

18° CONGRESSO NAZIONALE SIMP 2015

 ASSISI

3-5 DICEMBRE 2015



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# 18° CONGRESSO NAZIONALE SIMP 2015



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## 1. 2D ULTRASOUND AND 3D “REAL TIME” ULTRASOUND WITH LIVE X-PLANE IMAGING TO VISUALIZE THE AORTIC ARCH AND THE DUCTAL ARCH: COMPARISON OF THE METHODS

### LISTA AUTORI

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### AFFILIAZIONI

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### INTRODUZIONE

Compare “real-time 3D echocardiography with live xPlane imaging” and “2D traditional imaging” in visualizing the ductal and aortic arches during the routine echocardiography of the second trimester of gestation.

The feasibility and the timing of the two procedures were compared, related to spine's position and operator's ability

### MATERIALI E METODI

Live xPlane and 2D ultrasound were used to display the ductal- and aortic- arch views in 54 women with uncomplicated, singleton pregnancies. At first, the position of the spine was described. Then, with 2D ultrasound, the time to visualize the ductal- and aortic-arches was evaluated, starting from the 4-chamber views. After that, with Live X-Plane imaging, the time from the 4 chamber views to 3VT, from 3VT to ductal arch and then from 3VT to aortic arch was evaluated. The exam is defined infeasible when the two arches aren't visualized in five minutes.

Echocardiographies were performed by two different operators: twenty-eight echocardiographies were performed by a first level's operator, while twenty-six by a second level's operator

### RISULTATI

The measurements with 2D ultrasound were performed in all 54 echocardiographies, while with live x-Plane it was performed in 45 of them, because of the fetal motion or position. The timing with 2D ultrasound is faster than with live x-Plane imaging in visualizing the arches, if the measurements start from the 4 chambers. Conversely, if the measurements start from the 3VT for the live xPlane, the difference is not statistically significant.

Two methods were compared between two operators: there is no statistically significant difference.

Regarding the position of the spine, live xPlane is faster when the spine is posterior and slower when the spine is anterior

### CONCLUSIONI

Live xPlane imaging is a novel and relatively simple method to visualize the ductal- and aortic-arch views, but is strongly dependent upon the fetal movement and position. For this reason, 2D ultrasound is better in the second trimester echocardiography. However this new method could be a useful tool in the screening of fetal conotruncal and aortic-arch anomalies



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## 2. A CONSERVATIVE PROTOCOL FOR THE MANAGEMENT OF POSTPARTUM HEMORRHAGE. EVALUATION OF ITS EFFECTIVENESS IN HIGH RISK PATIENTS

### LISTA AUTORI

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### AFFILIAZIONI

Struttura Complessa di Clinica Ostetrica Ginecologica Ospedale Santa Maria della Misericordia, Università degli studi di Perugia.  
Direttore Prof. G. C. Di Renzo

### INTRODUZIONE

Postpartum hemorrhage (PPH) is the leading cause of maternal death worldwide. All pregnancies are at risk of PPH, but the main causes are represented by placenta previa/accrete retention of placental cotyledons or flaps, lacerations of the soft tissues of the birth canal, uterine atony, uterine rupture and coagulopathies. Several maternal factors, play an important role as risk factors. Placenta previa is the main condition related to the risk of severe hemorrhage. One of the most dreadful complications of placenta previa is its association with accretism.

The treatment of massive PPH can be summarized in two points: replacement of circulating blood volume to maintain perfusion and tissue oxygenation; stop the bleeding by treating the causes or using surgical procedures.

Treatment options of PPH during cesarean section provide, first of all, conservative management: uterotonic drugs, external compression with specific uterine sutures (B-Lynch, Hayman, Cho), intrauterine packing and selective devascularization by ligation or embolization of the uterine arteries or of the internal iliac arteries in relation to the amount of bleeding and to the success of procedures to reduce bleeding. Failure of these options necessitates hysterectomy.

The aim of the study is to report our experience with a conservative management protocol to treat PPH in cases of high risk patients with the diagnosis of placenta previa major. The presents conservative approach is characterized by a philosophy of liberal use of resources and treatment options/devices with the contemporary involvement of all professionals in a multidisciplinary approach

### MATERIALI E METODI

Retrospective analysis of 55 patients with placenta previa major who underwent cesarean section at the Maternity Hospital of Perugia between January 2009 and June 2012 were carried out. The patients were included in a diagnostic-therapeutic protocol for the prevention and management of PPH that consisted in a conservative procedure managed by a multidisciplinary team.

The protocol for management of PPH used in our institution is shown in Figure 1 and can be briefly summarized as follows: preliminary prophylactic transfemoral/transomeral catheterization, cesarean section, use of multiple square endouterine hemostatic sutures, application of an intrauterine Bakri balloon combined with B-Lynch suture. In case all the previous maneuvers failed, devascularizing ligature/selective embolization of the uterine arteries was performed. When even the previous described procedures failed, hysterectomy were done.

Maternal hematologic parameters monitoring was carried out 24 hrs before cesarean section and 2 hrs after the procedure, then every 2-4 hrs for the following 24 hrs, in relation to clinical conditions/blood loss and, finally, at 48 hrs. Blood transfusion was performed only in case the hemoglobin values dropped above 7 g/dl and/or hematocrit value was less than 21%. Bakri balloon was removed 24 hrs from delivery, 30 minutes after rectal administration of misoprostol 400 mcg

### RISULTATI

In four cases we used selective embolization of the uterine arteries (7.2 %). In three cases, we performed hysterectomy (5.4 %). In two of the three cases, due to a massive blood loss, hysterectomy was performed immediately after extraction of fetus and placental delivery. In one case even if embolization of uterine arteries were performed, the bleeding did not stop, and therefore hysterectomy and following embolization of internal iliac arteries was done due to massive bleeding from implants of pelvic endometriosis. Fourteen patients (25.4%) underwent intraoperative or postoperative blood transfusion. Four patients (7.3%) were admitted to the general intensive care unit for one day y, due to postoperative hemodynamic instability

### CONCLUSIONI

With this study we evaluate the effectiveness of the use of a conservative management protocol which should represent the leading aim for treatment of PPH in high risk patients with placenta previa/accreta and/or with other risk factors. The aim of the management of PPH is to apply conservative intervention and use the hysterectomy as the last possible treatment option. The results of our conservative protocol are encouraging and suggest that there is a need that all tertiary level obstetric units must have the facilities, professionals and equipments in place to manage properly this emergency



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## 3. VALUTAZIONE DELL'OUTCOME OSTETRICO NEI NATI DA GRAVIDE HIV POSITIVE IN UN UNICO CENTRO OSTETRICO

### LISTA AUTORI

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### AFFILIAZIONI

Fondazione Policlinico Universitario "A. Gemelli", Università Cattolica del Sacro Cuore, Roma, Italia

### INTRODUZIONE

In letteratura sono presenti numerosi Studi relativi circa l'effetto che l'infezione da Virus dell'Immunodeficienza Umana (HIV) può avere sull'outcome della gravidanza. Si tratta di dati talora discordanti ma è stata riportata una maggiore incidenza di parto prematuro, basso peso fetale alla nascita, e morte neonatale entro l'anno di vita.

Lo studio da Noi condotto è stato finalizzato a valutare i principali esiti ostetrici delle donne in gravidanza sieropositive seguite presso il Policlinico Gemelli ma in particolare ad osservare la crescita fetale e il peso all nascita, confrontandolo con un gruppo di donne contemporaneo non HIV+ adeguatamente selezionato

### MATERIALI E METODI

Si è trattato di uno studio caso-controllo che ha valutato i casi nati da donne HIV+ confrontandoli con casi di gravide non HIV+, con un rapporto 1:2.

Il gruppo di studio ha incluso 159 gravidanze con data compresa tra Gennaio 2002 e Novembre 2011, tutte con espletamento del parto mediante esecuzione di Taglio Cesareo poiché intercorso nel periodo sostanzialmente precedente l'introduzione di protocolli di assistenza che includono la possibilità di parto vaginale in gravide HIV+.

Di entrambi i gruppi si è considerato i seguenti outcome: peso alla nascita, punteggio di Apgar al 1° e al 5° minuto, e esecuzione di TC urgente. Il peso neonatale è stato valutato sia come valore assoluto, sia secondo riferimento alla scala di centili; ed, in secondo luogo, il peso è stato confrontato in merito all'incidenza di casi affetti da iposviluppo, considerando separatamente sia un cut-off di un peso < al 5° che < al 10° centile.

Il punteggio di Apgar è stato confrontato sia in valore assoluto, sia valutando i neonati che presentavano un indice Apgar < 7.

Da ultimo è stata valutata l'epoca gestazionale al parto, sia in settimane assolute che considerando come cut off una epoca gestazione inferiore a 37settimane+0giorni

### RISULTATI

L'analisi univariata ha dimostrato:

- centile del peso significativamente minore nella popolazione delle gravide sieropositive rispetto ai controlli ( $p < 0.001$ )
- non è stata riscontrata, tuttavia, una correlazione tra iposviluppo (inferiore al 5° e 10° centile) e sieropositività materna.
- non è stata riportata nessuna differenza statisticamente significativa tra i singoli parametri biometrici fetali considerati ed i dati di velocimetria Doppler tra il gruppo di studio ed il rispettivo controllo.

Utilizzando l'analisi univariata l'indice di Apgar al 1° minuti è risultato significativamente minore nel gruppo di studio rispetto ai controlli, laddove utilizzando una analisi multivariata, la significatività comprende l'indice sia al 1° che al 5° minuto. Considerando i neonati con Apgar < 7, solo il punteggio al 5° minuto risulta correlato alla positività materna.

In merito all'EG al parto, i dati riportano un correlazione significativa sia in termini di settimane assolute, che considerando il gruppo della donne che hanno partorito pre-termine epoca gestazione inferiore a 37settimane+0giorni

### CONCLUSIONI

Nella nostra esperienza, i nati da madri sieropositive presentano un peso alla nascita, sia in valore assoluto che espresso in centili, significativamente inferiore rispetto a quello dei controlli pur in assenza di un aumentato rischio di iposviluppo fetale.

I nostri risultati con particolarmente rilevante circa il dato ottenuto in riferimento al centile del peso alla nascita, che, riferito all'epoca gestazionale, risulta evidentemente inferiore nel gruppo di Studio.

Circa l'epoca gestazionale il dato più significativo rimane la differenza in merito al parto pretermine non è giustificata dalla pianificazione del taglio cesareo elettivo.

In relazione all'osservazione relativa al punteggio di Apgar si ritiene interessante un approfondimento riguardante le sequelae a lungo termine che potrebbero verificarsi



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## 4. ASPHYXIATED NEONATES: HOW A HEALTH CARE NETWORK CAN IMPROVE THEIR MANAGEMENT

### LISTA AUTORI

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### AFFILIAZIONI

PH\_Net Study Group: Fondazione MBBM, Monza; Ospedale Carate; Ospedale Desio; Ospedale Vimercate; Università Milano-Bicocca, Italia

### INTRODUZIONE

Neonatal Encephalopathy (NE) in the term infant describes a clinically defined syndrome of disturbed neurological function in the earliest days of life that can be caused by intrapartum asphyxia and manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, sub-normal level of consciousness and often seizures. It can result in long-term neurological sequelae as cerebral palsy. The objectives of this study were: to describe the characteristics and short-term outcomes of children with perinatal hypoxia born in a health care network composed by three I level centers and a II level referring hospital; to estimate the incidence of perinatal hypoxia and NE in this territorial area according to the presence of antepartum and/or intrapartum risk factors and to the level of assistance; to evaluate the value of the Thompson Score in the diagnosis of NE

### MATERIALI E METODI

Perspective study that involves 4 hospitals: San Gerardo Hospital (HUB center, II level), Desio, Vimercate and Carate Hospitals (SPOKE centers, I level) being part of the same health care network which include the STEN service (transportation service for neonatal emergency) and offers therapeutic hypothermia. All term ( $\geq 35$  weeks, birth weight  $\geq 1800$ , no malformation incompatible with life) infants born between 01/07/2014 and 31/08/2015 with birth asphyxia, defined as umbilical artery pH  $\leq 7.0$ , BE  $\leq -12$  mEq/L, 10 minute Apgar score  $< 5$ , or need for resuscitation at birth longer than 10 minutes, were included in the study. All asphyxiated neonates were admitted to a specific neonatal monitoring protocol, including clinical, biochemical and instrumental evaluations and follow-up at least until 12 months. All neonates were monitored with Thompson score and NE was diagnosed using the modified Sarnat&Sarnat classification. Data on maternal complications during pregnancy, characteristics of labor, mode of delivery, heart rate monitoring, sentinel events, presence of meconium, cord pathologies, placental findings and neonatal outcomes were prospectively recorded

### RISULTATI

The incidence of birth asphyxia in term neonates during the study period was 20‰ (181/9027). Nine cases of NE (1‰) were diagnosed, and Thompson score correctly identified 7/9 cases (6 cases with a maximum score  $\geq 7$ , 1 case with a maximum score of 6). The Thompson score showed a statistically significant relation with the value of pH ( $p < 0.001$   $R = -0.28$ ) and with the value of BE ( $p = 0.04$   $R = -0.16$ ). As shown in the figure A, the Thompson score tends to get better or remain stable over time. All cases of NE reported a value of pH  $\leq 7.00$  and/or a value of BE  $\leq -12$  mEq/L and they were admitted to cooling within 6 hours. Fourteen neonates registered an Apgar score  $< 7$  at 5 min, 7 of them developed NE, while a score  $< 5$  at 10 min was recorded only for 2 newborns who both presented NE. 45% of the cases of NE were preceded by a sentinel event. 22% of NE occurred in low-risk pregnancies; these cases were classified as moderate NE

### CONCLUSIONI

The Thompson score shows a high predictive power of need for therapy and neurological outcomes, even in the first hours of life. The relationship between BE and Thompson score and NE was weaker than that of pH, suggesting that the cut-off of BE may be poorly specific in identifying cases at worse prognosis. The high rate of operative deliveries is justified by the presence of critical antenatal conditions, as in case of suspected fetal distress, requiring a rapid accomplishment of the delivery. 22% of NE occurred in low-risk cases underlying the importance of early diagnosis in all neonates, regardless of the presence of pregnancy risk factors, and suggesting that the perinatal outcome also depends on factors still unclear. We confirm the relation between tachysystole and inflammation as risk factors of perinatal hypoxia. The CTG monitoring demonstrated low sensibility in recognizing asphyxiated babies. In fact, although characterized by an high negative predictive value, in our series, three babies who developed NE, presented a normal CTG during labor and during the last 60 minutes before the delivery. This confirms the unreliability of this instrument. The presence of the network granted adequate opportunity of care to all asphyxiated babies. The policy of sharing care protocols and the cooperative management system between centers for cases at higher risk have proven winning



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## 5. ATYPICAL HEMODYNAMIC PATTERN IN FETUSES WITH HYPERCOILED UMBILICAL CORD AND GROWTH RESTRICTION

### LISTA AUTORI

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### INTRODUZIONE

Intrauterine growth restriction (IUGR) is one of the main causes of neonatal mortality and morbidity and it continues to represent a challenge for prenatal medicine. The pathophysiology of IUGR is primarily related to placental insufficiency, but it can be the result of different pathological processes that can produce completely different fetal hemodynamic modifications which vary in relation to the quality as well as to the chronology of the hemodynamic events. Several studies have shown the classical progression of the hemodynamics in IUGR fetuses with utero-placental insufficiency. Also Umbilical cord hypercoiling (abnormal spiral twisting of the umbilical cord) has been associated with fetal demise and intrauterine growth restriction (IUGR).

Several studies have been published in the scientific literature regarding the pathologies associated with the alterations of the umbilical cord. Some of these studies investigate the effects of these abnormalities on fetal hemodynamics. However, all previous studies investigate only partially fetal hemodynamics, often with equivocal results, focusing the attention on some particular districts/ vessels without taking into account the hemodynamic profile of the uterine arteries. The purpose of this study was to describe the whole hemodynamics in IUGR fetuses with umbilical cord hypercoiling and the correlations with the hemodynamic profile of maternal uterine arteries

### MATERIALI E METODI

Our study consisted of 102 pregnant women with a single pregnancy affected by intrauterine growth restriction (IUGR) observed between January 2009 and January 2010, who were managed at our Prenatal Medicine Center.

Eighty percent of these cases (81 patients) were followed in our center from the beginning of the pregnancy and the remaining twenty percent (21 patients) was referred to our institution with suspected IUGR for further investigation.

The criterion used for the diagnosis of IUGR was the demonstration of an abdominal circumference (AC) two standard deviations below the biometric curve of reference values, adapted for each gestational age, in pregnancies correctly dated by ultrasound in the first trimester.

Sonographic examinations were performed using either GE Voluson E8 or Philips iU22 ultrasound equipment. All the hemodynamic evaluations were performed with a multi-frequencies (4-8 MHz) convex trans-abdominal transducer.

Patients with chronic maternal pathologies such as renal insufficiency, diabetes mellitus, chronic anemia, hemoglobinopathy, systemic lupus erythematosus, thrombophilia and antiphospholipid syndrome were excluded from the study. Furthermore, the patients enrolled in our study were screened for history of alcohol, cigarette and illicit drugs use. Infective pathologies (CMV, Toxoplasma gondii, Rubella, Parvovirus B19, Trypanosoma cruzi and Treponema pallidum) were screened for as well.

Following the diagnosis of IUGR, Doppler ultrasound velocimetry was performed biweekly or once a week depending on the severity of the maternal and fetal clinical conditions, examining the flow velocity waveform and indices of the uterine arteries, umbilical arteries and vein, fetal cerebral arteries and fetal venous system.

The most common etiology of IUGR is the utero-placental insufficiency and this situation itself can be secondary to numerous pathologies, which involve a reduced supply of oxygen and nutrients from the mother to the fetus through the placenta.

In our cases the identified cause of IUGR was placental insufficiency in all but 7 patients, in whom no pathophysiologic reasons could justify the clinical condition and the growth restriction.

All patients underwent repeated ultrasound and umbilical cord hemodynamic evaluation, in order to monitor the fetal condition and to plan the timing and mode of delivery.

The districts investigated were the uterine arteries, umbilical vessels, middle cerebral artery, ductus venosus and inferior vena cava. We recorded the maximum velocity flow in cm/s and the pulsatility index of the umbilical arterial vessels and fetal venous vessels. Furthermore, we evaluate the blood velocity in different segments of the umbilical vein end we documented the presence/absence of its pulsations. Finally, we evaluated the resistance and the pulsatility index of the uterine arteries.

For all the examined vessels, we performed a qualitative assessment of the Doppler waveform profile (e.g.: pulsation in the umbilical vein; absent/reverse flow in the umbilical arteries; absent/reverse flow in the ductus venosus; percentage of reverse flow in the inferior vena cava; etc.). The angle of insonation was kept below 30°.



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For all patients we performed an ultrasound scan of the longitudinal fields of the umbilical cord, with high resolution and we calculated the ante-partum coiling index as the reciprocal of the distance between two consecutive coils, from the inner edge of a venous or arterial wall to the outer edge of the next coil. The diagnosis of hypercoiling was accepted for values of coiling index superior to 0.60 (> 90th centile), and that of hypocoiling for values inferior to 0.20 (< 10th centile).

According to these criteria, we found an abnormal coiling index (> 90th centile) in 7 patients without the pathognomonic hemodynamic signs that characterize the IUGR fetuses with placental insufficiency

## RISULTATI

In 2 of the 7 patients the diagnosis of hypercoiling was made during the 20-22 week ultrasound scan and severe oligohydramnios and IUGR have been already present. For the remaining 5 patients, the diagnosis of IUGR was made between 29 and 34 weeks of gestation. By amniocentesis (when performed) microbiological culture and fetal karyotyping resulted negative and the 20-22 week ultrasound were negative. The ultrasound scans of all patients presented the image of a tangled umbilical cord with hypercoiling. The medium umbilical coiling index (UCI) was 0.71, above the 90th centile. The hemodynamic study of the cord in all these patients showed an abnormal fetal waveform pattern, in the presence of a normal impedance to flow in the utero-placental district. The fetal hemodynamics of the middle cerebral arteries, umbilical arteries and the inferior vena cava presented normal waveform profiles. The waveform evaluation of the umbilical cord showed, in some hypercoiled segments, an abnormal venous umbilical cord pulsatility. Unexpectedly, the waveform profiles of the ductus venosus showed a reduction of the flow and/or a reverse flow during atrial contraction. The two patients with early onset IUGR showed a particular deteriorating evolution of the hemodynamic profile at 34-35 weeks of gestation. In consideration of the hemodynamic pattern a cesarean section was performed. Birth-weight of the newborns were respectively 1740g and 1810g with an APGAR score of 8-10 and 6-10 respectively. The umbilical cord histological examination at birth confirmed the hypercoiling with reduced Wharton's jelly.

The five patients with late onset of IUGR showed hemodynamic alterations in the hypercoiled segment of the cord characterized by high velocity, pulsations and reverse and/or reduction of flow during atrial contractions in the ductus venosus. Three of these late onset IUGR patients did not show deterioration of the hemodynamic profile until the term of pregnancy. The other patients with late onset IUGR underwent cesarean section, one at 32 weeks of gestation the neonate had a birth-weight of 1240g and an APGAR score of 6/8 and the other at 35 weeks of gestation. The pathology report associated the stillbirth only to the presence of a hypercoiled umbilical cord

## CONCLUSIONI

In this study we identified an "atypical hemodynamic pattern" in IUGR fetuses associated with hypercoiled umbilical cord. In these IUGR cases hypercoiling was considered the only etiological factor for the growth restriction. In these fetuses, the pathognomonic features observed were normal utero-placental blood flow, pathologic hemodynamic patterns in the venous districts before any significant alterations in the hemodynamic profile of the fetal arterial vessels.

In particular we found a pulsatility profile with an increased flow velocity in the hypercoiled segments of the umbilical vein and alterations of the waveform of the ductus venosus, in the presence of a reverse flow especially when growth restriction became evident (Figure 1).

Our hypothesis is that this atypical pattern is due to the presence of hypercoiling with torsion, spiralization and compression of the umbilical cord vessels that can lead to fetal oxygen deficiency and IUGR.

Increased venous blood flow has been explained by the pulsometer effect, where increased coiling allows arterial pulsations to have more effect on the venous blood flow increasing blood flow velocities.

Whether this is a reflection of increased after-load caused by umbilical arterial compression or decrease pre-load due to reduction of umbilical vein return or, finally, due to myocardial failure from chronic hypoxia caused by the decrease in venous blood flow from hypercoiling is still unclear and under investigation.

In our series it seems that one of the earliest hemodynamic alterations is an altered waveform profile in the ductus venosus and an increased venous velocities and pulsations in the umbilical vein. We speculate that this may be due to an early decrease of the venous return from the umbilical. It seems likely that the further hemodynamic changes in the fetal arterial vessels and inferior vena cava are secondary to the increased after-load due to umbilical artery stenosis and, later on, to the hemodynamic decompensation caused by incipient heart failure (Table I).

In conclusion, IUGR fetuses with hemodynamic alterations that involve the venous system, without alterations of the arterial system and the uterine arteries, are at potential hypoxic risk because of cord hypercoiling



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## 6. **AUTOLOGOUS VERSUS HETEROLOGOUS GAMETE USE IN IVF SETTING: WHICH LINK WITH POST-PARTUM MATERNAL DEPRESSION?**

### **LISTA AUTORI**

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### **AFFILIAZIONI**

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### **INTRODUZIONE**

Post-partum is one of the most sensitive periods for the emotional stability in women' reproductive life; the deep neuro-hormonal changes that occur in this time-window may cause a breakdown in the mental balance of women, facilitating the onset of new mental problems and the recurrence or the eventual exacerbation of previous psychological disorders. A percentage of mothers estimated about 10-15% experience in the first twelve months after delivery severe psychic symptoms that are typical of major depression, disease known as postpartum depression (PPD). At this regard literature is unanimous in asserting that, in addition to severe damages to maternal health, PPD is able to affect the well-being of the whole family of the affected woman. In fact, recent studies emphasize how this disease may damage social and occupational functioning of mothers, the relationships between family members and alter language, emotional and cognitive skills of children. Among the risk factors for the onset of PPD some Authors reported old age, obstetric complications, psychiatric disorders before or during pregnancy, previous PPD, low social class, multiple births, although the debate on the real impact of these factors is still open. Moreover, disputes arise from literature analysis concerning the possible role of the way of conception as a risk factor for PPD development. In this respect we conducted a study aimed to investigate any differences in PPD incidence among patients who conceived spontaneously, with homologous IVF and heterologous IVF. The first objective of our study was to assess the mental state of patients after delivery, at 1, 3, 6 and 12 months stratifying patients according the way of conception. Secondary objectives were to verify any possible correlations with obstetrics, individual, environmental, educational risk factors and PPD and to evaluate the duration and way of feeding in our study population

### **MATERIALI E METODI**

We conducted a retrospective cohort study on women who delivered at the Obstetrical Clinic of Padua, a Level III hospital, in the Department of Woman and Child Health, Padua, Italy from January 2011 to September 2013. We considered eligible women with both singleton or multiple pregnancies, irrespective of gestational age and way of delivery. We excluded patients with poor comprehension of Italian language and women with documented psychological or psychiatric disorders before pregnancy. All recruited women were administered EPDS (Edinburgh Postnatal Depression Scale, a validated questionnaire investigating the psychological postpartum status) at time of dismissal, 1 month, 3 months, 6 months and 12 months after childbirth. Except for the first questionnaire before hospital discharge, the repetition of the test at 1, 3, 6 and 12 months was realized through a telephonic interview. EPDS is composed by 10-item investigating different female psychological feelings (anhedonia, self-blame, anxiety, fear, panic, inability to cope, difficulty in sleeping, sadness, tearfulness and thoughts of self-harm). Each question is scored from 0 to 3 points, with a total maximum of 30 points. Patients were considered not affected by post-partum depression when the total score was less than 10 points; if the total score exceeded 10 points, patients were considered affected by depression and re-evaluated in order to identify cases at risk of severe depression and/or suicidal instinct. Patients included in the study were stratified in 3 different groups depending on the way of conception: Group\_A included women with spontaneous pregnancy, Group\_B women who got pregnant through homologous IVF, Group\_C women who achieved pregnancy through heterologous IVF. For each woman we collected data about general characteristics (age, education level, residence, type of work, days of work during pregnancy, marital status), partner's characteristics (age and level of education), obstetric history (parity, years from the previous delivery, course of the last pregnancy, way of conception, pregnancy complications, number of obstetric ultrasound examinations, gestational age at delivery, type of labor, fetal presentation at birth, delivery complications, intrapartum analgesia), neonatal features (number, sex, weight, length, Apgar score at 10 minutes). Finally, we collected data about breastfeeding such as duration in months and modality of feeding (natural, combined natural/artificial, only artificial)

### **RISULTATI**

245 patients were included in the study, 105 in Group\_A (spontaneous pregnancy), 119 in Group\_B (homologous IVF) and 21 in Group\_C (heterologous IVF). No difference emerged about maternal education and partner's work, while significant differences emerged concerning maternal and partner's age [ $p < 0.001$ ], place of residence [ $p < 0.001$ ] and type of mother's work [ $p < 0.01$ ]. The patients showed a rising trend in maternal age from Group\_A to Group\_C, while Group\_B showed a higher mean paternal age in comparison to other groups. Regarding the residence, 24.8% of patients included in Group\_A lived in a city in comparison to 77.3% and 52.4% of Group\_B and Group\_C. Differences emerged between Groups A, B and C about number of unemployed women (21.9%, 12.6%, 0%)

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and freelance women (58.1%, 73.9%, 71.4%). Concerning obstetrical history, higher number of previous deliveries was observed in Group\_A [ $p < 0.05$ ], number of previous cesarean sections [ $p < 0.05$ ], number of live births [ $p < 0.001$ ], number of working weeks in the course of pregnancy [ $p < 0.001$ ], incidence of gestational diabetes [ $p < 0.05$ ], gestational age at birth [ $p < 0.001$ ], elective caesarean section [ $p < 0.05$ ], spontaneous delivery [ $p < 0.01$ ], demand for intra-partum analgesia [ $p < 0.001$ ], number of live births, percentage of multiple pregnancies [ $p < 0.001$ ], neonatal birth weight [ $p < 0.001$ ], neonatal birth length [ $p < 0.001$ ]. EPDS score evaluation showed significant differences between groups at the time of hospital discharge and 12 months after delivery, while at 1, 3 and 6 months no difference was recorded. In detail, at the hospital discharge a score higher than 10 points was observed respectively in 24.8% in Group\_A, 38.7% in Group\_B and 19% in Group\_C [ $p < 0.05$ ], with 2 cases of patients with suspected suicidal intent both in the Group B. Differently, after 12 months the total score was higher than 10 points in 13.3% of Group\_A, 3.4% of Group\_B and 4.8% of Group\_C. PPD risk was found to be related to maternal age, low parental education, nulliparity, preterm delivery, low fetal weight at birth, multiple pregnancy and multiple births, low pain threshold and high demand rate of analgesia intrapartum [ $p < 0.05$ ]. Concerning lactation, no significant differences in both the duration in months, and the type of feeding among groups

## CONCLUSIONI

Our study shows that the way through conception is achieved can profoundly affect the psychological condition of women in the post-partum period. In particular, the long and stressful path of couples who conceive with homologous fertilization seems to increase the risk of PPD immediately after birth, while the joy of the growing-up child seems to mitigate this negative psychic effect in the following period. In fact, in our experience women who conceived spontaneously showed 12 months after birth an EPDS total score even worst in comparison to both homologous and heterologous IVF Groups, suggesting a lower risk of PPD in these patients. In disagreement with other studies, we found no significant differences regarding the duration and mode of breastfeeding among the various Groups of patients. In other hand, however, a strong positive association was found between PPD and advanced maternal age, nulliparity, low birth weight, pre-term delivery, multiple pregnancy and multiple births, confirming that the maternal age at the time of conception and obstetric history can be critical factors for the risk of developing mental disorders in the post-partum period



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## 7. **BREASTFEEDING OF THE INFANTS BORN FROM WOMEN IN THERAPY WITH SELECTIVE SEROTONIN REUPTAKE INHIBITORS DURING PREGNANCY**

### **LISTA AUTORI**

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### **AFFILIAZIONI**

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### **INTRODUZIONE**

The prevalence of depressive symptoms and major depression during pregnancy has been estimated as high as 7-20%. Selective Serotonin Reuptake Inhibitors (SSRIs) are commonly used and prescribed (2.5% of pregnancies) as they are considered the safest antidepressants during pregnancy. Some adverse obstetric effects have been described. Breastfeeding is generally not recommended due to insufficient data regarding safety of the antidepressants secreted in breast milk, although they have been shown to prevent postpartum depression. As well, depressed women who breastfeed their baby show reduction of depressive symptoms.

In September 2009 we started the Antenatal Clinic dedicated to evaluate pregnant women with a diagnosis of depression receiving SSRI. We supported the women during their pregnancies and postpartum, especially by offering them advice about breastfeeding while receiving antidepressant therapy

### **MATERIALI E METODI**

From September 2009 to December 2014 we recruited 43 women receiving SSRI during pregnancy and breastfeeding and analyzed effects on the newborns fed with human milk. We investigated the plasmatic level of the SSRI in the infant blood after a week of breastfeeding and collected data about adverse effects on the newborns

### **RISULTATI**

Of the 43 women of the study, 31 decided to breastfeed their babies at delivery (72%). 10 infants needed a supplementation with formula due to neonatal comorbidity. A week after the discharge, at the pediatric check, the percentage of breastfeeding with maternal satisfaction was 70%.

The plasmatic levels of the drugs in the newborns were lower than therapeutic range and no adverse events were detected

### **CONCLUSIONI**

Depression in pregnancy, when not treated, can lead to harmful behaviors influencing neonatal outcomes. Breastfeeding is often considered more stressing than the use of formula feeding; thus, women using SSRI are influenced in their choice to feed their babies with formula. This work demonstrates that mothers receiving SSRI, when properly treated during pregnancy and followed up in postpartum, can breastfeed their babies with no adverse effects on the infant and positive effects on the mother. Moreover, 70% of exclusive breastfeeding is a high percentage when compared to Unicef recommendations on physiological neonatal breastfeeding (74%)



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## 8. **BREASTFEEDING THE LATE PRETERM INFANT: THE EXPERIENCE OF A BABY FRIENDLY HOSPITAL FROM 2012 TO 2014**

### LISTA AUTORI

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### INTRODUZIONE

The advantages of breastmilk feeding for premature infants are even greater than those for term infants; however, a large body of literature in the past 5 years documents the increased risk of morbidity and even mortality of the late preterm infant (34-36 weeks of gestational age) often related to feeding problems, especially when there is inadequate support of breastfeeding. Establishing breastfeeding in the late preterm infant is frequently more problematic than in the full-term infant. Because of their immaturity, late preterm infants may be sleepier and have less stamina and more difficulty with latch, suck, and swallow than a full-term infant. Late preterm infants are also more likely to be separated from their mother for evaluation and treatment of medical problems. All infants, including late preterm infants, have a greater chance of exclusive breastfeeding in hospitals that adhere to the Baby Friendly Hospital Initiative.

### Purpose

To describe the prevalence of breastfeeding at discharge among late preterm infants born in our Obstetric Clinic from 01/01/2012 until 31/12/2014

### MATERIALI E METODI

206 infants born between 34-36 weeks of gestational age in our Obstetric Clinic were enrolled. The data concerning gestational age, comorbidity and breastfeeding / combined / formula feeding at the discharge were collected and analyzed with Microsoft Excel®

### RISULTATI

During the study period the percentage of breastfeeding at discharge was 77.2%: 65 (31.5%) infants were fed exclusively with maternal milk; 94 (45.6%) needed a supplementation with formula. 39 (18.9%) were fed exclusively with formula. 8 infants were transferred to other hospitals so it was not possible to collect any data about feeding at their discharge

### CONCLUSIONI

Future research is needed to establish the best methods for monitoring the late preterm infant in the first days of life and specifically initiation of breastfeeding. The use of combined breastfeeding and formula feeding is often due to comorbidity and prematurity. Mothers feeding late preterm infants need to be supported even by the use of appropriate feeding plans in order to promote exclusive breastfeeding as soon as possible, before and after discharge



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## **9. BRONCHOPULMONARY DYSPLASIA AND PROLONGED INTUBATION: A CASE-REPORT**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Bronchopulmonary dysplasia (BPD) is a chronic respiratory disease that results as consequence of perinatal/neonatal lung injury and involves many respiratory childhood sequelae. The incidence is increasing as the survival of extreme premature infants improves and its clinical presentation is milder than the original description of Northway and collaborators. The diagnosis of BPD is currently based on the need of supplemental oxygen for at least 28 days after birth, and its severity is graded according to the respiratory support required at 36 postmenstrual weeks

### **MATERIALI E METODI**

M.R. is a male infant, born preterm from a multiple pregnancy by emergency caesarian section (gestational age: 29 weeks, birth weight: 1110 g, APGAR score: 7I – 8V). In the delivery room he needed non invasive respiratory care. Due to the prematurity, he was admitted to the neonatal intensive care unit, where respiratory condition worsened and he started high-frequency ventilation (HFOV), after two doses of exogenous surfactant. The first chest X-ray demonstrated signs of respiratory distress syndrome and beginning of cardio-circulatory failure. Clinical course was characterized also by severe IVH with hydrocephalus and the need of ventriculo-peritoneal drainage. The baby received oxygen during the first 28 days of life, so BPD was diagnosed. He was in room air at 36+1 weeks of PMA. After five months, due to the persistent inspiratory effort and several episodes of apnea, suspecting tracheomalacia, further diagnostic studies were required. The bronchoscopy revealed the presence of numerous ductal, obstructive, sub-glottic cysts and tracheal cysts too, although smaller than the larynx. The cysts were removed by laser diodes, even if some not obstructive micro-cysts still remained in loco. The patient needed invasive ventilation for 24 hours, than he was extubated without complications. One month later, the patient came back for endoscopic follow-up: ductal, subglottic, small size cysts without influence on respiratory dynamics were found

### **CONCLUSIONI**

Acquired subglottic ductal cysts may be the consequence of prolonged intubation in preterm infants, most commonly associated with a laryngeal intubation trauma; they have been reported with increasing frequency during the past two decades. The majority of them are small and not significantly airway obstructive; sometimes cysts shrink or completely regress. Although cysts may resolve without therapy, careful follow-up and treatment of potentially obstructing complications are recommended. Diagnostic evaluation is mandatory in case of inspiratory effort in newborns with BPD, mostly if symptoms happen after well being period



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## **10. CARBETOCIN IN THE PREVENTION OF POSTPARTUM HEMORRHAGE IN PREGNANT WOMEN WITH TWINS DURING CESAREAN SECTION**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Multiple pregnancy is a pregnancy of a high risk, which is associated with a manifold increase of obstetrical and perinatal complications. The incidence of early postpartum hemorrhage in multiple pregnancies exceeds the frequency of bleeding in singleton pregnancies

### **MATERIALI E METODI**

The purpose of the study is to evaluate the effectiveness of Carbetocin use in prophylaxis of early postpartum hemorrhage in women with multiple pregnancy.

The study was conducted in Rostov-on-Don Perinatal Centre (Rostov-on-Don, Russia) and was retrospective. The study included 102 pregnant with twins, delivered in the Perinatal Centre by cesarean section. Group I included 74 pregnant women, who were introduced Carbetocin (intravenous 100 mcg) at the time of caesarean section immediately after birth of the baby. Group II included 28 patients who were administered 10 units of Oxytocin by slow intravenous injection after removal of the fetus, followed by slow intravenous infusion of postoperative 5 units of Oxytocin

### **RISULTATI**

We evaluated the frequency of postpartum hemorrhage, blood loss during cesarean section, the frequency of use of an intrauterine balloon, side effects and frequency of hysterectomy. Qualitative characteristics were compared using Fisher's criteria, quantitative - using the Mann-Whitney test.

Intraoperative blood loss in patients of both groups did not differ - in Group I –  $940.5 \pm 257.9$  ml, in group II –  $964.3 \pm 342.4$  ml ( $p > 0.05$ ). Early postpartum hemorrhage was detected in 2 patients (3%) of group I and in 4 patients (14%) of group II ( $p = 0.0397$ ). Uterine balloon tamponade in group I was conducted in 11 women (14.8%) and in group II – in 3 women (10.7%) ( $p > 0.05$ ). Hysterectomy due to hypotonic uterine bleeding was performed only in 2 patients of group II (7.1%), which is significantly more frequent in comparison to I group ( $p = 0.0272$ )

### **CONCLUSIONI**

Analysis of the data showed that the use of Carbetocin is more effective than the use of Oxytocin for the prevention of early postpartum hemorrhage, which can be the reason of hysterectomy, in the surgical delivery of women with multiple pregnancy

## 11. COMPUTERIZED FETAL HEART RATE ANALYSIS DIFFERENCES ACCORDING TO PARENTAL ETHNICITY

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### INTRODUZIONE

Fetal heart rate (FHR) monitoring in clinical practice has provided the most reliable indicator of fetal wellbeing in clinical practice, however its control mechanisms are still poorly understood. Cardiotocography (CTG) monitoring of FHR is a noninvasive method that has recently been augmented by advances in computerized CTG analysis, with recent ultimate generation technology superseding past inefficiencies to demonstrate superior results with respect to visual analysis 1.

Ethnic origin has been demonstrated as being an independent factor for the development of many clinical conditions, such as hypertension, diabetes, atherosclerosis and coronary heart disease, in black newborns, children, adolescents and adults. Ethnic disparities have also been advocated as a co-factor in many pregnancy complications.

Only a few studies have investigated whether the ethnic race by itself could lead to a bad nonstress test (NST) when excluding all the other cofactors.

The aim of this study was to verify if the maternal and paternal ethnic origin could influence the fetal computerized CTG (cCTG) in singleton pregnancies and excluding other cofactors

### MATERIALI E METODI

This is a retrospective study comparing the results of the cCTG of pregnant patients at 37-42 weeks in two maternal-fetal medicine centers in northern Italy (Udine and Pordenone) according to parental ethnicity. The NST was done on a routine basis after the 37th gestational week, according to the national guidelines. Ethnicity was categorized as Black (group B, including all African States,) and White (group W, including all European States). Only pregnant patients with the same ethnicity of the father were included in the study. Other inclusion criteria was a singleton pregnancy after 37 week with absence of any maternal and fetal morbidity. The cCTG (8002 Sonicaid Fetal Care System) was performed to analyze the variables of FHR. The cCTG variables analyzed were % of signal loss, number of contractions, basal FHR, number of accelerations (10-15 bpm and > 15 bpm), number of decelerations, length of high variation episodes, short term variability (STV), total trace duration time, and number of fetal active movements.

A Patient's data was not normally distributed and therefore was described with median [25°-75° percentile]. The Mann-Whitney non parametric test for continuous data and Chi-square test were used to compare the two groups. A p-value < 0.05 was considered statistically significant. The software SPSS v. 22.0 (IBM, Chicago) was used for the statistical analysis

### RISULTATI

Group B and W were matched for gestational age, BMI, fetal sex and smoking. Parity was higher in Black women but this factor is not believed to influence cCTG results. The most representative State of origin in group B was Marocco (37 %), and Italy (76 %) for group W (data not shown).

When the two groups were compared, the cCTG results were the same regarding % of signal loss, number of contractions, basal FHR, number of accelerations (10-15 bpm and > 15 bpm), number of decelerations, length of high variation episodes, STV and total trace duration time (Tab.2). Long term variability was always > 5 bpm and as such it was not included in the analysis. Statistically significant differences were recorded in the number of fetal active movements (20 [8 – 35] in group B vs 39 [19.2 – 73.5] in group W) and minutes of low variation (0 [0 – 11] in group B vs 0 in group W [0 – 0]) (Tab.2)

### CONCLUSIONI

In this study a significantly lower number of active fetal movements and longer periods of low variation in cCTG was found in Black patients compared to White patients. This is the first time, to our knowledge, that both maternal and paternal ethnicity has been considered. Paine et al. in 19882 was the first to hypothesize that race was a significant co-factor influencing NST results.

Racial differences in the adult population is a well known risk factor for cardiovascular risk and for heart rate variability3. Recent evidence has suggested that these differences are present only because of the influence of the individual genetic variance regardless of other cardiovascular factors4. We speculate that the same genetic racial disparity exists in fetal life and can be detected by modern ultra-sensitive cCTG.

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Moreover, this is the first time that the newer generation of cCTG has been adopted to report ethnic differences in a pregnant population. One strength of our study is that the ethnic origin of both parents was considered. Fetal DNA is equally derived from the mother and father's contribution. We acknowledge the limitations of our study, primarily its retrospective nature and the low number of patients in each group. Though the clinical use of the CTG has undoubtedly benefited patients, criticism remains regarding its use and reliability, mainly with regard to its false positive rate. Identifying factors responsible to variance in objective analysis of CTG results is important in improving patients' outcomes. Our study lends further evidence as to the importance of ethnicity in clinical cCTG interpretation. Further studies are needed to confirm our finding in a larger population



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## 12. CONGENITAL CYSTIC ADENOMATOID MALFORMATION: A MULTIDISCIPLINARY DISEASE

### LISTA AUTORI

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### INTRODUZIONE

Congenital cystic adenomatoid malformation (CCAM) of the lung, is a rare anomaly of the lower respiratory tract characterized by cystic adenomatous overgrowth of the terminal bronchioles and airspaces. Approximately 80% of CCAM cases are usually identified during the first 2 years of life, and typical manifestations include progressive respiratory distress or recurrent respiratory tract infection. Since the technological advancement of ultrasound examination, CCAM has been increasingly diagnosed on routine prenatal examinations. Fetal MRI should be useful to differentiate CCAM from other lung lesions such as congenital lobar emphysema, pulmonary sequestration, diaphragmatic hernia, and bronchogenic cysts. Some CCAM lesions present only at birth with respiratory distress symptoms but are confirmed by an abnormal chest radiograph or a more definitive TC scan

### MATERIALI E METODI

We present a case of CAM TYPE I with signs of respiratory distress immediately after birth, treated by surgical excision

### RISULTATI

ZM was born by elective caesarean section for a cystic lung lesion in the right lobe of the lung identified during on a routine prenatal ultrasound. The mother's prenatal history was unremarkable. The fetus and cyst were followed in utero by serial ultrasound examination until the time of delivery. No complications were documented throughout the pregnancy. At birth the baby presented signs of respiratory distress: nasal flaring, rapid breathing, unusual breathing movement so he was intubated and assisted respiratory support was started. Chest x-ray showed a cystic lesion of 45 mm occupying the medium and lower right lobe of the lung with mediastinal shift. So a computed tomography scan with contrast was performed. It identified a macrocystic lesion with multiple large cysts inside that was of 48 mm in diameter occupying the medium and basal right lobe with vascularization supported by peripheral branches arising from the branch pulmonary artery. In the second day of life the child had a clinical deterioration so an intrathoracic surgery to resect the congenital cystic lung lesion was performed and a chest tube was placed.

The post-operative course was uneventful with gradual resolution of respiratory distress. So, on post-op 6 day it was possible to extubate the child and remove the chest tube. Histological examination confirmed the diagnosis of CAM TYPE I. The examination for additional malformations were negative. The follow-up carried out after discharge did not show the occurrence of post-surgical complications and/or infection

### CONCLUSIONI

CCAM is a condition that can cause progressive respiratory distress so its diagnosis can be done prenatally. Differential diagnosis is important to exclude pathologies that require immediate surgical intervention. Some CCAM lesions present at birth with respiratory distress symptoms, allowing early diagnosis and optimal patient management. For these reasons a multidisciplinary management is necessary after a prenatal diagnosis of CCAM

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## 13. DELIVERY OUTCOME IN UNCOMPLICATED TERM PREGNANCIES: ART VS SPONTANEOUS CONCEPTION

### LISTA AUTORI

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### INTRODUZIONE

After more than 30 years of in vitro fertilization (IVF), there is consistent evidence that pregnancies after assisted reproductive technologies (ART) have a higher risk of adverse obstetrical and perinatal outcomes such as preterm birth, hypertensive disorders, placental disorders and low birth weight infants. However, few studies have investigated specifically the influence of ART conception in delivery and postpartum outcomes, with controversial results. Thus, the aim of the study was to evaluate the delivery outcome of uncomplicated term pregnancies after IVF/ICSI conception in comparison with matched controls from spontaneous pregnancies

### MATERIALI E METODI

A total of 10860 deliveries, from 1 January 2010 to 31 December 2014 were subjected to retrospective analysis. A matched case-control study was performed. Single pregnancies with autologous IVF/ICSI conception, uncomplicated until delivery, were included in the study as cases (n=188). Single pregnancies with spontaneous conception, uncomplicated until delivery, were enrolled as controls, allowing a 1:7 ratio (n=1168). Cases and controls were matched for age and BMI. Exclusion criteria: multiparity, pregravidic diseases, obstetric complications until delivery, fetal malformations, elective cesarean section. Outcome measures: induction of labour, length of active phase of labour, mode of delivery, retained placenta, postpartum hemorrhage, episiotomy and third/fourth degree perineal tears, neonatal birth weight, Apgar score, umbilical cord blood gas analysis

### RISULTATI

Women with IVF/ICSI conception had a higher incidence of failed induction compared to controls ( $p=0.01$ ) and they underwent more frequently to prelabor CS, mostly for abnormal fetal heart rate ( $p=0.0002$ ). In addition, cases had a higher incidence of retained placenta ( $p=0.03$ ) with a higher incidence of postpartum hemorrhage ( $p=0.0005$ )

### CONCLUSIONI

Women with uncomplicated IVF/ICSI term pregnancies had a higher incidence of failed induction, if labour was induced for prolonged prelabor rupture of membranes or postdate pregnancies. In addition, they underwent more frequently to prelabor CS, mainly for abnormal fetal heart rate during antepartal CTG. They had also a higher risk of retained placenta and postpartum hemorrhage. Thus, pregnancies conceived by autologous IVF or ICSI, even if uncomplicated until delivery, need to be counselled about the higher risk of peripartum and postpartum complications



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## 14. DETERMINATION OF HEART RATE IN INFANTS NEEDING RESUSCITATION AT BIRTH – METHOD COMPARISON IN A LOW INCOME COUNTRY

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### INTRODUZIONE

Intrapartum-related events, previously called “birth asphyxia”, account for a quarter of neonatal deaths.<sup>1</sup>

Initial assessment of breathing and heart rate (HR) is an essential part of newborn resuscitation.<sup>2</sup>

The International Guidelines for Neonatal Resuscitation state that auscultation of the precordium should remain the primary means of assessing HR.<sup>2</sup>

Although based on a very low quality of evidence, recent literature suggests that electrocardiogram (ECG) can be used to provide a rapid and accurate estimation of HR.<sup>3,4</sup>

Algorithms for neonatal resuscitation adapted to low resource settings include HR evaluation by auscultation or umbilical cord palpation at about one minute of life.<sup>5-7</sup>

In low resource countries, a stethoscope is rarely available and HR is routinely detected by palpation of the umbilical pulse.

Although this is preferable to other palpation sites (i.e. femoral and brachial artery), there is a high likelihood of underestimating HR with palpation of the umbilical pulse in healthy infants.<sup>8,9</sup>

Previous studies conducted in manikins and healthy infants showed that about half of the times HR detection methodology is wrongly executed.<sup>8-10</sup>

Our hypothesis is that palpation of the umbilical cord could further underestimates HR when used in neonates with bradycardia. The accuracy of clinical HR assessment in infants needing resuscitation at birth remains to be determined.

This study was designed compare two different methods (auscultation and umbilical cord palpation) of HR estimation in newborn infants needing resuscitation, in order to determine which method is most suitable for use in clinical practice

### MATERIALI E METODI

This is a single centre, prospective, randomized clinical trial comparing two methods for assessing HR in infant newborns needing resuscitation at birth. The study will be conducted at the Central Hospital of Beira in Mozambique (5.555 deliveries - CUAMM data 2013), which is a governmental hospital (III level) (Mozambique: neonatal deaths, 34% of all under-5 deaths; neonatal mortality rate: 30 per 1000 live births; source: Countdown to 2015, The 2014 Report).<sup>11</sup> This study will be part of a collaborative project between the Beira Central Hospital and Doctors with Africa CUAMM, a non-governmental organization.<sup>12</sup>

Infants satisfying the following inclusion criteria (being born infants, needing for resuscitation and with parental informed consent signed) will be eligible to participate in the study.

Patients with major congenital malformations or without parental informed consent will be excluded from the trial.

The sample size could not be estimated using mathematical methods because of the lack of data about accuracy in HR estimation by auscultation and umbilical palpation in newborn infants needing resuscitation. Therefore, we plan to enrol 60 subjects (30 in the stethoscope group and 30 in the palpation group) according to a previous study on healthy infants at birth.<sup>9</sup>

Eligible infants will be randomly assigned to auscultation or palpation group in a 1:1 ratio according to a computer-generated, randomized sequence.

The primary outcome measure will be the degree of agreement as regards the categorisation of the HR obtained by auscultation or palpation compared with the HR as determined by ECG. The HR - beats per minute (bpm) - will be categorised as either not palpable, 100 bpm. The values of 60 and 100 bpm were chosen as they are recommended in the guidelines for determining the need to intervene.<sup>2,6,7</sup> HR will be detected at 60, 90, 120 seconds and at 5 minutes of life. Among secondary outcomes will be evaluated mortality, severe asphyxia, age at discharge.

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The degree of agreement between categorical HR by auscultation and by ECG will be evaluated using Cohen's Kappa coefficient, with a value greater than 0.8 indicating good agreement. The same approach will be used to evaluate the agreement between umbilical cord palpation and ECG. The two Kappa coefficients will be compared using the test for equal Kappa coefficients, that under the null hypothesis of equal coefficients in the two groups has an asymptotic chi-square distribution with 1 degree of freedom. A p-value less than 0.05 will be considered significant. Categorical data will be expressed as number and percentage and compared using Fisher test. Continuous data will be expressed as mean and standard deviation or median and interquartile range (IQR). Normality assumption of continuous variables will be evaluated using Shapiro-Wilk test. Continuous data will be compared using Student t test or Mann-Whitney non parametric test. Correlation between continuous data will be evaluated using Pearson correlation coefficient or Spearman correlation coefficient. Statistical analysis will be performed using R 2.12 language

## **RISULTATI**

In this trial, we will compare the accuracy of assessing HR in neonates needing resuscitation at birth by the two recommended methods. The findings of this study will be important for other units/settings in high as well low resource countries where HR estimation is routinely done by auscultation and/or palpation

## **CONCLUSIONI**

There are unique features of this trial compared to prior studies on HR assessment of neonates at birth. World Health Organization guidelines recommend to detect HR by auscultation and/or palpation, but evidence for this practice is lacking. Based on the results of the present study, we could speculate whether the availability of a stethoscope is mandatory for management of neonates needing resuscitation at birth



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## **15. DIFFERENTIAL EXPRESSION OF OSTEOPONTIN IN MODELS OF PHYSIOLOGICAL AND PATHOLOGICAL PLACENTATION: A PRELIMINARY INVESTIGATION**

### **LISTA AUTORI**

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### **AFFILIAZIONI**

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### **INTRODUZIONE**

The placenta forms the interface between maternal and fetal circulation and it is critical for the establishment of a healthy pregnancy. Trophoblast cell proliferation, migration and invasion into the endometrium are fundamental events in the initiation of placentation. Placental development is highly regulated spatially and temporally by numerous factors which can ultimately determine the success or failure of pregnancy. Recently, osteopontin (OPN), a secreted extracellular matrix protein involved in adhesion and signal transduction, has been shown to promote trophoblast invasion in-vitro, however its precise role in-vivo is unknown. OPN is also present in the endometrium where it is indicative of a decidualization-like process during pregnancy acting as a pro-inflammatory Th1 type cytokine. The aim of our study was to determine OPN role in placental development, characterizing its differential expression in models of aberrant placentation as Preeclampsia (PE) with Fetal Growth Restriction (FGR) and Egg Donation (ED) with PE, compared to physiological and PE pregnancies with Appropriate for Gestational Age fetuses (PE-AGA)

### **MATERIALI E METODI**

Placentae from PE (FGR n=8; AGA n=8), ED (n=8) and physiological control (CTRL, n=13) pregnancies were collected. OPN gene expression levels were determined by Real Time PCR using commercially available TaqMan probes (Life Technologies, Italy). For the relative quantitation, PCR signals were compared among groups after normalization using ribosomal 18S RNA expression as internal reference (Life Technologies, Italy)

### **RISULTATI**

Real Time PCR showed a decreased OPN expression in PE-FGR and ED-PE relative to physiological (1,25 and 1,3 fold decrease, respectively) and PE-AGA (1,19 and 1,24 fold decrease, respectively) placentae. In contrast, OPN mRNA levels were similar in PE-AGA relative to control placentae

### **CONCLUSIONI**

Herein, we characterized, for the first time to our knowledge, differential OPN expression in PE-FGR, PE-AGA and ED-PE placentae. Interestingly, placental OPN reduction in PE-FGR and ED-PE pregnancies, characterized by aberrant placental development, suggest OPN as a key player for appropriate placentation. As expected, OPN expression was not different in PE-AGA relative to physiological placentae, emphasizing the "maternal" origin of preeclampsia without placental compromise. Further studies are required

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## 16. DISTANCE BETWEEN DELIVERY ROOM AND NICU: INFLUENCE ON AIRWAYS MANAGEMENT

### LISTA AUTORI

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### INTRODUZIONE

A short distance between the delivery room (DR) and the neonatal intensive care unit (NICU) should be recommended in order to minimize potential problems during intrahospital transport. In extremely low birth weight infants (ELBWI), the respiratory support with nasal CPAP instead of intubation at birth reduces the outcome mortality/BPD. We hypothesized that a significant distance between DR and NICU could lead the team to intubate the patient in order to achieve a safer transport to the NICU.

The aim of this study was to assess whether the distance between the delivery room and the NICU may influence the airway management of ELBWI at birth

### MATERIALI E METODI

In our institution, there are 2 delivery rooms located at different distance from the NICU: delivery room A is situated under the NICU to which is connected by 1 elevator; delivery room B is connected to the NICU by an underground corridor (70 meters) and 3 elevators. We retrospectively reviewed medical records of all preterm infants  $\leq 28$  weeks gestation and/or birth weight  $\leq 1000$  g admitted to the NICU of the Department of Women's and Children's Health, University of Padua, between January 1, 2005 and December 31, 2013. For each infant, born in the delivery room A or B, we collected: maternal history, birth weight, gestational age, time of birth, time of NICU admission and type of respiratory support

### RISULTATI

Of the 470 ELBWI included in the study, 329 (70.0%) and 141 (30.0%) were born in delivery room A (group A) and B (group B), respectively. The 2 groups were comparable for gestational age ( $p=0.26$ ), sex ( $p=0.67$ ), proportion of SGA ( $p=0.91$ ) and twin pregnancy ( $p=0.15$ ), need for resuscitation ( $p=0.42$ ). Birth weight ( $p=0.022$ ) and Apgar score at 5 minutes ( $p=0.037$ ) were significantly lower in infants born in delivery room B than those born in delivery room A. Admission times were 20 min (16-27) and 26 min (20-34),  $p<0.001$ .

Regarding airway management: infants in spontaneous breathing at NICU admission were 35 (10.6%) and 11 (7.8%) for group A and B, respectively; infants on n-CPAP ventilation were 106 (32.2%) and 39 (27.7%), respectively; while infants on endotracheal ventilation were 188 (57.1%) and 91 (64.5%), respectively. These differences were not statistically significant ( $p=0.3$ ). Intubation rate in DR was 55.8% (n. 184) and 65.2% (n. 92) for group A and B, respectively ( $p=0.066$ )

### CONCLUSIONI

The distance between the DR and the NICU does not affect the airways management of ELBWI



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## **17. DOPPLER VELOCIMETRY AND ADVERSE OUTCOME IN LABOR INDUCTION FOR LATE ONSET IUGR**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Late onset intrauterine growth restriction (late IUGR) represents one of the main causes of perinatal morbidity/mortality. No guidelines are available on labor induction in late IUGR, even if induction at 37-38 weeks gestation is suggested. The aim of the study is to identify the maternal-fetal and medical factors related to adverse outcome in case of labor induction for late IUGR

### **MATERIALI E METODI**

The study includes 169 cases of late IUGR, which were retrospectively revised on parity, fetal weight percentile<sup>3</sup>, start of induction, use and type of augmentation. All the variables were matched with the following adverse outcomes: cesarean section (CS) or vacuum extractor delivery (OD) for non-reassuring fetal status or mechanical dystocia; neonatal intensive care unit (NICU) admission; Apgar score <7 at first and fifth minute; umbilical artery (UA) pH < 7.10

### **RISULTATI**

Induction of labor was performed in 100 cases (59.2%), while 21.3% had spontaneous vaginal delivery and 19.5% underwent elective CS. A regular vaginal delivery occurred in 65% of cases from the induction group, while the rate of CS and OD was 30% and 5% respectively. Apgar score at 1st minute <7 and UA pH 95° centile (CS p=0.04/0.007; NICU p=0.004), MCA PI < 5° centile (CS p=0.04/0.024; NICU p=0.02), CPR < 5° centile (CS p=0.005/0.001; NICU p=0.005) were significantly associated with the adverse outcomes considered

### **CONCLUSIONI**

Doppler velocimetry of UA, MCA and CPR are potentially useful tools for the identification and management of the late term IUGRs, so further prospective dedicated trials are expected



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## 18. DUODENAL DUPLICATION: A CLINICAL CASE

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### INTRODUZIONE

Intestinal duplications are rare congenital GI (gastro-intestinal) malformations; they are ubiquitous, with an incidence of 1:25,000 births. Among those, duodenal duplications are extremely rare (6.5% of cases), generally localized in the medial and posterior part of the 2nd and 3rd portion of the duodenum. Usually they are incidental findings and symptoms, like mass effect or the presence of heterotopic gastric mucosa, are rare. If detected prenatally, such forms, predominantly cystic, may show the characteristic double bubble sign and enter into the differential diagnosis with duodenal atresia. We present the case of a newborn with prenatal diagnosis of double bubble proved to be a duodenal not symptomatic duplication at birth

### MATERIALI E METODI

Clinical case: F.R. was born at term by spontaneous delivery. The pregnancy was normal without prenatal exposures to toxic; TORCH and vaginal swab were negative. Prenatal ultrasound at 34+3 weeks, showed a rounded anechoic area (18x15 mm), with a "double-bubble" image, near the first part of the duodenum, arousing the suspicion of duodenal atresia. At birth: good adaptation to extrauterine life, normal auxological data, meconium emission in the delivery room, absence of gastric retention. Serial XR performed at 2, 8 and 24 hours of life and a GI-XR with contrast performed at 48 hours of life, showed no signs of intestinal occlusion or pneumoperitoneum. Abdominal ultrasound, performed at 24 hours of life, showed an oval anechoic area (25 mm), well cleaved, with a thin wall, located between the stomach, the pancreas tail and the spleen, compatible with a "duodenal duplication cyst." Abdomen MRI with contrast confirmed ultrasound data. There were not additional malformations. Follow-up is negative for complications and the cyst appears losing ground, so it was decided to not perform surgical excision till now and to postpone surgery until year of age when it will be performed with minimally invasive techniques

### CONCLUSIONI

Conclusions: Prenatal diagnosis of cystic duodenal duplication enters the differential diagnosis of duodenal obstruction, if it occurs with ultrasound image of gastric double bubble. The risk of occlusion by mass effect is high at birth, so a careful multidisciplinary management involving obstetricians, neonatologists and surgeons, is critical for these patients. In our case, the absence of symptoms and a careful follow-up allowed us to delay surgery till a year old. Without occlusive problems, laparoscopic surgery is the first choice in children.



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## 19. ECLAMPSIA, MATERNAL AND NEONATAL OUTCOMES: COMPARISON OF TWO EXPERIENCES OF A TERTIARY CENTER

### LISTA AUTORI

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### INTRODUZIONE

Eclampsia is defined as the development of convulsions and/or unexplained coma during pregnancy or postpartum in patients with signs and symptoms of preeclampsia (1). Eclampsia should be considered also when hypertension (16% of cases) or proteinuria are absent (14%) (2). Eclampsia may occur before birth (45%), during labour (19%) or after delivery (36%) (3). In Western countries eclampsia is a rare condition (in Europe about 1 in 2000-3000 births), thanks to a better quality of perinatal care and effective guidelines which recommend use of magnesium sulphate for the prevention of eclampsia itself (3;4;5). However, it is still an important cause of maternal and perinatal mortality and morbidity, resulting in 10-15% of maternal deaths and in about 2-20% of perinatal mortality (4;6;7). In 2015, in our Department there were two cases of eclampsia in pregnancy, in very different clinical settings; aim of this report is to analyze the clinical management and maternal and perinatal outcome, in relation to the effectiveness of the guidelines in use and literature data

### MATERIALI E METODI

We analyzed two cases of eclampsia occurred in 2015. Our department provides procedures and standardized guidelines for both the management of the hypertensive emergencies in pregnancy and in puerperium, and for the prophylaxis and treatment of eclampsia in case of severe pre-eclampsia, based on national and international guidelines (8;9;10;11). In particular, therapy of eclampsia consists in infusion of magnesium sulphate (dosage: 4 grams i.v. loading dose over 10-15 minutes, followed by 1g/hour as a continuous intravenous infusion via pump for 24 hours). In all cases of severe preeclampsia, an "eclampsia emergency kit" (which includes all needed drugs such as magnesium sulphate, calcium gluconate, diazepam and equipment such as syringes, swabs, intravenous lines, etc.) is available near the patient's bed to facilitate rapid intervention (Figure 1)

### BACKGROUND

CASE 1: A 34-years old nulliparous woman was admitted at 39+4 gestational weeks because of headache and high blood pressure levels (140/100 in two measurements) without proteinuria and with normal value of platelets, hepatic enzymes and renal function. The diagnosis of gestational hypertension was made, and induction of labour with vaginal prostaglandins was started. Intensive monitoring of blood pressure was performed, with normalization of blood pressure without antihypertensive therapy; however, the headache persisted and subsequently photophobia occurred. Electronical fetal heart rate monitoring (cardiotocography) was always normal. During second stage of labour, after one hour of active pushing it was decided to augment labour with oxytocin. After two hours a blood pressure of 170/105 was detected and six minutes later tonic-clonic seizures with loss of consciousness occurred. The patient was positioned on the left lateral position, the attack dose of magnesium sulphate was administered, and the Anesthesiologist arrived promptly since already present in the delivery ward. Eclamptic convulsions lasted about 10 minutes, during which it was impossible to register the fetal heart rate but, immediately after, CTG trace was restarted and it was normal (Figure 2). In consideration of the maternal clinical conditions and the stage of labour (second stage lasting about 3 hours with presenting part at +1 level), an emergency cesarean section was performed with the patient under general anesthesia.

CASE 2: A 37 years old woman, with three previous spontaneous vaginal deliveries uncomplicated by hypertensive disorders was admitted at 34+5 gestational weeks for proteinuria of 0,30 g / 24 h and elevated blood pressure (140/100), with normal liver and kidney function, leading to hospitalization for mild pre-eclampsia. A significant proteinuria (0.82 g / 24 h) was confirmed. The following days the patient complained of headache associated with hypertensive peaks with values up to 190/105, treated with intravenous infusion of labetalol and serial monitoring of blood tests, resulting always within normal limits. During hospitalization antenatal steroids to reduce neonatal morbidity were administered and fetal well-being was monitored by cardiotocography, that was always normal, and by ultrasound scans that detected fetal abdominal circumference at the 10th percentile, oligohydramnios and velocimetry of the umbilical artery at the 90th percentile.

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On the 9th day, at 36+1 weeks of gestation, an eclamptic seizure occurred; the “eclampsia emergency kit” was readily available near the bed of the patient allowing a quick start of the magnesium sulphate infusion. The woman was promptly placed on the left lateral position. After about 2 minutes the Anesthesiologist arrived. At the end of the crisis the patient was in a drowsy state, the uterus was contracted, and there was no possibility to record the fetal heartbeat with CTG; therefore an ultrasound was performed with detection of fetal bradycardia (40-60 beats per minute). An emergency cesarean section was performed for suspected placental abruption, with the patient under general anesthesia

## RISULTATI

CASE 1: After 16 minutes from the eclamptic fit, a male infant of 3820 grams was delivered. Apgar score at the 1st minute was 9 and at the 5th minute was 10, arterial pH was 7.19 with excess bases of -6.8. The baby did not require care in the Neonatal Intensive Care Unit (NICU). The patient was transferred to the Intensive Care Unit (ICU), for postoperative monitoring. Magnesium sulphate infusion was maintained for 24 hours and afterwards she returned to the Obstetric ward in hemodynamically and neurologically stable conditions. An hypertensive crisis occurred after 50 hours from the cesarean section, with 2 measurements > 160/110, and was treated with oral nifedipine at first and later with oral labetalol. Proteinuria, which was absent at admission, was detected at a level of 1.78 g/24 hours, allowing for a diagnosis of preeclampsia. The other blood tests for preeclampsia were normal. The patient underwent neurological investigations, with the performance of an electroencephalogram (EEG) that detected electrical irritant alterations; she was submitted to a cerebral magnetic resonance imaging (MRI) that resulted normal. She was discharged on the eleventh day with oral antihypertensive therapy. At 2 months after birth there was normalization of proteinuria and blood pressure and antihypertensive therapy was stopped.

CASE 2: Intraoperative diagnosis of placental abruption was confirmed; after 12 minutes from the eclamptic fit, a female infant of 1950 grams was delivered. Apgar score at the 1st minute was 8 and at the 5th minute was 10, arterial pH was 6.94 with excess bases -13; the newborn was transferred to the NICU. The woman was transferred in the ICU for monitoring and maintained the magnesium sulphate infusion for 24 hours. Subsequently, the patient underwent neurological investigations that resulted normal. She was discharged on the seventh day without antihypertensive therapy. Two months after birth blood pressure and proteinuria were normal. Histological examination of the placenta has subsequently confirmed the diagnosis. The baby was discharged on the seventh day with the diagnosis of mild prematurity and mild cerebral periventricular hyperechogenicity, in good general conditions. Subsequent follow-up at 2 months was normal

## CONCLUSIONI

In the first case eclampsia occurred at term of pregnancy during second stage of labour, in a patient previously managed for gestational hypertension; the detection during puerperium of a significant proteinuria allowed the diagnosis of preeclampsia only after delivery. In the second case, eclampsia occurred in a different clinical setting where a symptomatic preeclampsia was already known in a preterm pregnancy with fetal growth restriction, oligohydramnios and pathological Doppler, and this may explain the worst obstetric and perinatal outcome. Eclampsia is complicated in 2-20% of cases by perinatal loss and neonates born to eclamptic mother are more likely to experience RDS (respiratory distress syndrome) and neonatal seizures independently of gestational age and birthweight (12). Although it is known that eclampsia is not a contraindication to vaginal delivery (13) and could be associated with better perinatal outcome (14), a recent study has shown that eclamptic women are significantly more likely to deliver by caesarean section compared to pre-eclamptic women (12). Cesarean delivery is recommended, after stabilization of maternal clinical conditions, in case of absence of maternal collaboration, signs of fetal distress or when vaginal delivery is expected to be too long, conditions that occurred in the two cases we have described (13).

Fortunately, in both cases, there were no maternal sequelae, although it is well known that eclampsia can be associated with neurological and cardiovascular morbidity and maternal mortality.

After the audit of the clinical management of the two cases, we concluded that the presence of guidelines procedures and updating of all staff have allowed rapid identification and treatment of eclampsia. However, in the first case the “eclampsia emergency kit” previously described was not immediately available since the admission diagnosis was gestational hypertension. Therefore this experience has prompted us to modify our procedures providing the availability of the “eclampsia emergency kit” not only for patients with severe preeclampsia but also for those with gestational hypertension, aware of the possibility of atypical manifestations of eclampsia (15)



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## **20. EFFECT OF A NEONATAL RESUSCITATION COURSE ON HEALTHCARE PROVIDERS' PERFORMANCES ASSESSED BY VIDEO RECORDING IN A LOW-RESOURCE SETTING**

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### **INTRODUZIONE**

We assessed the effect of an adapted neonatal resuscitation program (NRP) course on healthcare providers' performances in a low-resource setting through the use of video recording

### **MATERIALI E METODI**

A video recorder, mounted to the radiant warmers in the delivery rooms at Beira Central Hospital, Mozambique, was used to record all resuscitations. One-hundred resuscitations (50 before and 50 after participation in an adapted NRP course) were collected and assessed based on a previously published score

### **RISULTATI**

All 100 neonates received initial steps; from these, 77 and 32 needed bag-mask ventilation (BMV) and chest compressions (CC), respectively. There was a significant improvement in resuscitation scores in all levels of resuscitation from before to after the course: for "initial steps", the score increased from 33% (IQR 28-39) to 44% (IQR 39-56),  $p < 0.0001$ ; for BMV, from 20% (20-40) to 40% (40-60),  $p = 0.001$ ; and for CC, from 0% (0-10) to 20% (0-50),  $p = 0.01$ . (Figure 1) Times of resuscitative interventions after the course were improved in comparison to those obtained before the course, but remained non-compliant with the recommended algorithm

### **CONCLUSIONI**

Although resuscitations remained below the recommended standards in terms of quality and time of execution, clinical practice of healthcare providers improved after participation in an adapted NRP course. Video recording was well-accepted by the staff, useful for objective assessment of performance during resuscitation, and can be used as an educational tool in a low-resource setting

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## 21. EFFECT OF HCV CHRONIC INFECTION ON SEMEN PARAMETERS

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### INTRODUZIONE

Although the incidence of hepatitis C has decreased in the last decades, it is estimated that about 3% of world population is still affected by HCV virus. Most of affected male is in reproductive age. Even though HCV sexual transmission is doubtful, HCV RNA can be detected in the semen of 11% - 31.6% of infected males.

Moreover, HCV RNA was found in semen plasma and in not-spermatic cells like lymphocytes, but not in sperm before and after swim-up. The aim of our study is to evaluate semen parameters of HCV positive patients compared to normal WHO 2010 semen parameters

### MATERIALI E METODI

This is an observational study including 58 patients enrolled from 2010 to 2015 in the Fertility Center, Luigi Sacco Hospital in Milan. All patients were diagnosed with HCV chronic infection, while exclusion criteria were coinfection with hepatitis B, HIV or presence of genital tract infection such as Mycoplasma or Chlamidia Tracomatis.

All semen analyses were performed by the same biologist and in the same laboratory, after 3-5 days of sexual abstinence

### RISULTATI

Table 1 shows the baseline characteristics of our study population.

Table 2 shows the comparison between semen parameters of HVC positive patients and WHO reference group.

The HCV group presents median semen parameters significant lower than median semen parameters according to WHO 2010 criteria. About 50% of HCV patients have morphology' and motility's values below the fifth percentile of WHO reference values

### CONCLUSIONI

Our study provides evidence that all semen parameters of HVC-positive men are impaired comparing to WHO 2010 reference values. Therefore a reduced fertility may be supposed in this group.

Oxidative stress as a host response to HCV core protein and subsequent reactive oxidative species produced could damage sperm DNA and alter sperm quality.

Concluding our Fertility Center strongly suggests reproductive counselling in all couples with HCV positive male partner who desire a pregnancy



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## **22. EFFECT OF PROPHYLAXIS WITH BETAMETHASONE ON BLOOD GLUCOSE LEVELS IN PREGNANT DIABETIC WOMEN AT RISK OF PRETERM BIRTH**

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### **INTRODUZIONE**

The hyperglycemia can worsen the metabolic control in patients with diagnosis of diabetes mellitus or with subclinical glucose intolerance. In pregnant women with diabetes, hyperglycemia induced by betamethasone it is not properly known.

This study aims to describe the pattern of maternal glucose response to betamethasone administration using a glucose monitoring system.

We compare the timing, duration, and severity of corticosteroid-associated hyperglycemia in healthy pregnant women with and without gestational diabetes and type 2 diabetes mellitus

### **MATERIALI E METODI**

a prospective observational trial was conducted among women with clinically diagnosis of preterm labor between 24 and 34 weeks gestation. Preterm labor was defined as  $\geq 4$  uterine contractions / 30 min and or cervical length  $< 25$  mm with or without uterine contractions. A total of 84 pregnant women were enrolled from January to Dicembre 2014.

They were divided into 4 groups of 21 patients. Group A: healthy women; Group B: Women diagnosed with gestational diabetes treated with diet alone; Group C: women diagnosed with gestational diabetes treated with diet and insulin; Group D: women diagnosed with type 2 diabetes mellitus in dietary restriction (n11) or in treated with insulin and diet (n10).

At the first visit during pregnancy the presence of a diabetes type 2, should be evaluated by determining the fasting glucose.

The finding repeated on two occasions for a blood glucose  $\geq 126$  mg/dl, allows diagnosis of diabetes. The diagnosis of diabetes type 2 can also take place through the execution of a random blood glucose (performed at any time of the day). The finding of a blood glucose  $\geq 200$  mg / dl, allows a diagnosis of overt diabetes after confirmation with fasting plasma glucose  $\geq 126$  mg / dl.

Gestational diabetes is diagnosed with an oral glucose tolerance test (OGTT) performed between the 24th and the 28th week of gestation. The OGTT was performed with 75 grams of glucose and venous samples were performed at the time 0', 60' and 120' for the determination of blood glucose in plasma. Gestational diabetes is diagnosed when one or more values are equal or higher than the threshold.

We evaluated 84 women consecutively selected with threatened preterm labor.

At hospitalization, all patients received corticosteroids prophylaxis (antenatal administration of 12 mg of betamethasone, followed by a second dose 24 hours later) to enhance lung maturation.

All women made a glycemic profile, by measuring capillary blood glucose before and 2 hours after meals during the 5 days of hospitalization. The results were examined with the Student's t test

### **RISULTATI**

Several, relatively short episodes of glucose elevation occur in response to corticosteroids, and are more pronounced in diabetic women. In group A, the patients showed no significant changes in blood glucose levels. In group B, it was necessary to add insulin treatment for 4 patients, while the usual dose of insulin was increased from 36% to 74% in the patients of group C and D to maintain blood glucose levels between 92 mg/dL and 126 mg/dL.

The most significant changes occurred after 2-4 days after administration of betamethasone

### **CONCLUSIONI**

Hyperglycemia induced by betamethasone is greater in patients with a diagnosis of gestational diabetes or type 2 diabetes mellitus receiving insulin and should only be administered during hospitalization for proper monitoring of maternal and fetal conditions.

The gynecologist should be sensitized to this issue recalling that corticosteroid therapy in patients with overt diabetes or glucose intolerance (and therefore at greater risk of illness) and in non-diabetic patients. Prophylaxis with betamethasone is a fundamental therapeutic step for threatened preterm labor, but it needs monitoring which can not be delegated to outpatient activities and home

## **23. EFFECTIVE ANATOMICAL AND FUNCTIONAL STATUS OF THE LOWER UTERINE SEGMENT AT TERM: ESTIMATING THE RISK OF UTERINE DEHISCENCE BY ULTRASOUND**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Between the 12th and 20th weeks of gestation, the uterine wall undergoes a thinning process, reaching a minimum value of approximately 10 mm and then remaining constant until term. The increase in uterine volume, particularly along the longitudinal diameter, implies changes within the uterine isthmus that gradually develop the so-called lower uterine segment (LUS). Anatomical features of the LUS (thinner muscle fibers, abundant elastic tissue, and poor large blood vessel density) make it the most suitable site for a transverse incision during cesarean section (CS). At the same time, these features also render the LUS a "locus minoris resistentiae" in subsequent pregnancies, which can result in uterine dehiscence or even uterine rupture. The real incidence of uterine dehiscence during subsequent pregnancies after CS is underestimated. In a pregnant woman with previous CS, the association between undergoing labor, uterine scarring due to previous CS, and a thin LUS is unclear. Sonographic measurement of the LUS at term might be useful in identifying women with the lowest risk of uterine dehiscence during labor. Although ultrasound evaluation could be useful in evaluating the LUS to assess the risk of uterine dehiscence or worse, a risk scale and homogeneous cutoff values are not yet available. The first aim of our study is to clarify the role of ultrasound evaluation of LUS at term in predicting the effective anatomical and functional status of LUS in pregnant women with or without previous CS. The goal is to find the most reliable cutoff value of total LUS and myometrial thickness that might predict uterine dehiscence at term. An additional purpose of this study is to evaluate the obstetrical factors involved in promoting a thinner LUS after CS deliveries

### **MATERIALI E METODI**

This was an observational case-controlled study conducted in pregnant women between 36 and 41 gestational weeks who were referred to the Obstetrics and Gynaecological Unit of Padua from January to October 2011. All patients were adequately informed of the aim of the study and gave their written consent. All patients enrolled in the study delivered by CS and were divided into two groups. Group A was composed of multiparous pregnant women with a single fetus who had previously delivered by CS (up to two) and who were not willing to attempt a vaginal delivery. Group B was composed of multiparous pregnant women with up to three vaginal deliveries. None of them had any uterine scarring due to previous surgery. Group A consisted of patients who had an elective planned CS, whereas group B consisted of pregnant women who demonstrated persistent nonreactive cardiotocographic trace and non-reassuring additional testing for fetal well-being, such as umbilical artery Doppler study during routine monitoring at term. Inclusion criteria for both groups were as follows: single physiologic pregnancy, informed consent to ultrasound measurement, and absence of idiopathic or secondary alterations in amniotic fluid volume. Regarding previous CS (group A patients), inclusion criteria were as follows: accurate surgical description of the procedure and indication for CS (breech presentation, estimated fetal weight >4,000 g, twin pregnancies, fetal malformations, previous CS when pluriparous, non-reassuring fetal heart rate, or uterine dystocia), detailed information about stage of labor in which CS was performed, transverse uterine incision in the LUS, uterine double-layer suture, and non-retroverted uterus. Exclusion criteria for both groups were as follows: pregnancy and previous uterine surgery other than CS (myomectomy, polypectomy, lysis of uterine synechia, or hysteroscopic metroplasty). All patients underwent ultrasound evaluation of the LUS. To minimize error, three LUS measurements were performed by the same skilled sonographer upon admission to the delivery room. The average value of three subsequent measurements was calculated using a 3.5 MHz abdominal convex probe AB2-7-RS, Voluson e6 compact (GE Health Care-2010) with an image magnification up to two-thirds of the screen and an insonation angle between 60 and 120 degrees. The thickness of the LUS and of its myometrial component were assessed by a sonogram perpendicular to the uterine wall, according to the technique proposed by Jastrow et al. To measure the size of the LUS, a cursor was positioned at the interface between the urine and the bladder wall and another was placed at the interface between the amniotic fluid and the deciduas. The myometrium was measured with the cursor at the interface of the bladder wall and the myometrium so that it included only the hypo-echogenic layer. To optimize the measurement of the LUS, the distension of the bladder was set up by a standardized procedure. The patient was instructed to empty her bladder and then drink 300 mL of water an hour before the examination. Age, parity, gestational age, maternal weight gain, neonatal weight at birth during the current pregnancy, neonatal birth middleweight in previous pregnancies, and type of delivery in previous pregnancies were assessed for all patients. Furthermore, inter-pregnancy time and distinguishing whether the previous CS was performed during labor were assessed for patients in group A.

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At the opening of the abdominal wall, the surgeon made an objective evaluation of the integrity and thickness of the LUS. The LUS was graded as follows: grade I indicates that the LUS was well-developed; grade II indicates that the lower segment was thin without visible content; grade III was assigned when the lower segment was translucent with visible content; finally, grade IV was assigned when well-circumscribed defects, either dehiscence or rupture, were present

## **RISULTATI**

94 patients were eligible for inclusion into this study. In particular 45 patients were included in the case group (group A) and 49 patients were included in the control group (group B). In group A, 75.5% of patients had had one previous CS, 17.8% two previous CS, and 6.7% both a CS and a vaginal delivery. In group B, 73.4% of patients had delivered only once, 13.3% twice, and 13.3% three times. There was a significant difference between group A and group B in terms of maternal age: 34.73 4.62 versus 31.12 5.22 years. There was no statistically significant difference between the two groups with regard to parity, gestational age, neonatal birth weight, neonatal birth middleweight during previous pregnancies, or weight gain during the current pregnancy. Sonographic measurements revealed significant differences between the two groups in LUS size (3.95 1.29mm in group A and 5.36 1.47mm in group B) and myometrial thickness (1.74 0.76mm in group A and 2.36 0.52mm in group B). With regard to LUS status grades III and IV of LUS were only observed in group A. In both groups, there was a statistically significant correlation between sonographic mean LUS thickness and surgical LUS grade at abdominal opening (4.11 1.18mm in grade I-II and 1.61 0.54mm in grade III-IV) and between sonographic mean myometrial thickness and surgical LUS grade (1.93 0.35mm in grade I-II and 0.41 0.13mm in grade III-IV). There was also a strong correlation between the inter-pregnancy time from the last CS and surgical LUS grade III or IV. Four out of five patients with grade III or IV had undergone a CS within the last 18 months ( $P<.01$ ). LUS thickness  $<3.0$ mm, myometrial thickness  $<1.5$ mm and an inter-delivery interval  $<18$ months, were statistically significant predictors of LUS grades III and IV. There was no significant correlation among parity, gestational age, neonatal weight at birth, neonatal birth middle-weight in previous pregnancies, maternal weight gain in the current pregnancy, and surgical LUS grade III or IV. Number of previous CS showed no correlation with surgical LUS status

## **CONCLUSIONI**

Sonographic evaluation of LUS may represent a noninvasive, reproducible, and safe technique for defining the risk of uterine dehiscence in women with previous CS, especially in those who have undergone a CS more than 18 months before. The utility of the sonographic definition of LUS status may be proposed when selecting the criteria of the guidelines for vaginal birth after CS because the benefits of vaginal delivery in terms of maternal and neonatal outcome and of early bonding and breastfeeding have already been established



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## **24. EFFECTS OF A LIFESTYLE PROGRAM IN OVERWEIGHT/OBESE WOMEN ON MATERNAL AND NEONATAL OUTCOMES: A CASE-CONTROL STUDY**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Obesity and excessive weight gain are two well-known risk factors for LGA babies and macrosomia. Recent evidences suggest that diet or exercise, or both, during pregnancy might be beneficial in reducing the occurrence of macrosomia, among other outcomes. The aim of this study is to evaluate the incidence of large for gestational age (LGA) babies, small for gestational age (SGA) babies and macrosomic babies among women undergoing a program of lifestyle consisting of a hypocaloric, low glycemic index diet and moderate physical activity, respect to a population of women of the same BMI category not undergoing the same program

### **MATERIALI E METODI**

This is a retrospective, case-control study. Women with BMI  $\geq 25$  Kg/m<sup>2</sup>, enrolled in a trial for the evaluation of the effects of a lifestyle program were included. These women were counselled by a dietitian during early pregnancy and were prescribed a hypocaloric, low-glycemic index diet (in observance of the recommended nutritional intake suggested by the national guidelines), and moderate physical activity, consisting of walking sessions lasting 30 minutes at least 3 times a week. Three women delivering subsequently, meeting the inclusion criteria (BMI  $\geq 25$  Kg/m<sup>2</sup>, singleton pregnancy, absence of chronic disease) and not undergoing any lifestyle program, were included as controls. The data, collected from the clinical charts, included: maternal weight and BMI before pregnancy and at term of pregnancy; occurrence of pregnancy complications, such as gestational diabetes mellitus (GDM), pregnancy induced hypertension (PIH) and preterm birth (PTB); newborns' weight and birthweight centile; LGA were defined if birthweight centile was  $\geq 90^{\circ}$ , SGA if birthweight centile was  $\leq 10^{\circ}$ , macrosomic if birthweight  $\geq 4000$ g

### **RISULTATI**

Three hundred and sixty women were included: 90 cases and 270 controls. Age at enrolment was not different between the two groups, while BMI was higher in cases ( $33.1 \pm 5.7$  Kg/m<sup>2</sup>) than in controls ( $31.6 \pm 5.2$  Kg/m<sup>2</sup>;  $p=0.018$ ), due to a higher prevalence of obese women in the first group (66.7% vs 54.8%;  $p=0.049$ ). Main outcomes are reported in table 1. GDM, PIH and PTB had a lower occurrence among cases. Gestational weight gain (GWG) and the percentage of women remaining within recommended ranges of GWG were not different between the two groups. Occurrence of LGA and macrosomic babies was lower in the group of cases, while the occurrence of SGA was similar in the two groups. At logistic regression, after correcting for GDM, BMI  $\geq 30$  Kg/m<sup>2</sup>, age  $\geq 35$  years and Caucasian ethnicity, the occurrence of LGA was still prevented by the lifestyle intervention (OR 0.104, 95% CI: 0.014-0.784). A similar result was found for macrosomic babies (OR 0.282, 95% CI: 0.082-0.961)

### **CONCLUSIONI**

Exposure to a hypocaloric, hypoglycaemic diet and physical activity started in early pregnancy reduces the occurrence of macrosomic and LGA babies among overweight/obese women, while it doesn't affect the occurrence of SGA nor GWG

## 25. EFFECTS OF HIV-1 INFECTION AND ANTIRETROVIRAL THERAPY ON SEMEN PARAMETERS AND SPERM DNA INTEGRITY

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### INTRODUZIONE

It has been estimated that 35 million people worldwide and 0.2% of Italian population has a chronic HIV-1 infection. The use of antiretroviral drugs has provided a noteworthy improvement in both the quality and the expectancy of life of people infected with HIV; therefore, as three quarters of infected people are in their reproductive years, many couples with an HIV positive partner can consider pregnancy planning. The aims of this study were twofold: the first aim was to assess the effect of HIV-1 infection on semen parameters; the second aim was to evaluate the effects of highly active antiretroviral therapy (HAART) on sperm DNA fragmentation comparing HIV-1 infected patients receiving HAART versus naïve HIV-1 infected patients

### MATERIALI E METODI

For the first aim of the study, we retrospectively analyzed semen samples obtained from 770 HIV-1 patients recruited between January 2005 and June 2015 in our Unit of Assisted Reproduction. Co-infections with HBV or HCV and genital tract infections represented exclusion criteria; all patients received HAART and had a CD4 count > 200 cells/mm<sup>3</sup>. Complete semen analysis was performed according to WHO 2010 recommendations, with each semen variable of the study population being compared with the WHO reference group. For the second aim of the study we performed a case-control prospective study. 75 men infected with HIV-1 were recruited between January 2010 and June 2015 in our Unit. 51 HIV-1 infected patients receiving HAART (Group A) were compared to 24 HIV-1 infected patients who did not receive HAART (Group B). Sperm DNA fragmentation and semen analysis was performed using chromatin dispersion test (SCD) to evaluate the effect of HAART on sperm DNA fragmentation

### RISULTATI

Median values of all assessed semen parameters were within a normal range, but significantly lower compared to WHO median values ( $p < 0.05$ ). In addition, for each semen variable, a significant proportion of HIV-1 infected patients had values below the 5° percentile of the WHO 2010 reference group ( $p > 30\%$  whereas in Group B 9 patients (37.5%) showed sperm DNA fragmentation > 30% ( $p < 0.02$ ) (Table 2). We did not observe any correlation between antiretroviral therapy and semen parameters

### CONCLUSIONI

Our study provides evidence that a significant proportion of HIV-1 infected patients have impaired semen parameters values below the 5° percentile of the WHO 2010 reference group and therefore a possible altered fertility. Oxidative stress, as a response to possible HIV mitochondrial damage induced by HAART, could damage sperm DNA and alter sperm quality. In addition, the results of our study demonstrate that sperm nuclear fragmentation rate increases in HIV-1 infected patients receiving antiretroviral therapy when compared to HIV-1 infected patients who do not receive therapy. Integrity of sperm DNA is also known to influence a couple's fertility and possibly predicts the chances of pregnancy and its successful outcome. In the light of these results, reproductive counselling is strongly suggested for all couples with HIV-1 male partner who desire a pregnancy

## **26. ELECTRONIC FETAL MONITORING DURING LABOR: COMPARISON OF ABDOMINAL FETAL ELECTROCARDIOGRAPHY AND DOPPLER CARDIOTOCOGRAPHY**

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### **INTRODUZIONE**

Electronic Fetal Monitoring (EFM) is the standard modality of fetal surveillance during labor. During the last 30 years cardiotocography (CTG) has become the most common method to monitor fetal health. Despite its benefits, it is well known that cardiotocography is often affected by poor quality of recording, mainly signal loss and maternal - fetal ambiguity, leading to difficulties in its interpretation. Monica AN24 is a recent non-invasive electronic fetal monitoring technique which is able to monitor both Fetal Heart Rate (FHR) by abdominal fetal ECG (abfECG) and uterine activity by electrosterography (EHG).

The aim of this study is to compare the signal quality of a abfECG system (Monica 24™) to the one of Doppler CTG monitoring

### **MATERIALI E METODI**

We enrolled 40 singleton pregnant women at term undergoing intrapartum fetal monitoring using both Doppler CTG and AN24. 12 patients were excluded because of a recording time below 30 minutes and 28 women were included in the study. Recordings from both methods were analyzed for signal quality and numbers of accelerations, decelerations and uterine contractions

### **RISULTATI**

Overall perceived signal quality was significantly higher with AN24 than with Doppler CTG (94.2% vs. 88.2%;  $p < 0.01$ ). AN24 leads to significantly lower estimation of large decelerations (5,2 vs. 8,3;  $p < 0.001$ ) and allows a better view of small accelerations and uterine contractions (Small acceleration: 31,2 vs. 9,6  $p < 0.001$ ; uterine contractions: 76,4 vs. 31,6  $p < 0.001$ ). Large decelerations and uterine contractions showed a similar trend also during the second stage of labor (large decelerations: 1,7 vs. 5,0  $p = 0.003$ ; uterine contractions: 22,4 vs. 7,1  $p < 0.001$ ), whereas signal quality of both abfECG and CTG was found to be equivalent during this stage (85.0% vs. 84.6%,  $p = 0.638$ )

### **CONCLUSIONI**

Our study shows that the use of non-invasive fECG allows better signal quality. This seems to be associated with a more accurate identification of uterine activity and with a lower estimation of decelerations. Consequently, the judgment of the tracks appears improved

## 27. ERYTHROPOIETIN USE AND INTRAOPERATIVE BLOOD SAVAGE IN A PREGNANT JEHOVAH'S WITNESS WITH SEVERE ANEMIA DUE TO BETA-THALASSEMIA

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### INTRODUZIONE

Anemia in pregnancy is seen often because of iron deficiency and the "physiologic dilution" that occurs in the third trimester. Other causes include genetic conditions, such as sickle cell anemia and thalassemias. The different hemoglobinopathies are among the most common inherited disorders worldwide. The geographical areas with the highest incidence of hemoglobinopathy include Central and Southeast Asia, Northern Africa, Pakistan and the Mediterranean region. Due to the migration of people from these countries, laboratory diagnosis and adequate treatment is of growing importance in North-western Europe.

B-Thalassemia, the most common congenital anemia, is caused by mutations that reduce or eliminate production of b-globin (1,2). During late stages of normal erythroid differentiation, haemoglobin synthesis is highly coordinated to minimize accumulation of free globin subunits (3,4). Intracellular accumulation of free a-globin chains and precipitation of a-globin-heme complexes on red cell membranes in b-Thalassemia generates proteotoxicity, inhibits late-stage erythroid differentiation, and is also thought to cause haemolysis of erythrocytes (1,2,5,6). Ineffective erythropoiesis (IE) is a hallmark of b-Thalassemia and promotes anemia and hypoxia. If prolonged, this condition can lead to erythroid hyperplasia in bone marrow and spleen, dysregulated iron homeostasis, increased levels of reactive oxygen species (ROS) in erythroid cells and additional complications.

In cases not responding to iron therapy, patients occasionally require a blood transfusion to restore adequate circulating red blood cell mass. In patients belonging to the Jehovah's Witness sect, transfusion of blood products is not allowed, and treatment of anemia in pregnancy may require use of erythropoietin

### MATERIALI E METODI

We report a case of a 39 years old woman, PARA 0, with a pregnancy obtained by ICSI and affected by Beta-Thalassemia, diagnosed during pregnancy with the execution of set-hemoglobin after detection of low hemoglobin values and hemoglobin mean cell content <27 pg at the first blood count control. At 16 weeks of gestation and five days it was therefore prescribed: folic acid, iron and vitamin B12 orally; however for "personal choice", the patient did not assume the prescribed therapy until the 20 weeks and 6 days of gestation, when, after further inspection of blood exams during the midwife visit, that revealed a value of Hemoglobin 8.3 g/dl, there was the further explanation of the necessity of taking such drugs.

The patient, for religious reasons (Jehovah's Witness), also refused blood transfusions despite having been informed by both the gynecologists and neonatologists of the need to resort to free a-globins in the case of detection, in the subsequent blood tests, of hemoglobin values below to 8 g / dl.

The patient underwent also consulting for hematologic evaluation of intravenous iron therapy. Meanwhile, the load curve of glucose (75g) was altered and the patient began insulin therapy, concurrently intravenous iron therapy.

At 25 weeks and 1 day of pregnancy the patient was admitted to the Department of Obstetrics Hospital of Treviso for detection of Hb 7.9 g / dl. Following the renewed refuse of blood transfusions, it is at this point opted for therapy with erythropoietin (Eprex 8000 IU, 1 fl subcutaneously for four weeks and, in the discharge, 2 fl subcutaneously / week) whose off-label use, however, is not supported by Literature data that take into account the specific event of anemia in pregnant patient bearer of beta-Thalassemia.

Blood tests have then demonstrated the following values:

- 29/11/2013: Hb 7.6 g / dl
- 03/12/2013: Hb 7.5 g / dl
- 12/09/2013: Hb 7.4 g / dl
- 16/12/2013: Hb 7.8 g / dl

During hospitalization the patient has also performed heparin therapy for the onset of a phlebitis at the left upper limb.

The patient has also performed a full abdomen ultrasound, infectious disease testing and gastroenterological counseling for ALT levels slightly above the normal range limits from the beginning of pregnancy (ALT 58) and suspected intestinal malabsorption syndrome, that however resulted negative.

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At 33 weeks and 4 days of gestation the patient began treatment with ursodeoxycholic acid for further rise in transaminases; the dosage of bile salts was slightly impaired (15.5 micromol / L). Therefore it proceeded to fetal RDS prophylaxis and programming of elective caesarean section in view of previous laparoscopic myomectomy performed in 2009 for removal of massive posterior fibroid (weight: 1,070 g). The patient accepted intraoperative blood salvage and gave her written consent before surgery.

At 34 weeks and three days of gestation, the patient underwent urgent cesarean section for repetitive decelerations in CTG. Cell Salvage during surgery allowed to give back to patient ml. 450 of red blood cells that were reinfused through a leucodepleting filter as the guidelines suggest in this setting (13). The Hb at discharge was 8.3 g/ dl

## RISULTATI

Jehovah's Witnesses religious conviction, refuses transfusion of whole blood, packed RBCs and plasma, as well as the administration of white blood cells and platelets. They also believe that the blood taken from the body has to be eliminated and therefore they are also opposed to those techniques of collection or hemodilution during surgical intervention that involved blood storage.

Doctors are therefore in front of an important ethical challenge facing these surgical patients.

The Beta-Thalassemia is a genetic defect that causes the reduction of the synthesis of polypeptide chains that combine to form hemoglobin and mostly affects people of Mediterranean, African and Southeast Asian.

In pregnancy the levels of hemoglobin and hematocrit are reduced "physiologically" for an increase of plasma volume, but also by the inadequate production of erythropoietin (7); so often the condition of Beta-Thalassemia is not responding, therefore, to the only martial intravenous administration.

The use of erythropoietin seems to be, therefore, a useful therapeutic option in pregnant patients who for religious reasons refuse blood transfusion. As a molecule of 30,400 Dalton, in fact, it does not cross the placental barrier in vivo (8).

Several studies focused on the possible use of recombinant human erythropoietin (rHuEPO) therapy for Beta Thalassemia in pregnancy. This treatment may result in decreases in the RBC demand and transfusion-induced iron overload, facilitating normal growth and development, and a better quality of life. By the way its use remain today controversial because of the resistance of the beta Thalassemia above all other hemoglobinopathies failing to respond to subministration of this drug. (9,10,11)

Jehovah's Witnesses allow the use of cell salvage during surgery, as long as the extracorporeal circulation is uninterrupted. This is why in our case, due to the values of hemoglobin of the patient, it has been used during caesarean section, the procedure of intraoperative blood salvage that consists in the collection, separation, washing and re-infusion of red blood cells through a device called "Cell-Saver"

## CONCLUSIONI

As seen in literature synthetic erythropoietin has been used successfully in patients with anemia. In pregnancy associated with renal failure and anemia, synthetic erythropoietin has been shown to be safe except for rare cases of hypertension. We treated anemia caused by beta-Thalassemia in pregnancy with synthetic erythropoietin to avoid a transfusion in a Jehovah's Witness and with the procedure of intraoperative blood salvage during a subsequent cesarean section. This procedure can be useful in obstetrics and during caesarean section than vaginal birth, especially if there are special conditions which, among other patients at high risk of intra and peripartum bleeding (i.e. placenta accreta, placenta praevia, the presence of bulky uterine fibroids) or with severe anemia in the peripartum, and patients who for religious reasons refuse blood transfusions from the donor.

The procedure of intraoperative blood salvage can reduce the incidence of infections and reactions to incompatible blood transfusion, but it is a procedure that has not yet adopted as routine by obstetrics because of the controversy surrounding the possible amniotic fluid embolism and the risk of hemolytic anemia for the newborn in future pregnancies of Rh-negative mothers as a result of the re-infusion of fetal cells in maternal circulation.

To cope with this latter case it is necessary, in fact, to administer within 72 hours, an appropriate dose of Ig anti-D (1500 IU anti-D Ig) to Rh-negative patients and subjected to intraoperative blood salvage because the device "Cell-Saver" it is not able to distinguish maternal red blood cells from fetal ones.

It should also be considered the limit of the procedure of intraoperative blood salvage as it requires a perfect interdisciplinary organization between surgeons, anesthetists and laboratory analysis, as well as a constant training of the staff to perform such procedures, that is not always easy and can be performed in emergency conditions only where there is the experienced staff (12)



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## **28. EVALUATION OF BIOCHEMICAL PARAMETERS OF RENAL IMPAIRMENT/INJURY AND SURROGATE MARKERS OF NEPHRON NUMBER IN IUGR AND PRETERM NEONATES AT 30-40 DAYS OF POSTNATAL CORRECTED AGE**

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### **INTRODUZIONE**

Prematurity and IUGR are associated with increased risk of developing renal postnatal injuries in the early postnatal period and in later life. In addition, newborns with the diagnosis of renal dysfunction and/or renal failure display higher rate of mortality. It is now clear that once renal functional impairment is established, it is often difficult to retard further disease progression. In view of that, it is crucial to identify in IUGR and preterm (PR) babies those individuals who may be subjected to future progression to renal failure as early as possible and take preventative measures before apparent renal dysfunction becomes established. Data concerning renal physiology in IUGR and PR neonates at the early postnatal period of 30-40 days of corrected age are limited and mostly concern PR babies. They are often lacking of correlation between biochemical parameters and nephron number (Nne), a data that could provide additional insight in order to better elucidate the high variability evidenced and/or to improve recognition of individuals at higher risk of renal failure. We here aimed to determine possible early asymptomatic onset of renal damage in IUGR and PR neonates at 30-40 days of postnatal corrected age measuring some urinary indicators of glomerular and tubular impairment/injury and looking for their association to predominant susceptibility factors of renal damage associated with low Nne (i.e. gestational age, GA, birth weight, BW, total renal volume, RV, and renal cortex volume, CV). For our purpose, we included urinary levels of total protein (TP), microalbumin ( $\mu$ ALB) and the activity of N-acetyl-b-D-glucosaminidase (NAG) and cathepsin B (CB)

### **MATERIALI E METODI**

Neonates at 30-40 days of corrected age without congenital abnormality or urinary tract infection were recruited from the newborn nursery at the S. Maria della Misericordia's Hospital in Perugia, Italy. They were grouped into three categories: IUGR (diagnosed by a birth weight below the 10th centile); PR and healthy controls defined as appropriate for gestational age (AGA, a newborn infant whose size is within the normal range for the gestational age). For each child, a first morning urine sample was obtained (using a U-bag collection device) and immediately stored at -4°C to avoid denaturation during the transport to the hospital. All samples were centrifuged at 1000g for 10 minutes at 4°C before storage at -80°C for later analysis. Urinary creatinine was measured using the Jaffé test. TP and  $\mu$ ALB were determined using nephelometric technology on a Beckman immunochemistry system and data were expressed as creatinine ratio (mg of TP o  $\mu$ ALB /mmol creatinine). NAG, CB activities were detected using specific fluorescent substrates and expressed as International Units (IU)/min mmol creatinine, in the case of NAG, and IU/h mmol creatinine, in the case of CB. GA was expressed as weeks and BW as grams. RV and CV were measured by echo 3-D combined with a general imaging 3D quantification software (Vocal II GE ULTRASOUNDS, USA)

### **RISULTATI**

AGA babies displayed higher levels of all surrogate markers of Nne (i.e. GA, BW, CV and RV) compared to IUGR and PR ones. Within LBW group, IUGR versus PR newborns exhibited significant lower levels of RV and CV and, of note, higher GA and similar BW. In terms of kidney function/dysfunction, in agreement with previous data, we found that reduced levels of Nne in IUGR and PR, compared to AGA, clearly associated to increased impairment/injury of tubule. IUGR and PR neonates, indeed, presented higher levels of the two lysosomal markers of tubular impairment/injury and CB activity, which significantly augmented in both IUGR and PR, strongly and negatively correlated with all surrogate markers of Nne (GA, BW, RV, CV). Within LBW newborns, IUGR versus PR demonstrated a more severe impairment/injury of tubule. In addition, IUGR presented the most elevated values of proteinuria

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## CONCLUSIONI

This study indicates that at 30-40 days of corrected age, kidneys of PR and IUGR neonates are characterized by a tubular impairment/injury that associates to reduced Nne. In IUGR this is more severe and possibly combined to concurrent increased glomerular permeability. This may allow to augmented risk of glomerular proteinuria, which could contribute to hyperfiltration, hypertension, glomerulosclerosis and renal disease in later life. Data also suggest that, together with the main surrogate markers of Nne (i.e. GA; BW; RV and CV), urinary CB activity may early indicate the risk of progression to renal disease in low birth weight neonates



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## 29. FERTILITY RATE AND SUBSEQUENT PREGNANCY OUTCOMES AFTER CONSERVATIVE SURGICAL TECHNIQUES IN POSTPARTUM HEMORRHAGE: 15 YEARS OF LITERATURE

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### INTRODUZIONE

Primary postpartum hemorrhage (PPH) is the most common major obstetric hemorrhage and cause of maternal mortality worldwide. The most significant risk factors include advanced maternal age, prolonged labour, pre-eclampsia, obesity, multiple pregnancies, birth weight >4,000 g, and previous PPH. When the bleeding is due to uterine atony, mechanical procedures and pharmacologic measures must be performed until the bleeding stops. If this procedure does not work intrauterine balloon tamponade is an appropriate first-line "surgical" intervention. If also this fails, the following conservative surgical interventions may be attempted: hemostatic multiple compressive or square suturing using procedures described by B-Lynch or Cho or other modified sutures; bilateral uterine artery ligation (BUAL) and stepwise uterine devascularization procedures; bilateral internal iliac artery ligation (BIIL); and angiographic selective embolization (ASE). Hysterectomy is the last measure to avoid maternal death. The aim of this review is to compare the effectiveness of conservative surgical techniques, separately or in combination, in regard to success rate (the ability to stop bleeding while preserving the uterus), fertility rate (subsequent pregnancies or the return of regular menstrual cycles), complication rate of the procedures, and outcome of subsequent pregnancies in terms of type of delivery and eventual delivery complications.

### MATERIALI E METODI

A systematic literature search was conducted in the electronic databases MEDLINE, EMBASE, ScienceDirect, and the Cochrane Library between March 1997, when B-Lynch and colleagues described his uterine compression suture for the first time, and March 2012.

All original descriptions, case reports, retrospective evaluations, and review articles of women who had been treated with uterine compression sutures, selective vessels embolization, and pelvic vessel ligation were analyzed. Key search terms included postpartum hemorrhage (PPH) in combination with uterine atony, placental abruption, placenta previa, previous PPH, elective/emergency cesarean section (CS), and retained placenta (accreta, increta, percreta); arresting the bleeding in combination with uterine vessel ligation, hypogastric ligation, uterine and pelvic vessel embolization, and uterine compression sutures; and failure rate and fertility rate in combination with postpartum hysterectomy, pregnancies after PPH, and pregnancy complications. A manual search of reference lists of included studies and review articles was also performed. Eligible articles included clear descriptions of PPH and its causes, details about the surgical procedures performed and a quantification of their failure rates, a quantification and accurate description of procedure complications, detailed descriptions of subsequent fertility rates (defined as the return of menses and/or subsequent pregnancies), and detailed data about subsequent pregnancy complications. We considered all conservative surgical hemostatic techniques used in PPH management.

Arterial ligation was analyzed by anatomic site and side: BUAL performed according to Waters and/or O'Leary's techniques, and BIIL performed according to Reich's technique. We also considered stepwise uterine devascularization procedures performed according to Tsurinikov's or AbdRabbo's technique. For compressive sutures, we considered B-Lynch's technique and its variations, such as Hayman's technique. We also considered Cho's and Pereira's techniques. Finally, pelvic vessel embolization was analyzed by anatomic site and side of ASE.

All techniques were compared in terms of success and complication rates in PPH management, fertility preservation rate, the subsequent pregnancy rate, and finally, the complication rate of subsequent pregnancies. Our search found more than 2,000 articles, but only 46 satisfied our selection criteria.

### RISULTATI

We found thirteen eligible articles regarding Pelvic Vessel Ligation. These techniques are the most commonly used in PPH due to uterine atony (33% of cases) in cases of placental disorders (placental accreta in 45% of cases and placenta previa in 9% of cases). The success rate ranges from 23% to 100%. In all the studies the surgeons performed a bilateral ligation. Eight of 13 study groups reported procedure complications: unintentional ureter ligation, injury to other pelvic vessels, and persistent bleeding followed by Sheehan's syndrome. The fertility rate ranges from 50% to 100%. At the next pregnancy, CS was performed in approximately 60% because there was a high incidence of intrauterine growth restriction (IUGR) and possible PPH recurrence.

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We found fourteen eligible articles described and compared different Uterine Compressive Sutures. These procedures are commonly used in cases of PPH due to uterine atony (80% of cases), followed by placental disorders, particularly placenta previa (12% of cases). The success rate ranges from 72% to 100%. Six of 14 study groups reported procedure complications: late PPH, infections, endometritis, and synechia. The fertility rate ranges from 10% to 100%, with lower performances for Hayman's and B-Lynch's modified procedures. Even if pregnancies after the procedure are mostly uneventful, the mode of delivery is often CS due not for an anatomic distortion of the uterus (dystocia), but chosen to ensure prompt management in the case of PPH recurrence.

Finally twenty-two articles described Angiographic Selective Embolization with a major preference for uterine vessels first and, when possible, unilaterally. Compared with the ligation procedure, embolization allows for a more selective approach, including the opportunity to identify the bleeding site before starting the procedure and monitoring the effectiveness after the procedure. The main indications was uterine atony after vaginal delivery (50% of cases). The success rate ranges from 75% to 100%. Ten of 22 studies reported procedure complications: accidental vessel puncture, extravasation of contrast medium, leg numbness, and perivascular hematoma. The fertility rate ranged from 12% to 100%, with a high rate of vaginal delivery in the subsequent pregnancies

## CONCLUSIONI

In conclusion, regarding the newer techniques described to stop bleeding after PPH, data on the efficacy and safety are mainly limited to small case series reported by the proponents themselves. In most studies, the short duration of follow-up represents the major limitation in obtaining adequate data about the subsequent return of menses, the pregnancy rate, and the outcomes of subsequent pregnancies. Frequently, preservation of fertility is evaluated indirectly by the uterine preservation rate without focusing on the return of menses or the rates and outcomes of subsequent pregnancies. Nevertheless, no randomized, controlled trials are available. On the basis of the data derived from the observational studies and case reports considered in our review of the current literature, we can conclude that compressive sutures and vessel embolization, when available, may be considered life-saving procedures by achieving the best hemostatic efficacy when pharmacologic uterotonic approaches fail. The few data on fertility preservation and return of menses showed that angiographic selective embolization and compressive sutures demonstrate a high effectiveness in preserving fertility, despite a large range of pregnancy rates in the different studies. Compressive sutures are associated with good pregnancy outcomes but an increasing rate of subsequent CS delivery. On the other hand, pelvic artery embolization is associated with subsequent placental disorders, leading to fetal growth restriction, preeclampsia, and placenta accrete and/or previa. Regardless of the technique used in the management of PPH, the risk of recurrent PPH is not negligible in subsequent pregnancies



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## 30. FETAL ABDOMINAL HYPERECHOGENICITIES: PRENATAL DIAGNOSIS AND CLINICAL SIGNIFICANCE

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### INTRODUZIONE

Echogenic bowel or liver defined as bowel or liver with a sonographic density equal to or greater than of surrounding bone. The differential diagnosis for this finding is broad and includes normal variant, primary gastrointestinal pathology, congenital viral infection, cystic fibrosis, aneuploidy and intra-amniotic bleeding. Hyperechoic liver lesions that often are identified as calcifications can be classified, according to their location, in three categories: peritoneal or surface, that can be a feature of meconium peritonitis with intestinal and peritoneal liver calcifications; parenchymal, that are a manifestation of intrauterine infection and primary or metastatic tumors; and vascular that include calcified portal or hepatic venous clots and foci of ischemic hepatic necrosis due to thromboembolism. The most important viral infection linkable with the onset of liver and bowel calcifications are: CMV infection, with increased bowel echogenicity, sometimes dilated bowel and liver calcifications; Herpes Simplex virus; parvovirus B19 virus with often associated meconium peritonitis and liver calcifications; embryopathy from VZV that including abdominal echogenic foci; Rubella virus; HIV, Toxoplasmosi infection; and finally minor infection as Adenovirus and Hepatitis A virus. The most common cause of Intra-abdominal fetal hyperechogenicity is peritoneal calcification resulting for small bowel obstruction, with perforation and subsequent sterile chemical meconium peritonitis. Causes of meconium peritonitis include ileal or jejunal atresia, volvulus and microcolon, also cystic fibrosis is associated with meconium peritonitis. Associated abnormalities are often detected in fetus with meconium peritonitis, particularly dilated bowel (27-29%). Hepatic echogenic lesions were reported in aneuploidy neonates with partial trisomy 14, trisomies 13,9,18,21 and monosomy X0

### MATERIALI E METODI

A pregnant 36-year-old thyroidectomized (for autoimmune thyroiditis) and parathyroidectomized woman with diabetes mellitus type I, celiac disease, referred to our Centre for Perinatal and Reproductive Medicine, in Perugia, to routine ultrasound scan in pregnancy. During morphological ultrasound (22 weeks), focal hyperechogenic lesions in the liver surface and heart wall were reported (Fig.1,2,3). Echogenic bowel or liver lesions were defined as bowel or liver with a sonographic density equal to or greater than of surrounding bone. The patient began closely monitoring with serial ultrasound examinations to check the evolution of the pathology or to evaluation others associated anomalies. The patient was investigated also for related infections, for cystic fibrosis and for karyotype

### RISULTATI

The focal hyperechogenic lesions in the liver surface and heart wall were confirmed during the following controls and dilatation of ileal bowel loops was demonstrated (Fig 4) with present peristalsis. Subsequent ultrasound scan showed diffuse hyperechogenicity involving liver, heart and, over late, in the whole abdomen, increased bowel dilatation was also reported. The patient was negative for toxoplasma, rubella, cytomegalovirus, herpes, HIV, Parvovirus B19, Varicella zoster virus (VZV), Rubella virus, Adenovirus and Hepatitis A virus investigation; she was negative for cystic fibrosis and she had normal karyotype investigated by amniocentesis. The induction of lung maturity was performed on 34 weeks for growing expansion of intestinal loops; after about ten days lung maturity was controlled by diagnostic amniocentesis for evaluation of the ratio L/S. Delivery, by caesarean section, occurred on 35 weeks and 6 days of gestation for increased dilatation of fetal bowel loops. At birth the infant showed a good adaptation to extrauterine life without the need for resuscitation (weight: 3,160 Kg, Apgar: 1° min 9, 5° min 10). In the first hours of life a progressive abdominal distension was shown with stagnant bile, so, after radiological study, the child was subjected to exploratory laparotomy on 11° day of life which confirmed a jejunal atresia type IV and double ileal atresia type I. Finally, the child also had a ABO incompatibility, patent foramen ovale (FOP) and alterations of glucose metabolism. The baby was discharged on 31° day of hospitalization, after surgical recanalization, with an appropriate follow-up program. At present the child is in good health

### CONCLUSIONI

Fetal abdominal echogenic lesions are relatively common ultrasound findings. In the absence of structural anomalies, chromosomal aberrations, viral infections and additional ultrasound findings are usually harmless and have a good prognosis. Investigation should include maternal and fetal serological tests for VZV, Parvovirus B19 TORCH, hepatitis, Rubella virus and Adenovirus; amniocentesis for fetal karyotyping, screening for cystic fibrosis and Doppler evaluation of the lesions. However even when seen as an isolated finding without apparently associated pathologies, serial follow-up ultrasound examinations are recommended. Indeed, the finding of hyperechoic lesions should never be undervalued, especially when related to other sonographic findings. In our case, in addition to hyperechoic lesions, important and progressive bowel expansion have been encountered, that despite the normal karyotype and negativity for screening of infection, indicated a major defect as the intestinal atresia. Early diagnosis or even a suspect allow, in this case, a better management of pregnancy and an prompt intervention on the newborn, with the possibility of the improving the outcome

## 31. FETAL GROWTH IN CYTOMEGALOVIRUS INFECTION: THE ROLE OF HYPERIMMUNOGLOBULIN THERAPY

### LISTA AUTORI

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### INTRODUZIONE

Primary cytomegalovirus (CMV) infection affects 0.3%–2.3% of pregnant patients with a different rate of vertical transmission in base of gestational age, and is the leading infectious cause of congenital neurological disabilities. Standard management of primary CMV infection is still controversial: pregnant women might be offered a limited range of medical therapies or the option to terminate pregnancy. Intravenous treatment with CMV hyperimmunoglobulin (HIG) could represent an important option, even if there are controversial results. Prenatal congenital infections caused by CMV is associated with, and account for, approximately 5 to 15% of intrauterine growth restriction. The aim of the study was to assess if intravenous hyperimmunoglobulin therapy could influence the intrauterine fetal growth

### MATERIALI E METODI

In 2014 we have enrolled consecutively all pregnant women with early and late primary maternal CMV infection. In early infection (Group 1), amniocentesis at 20 weeks was performed to assess the presence of the virus in the amniotic fluid. In case of positivity the patient was subjected to monthly ultrasound scans and fetal MRI (at the diagnosis and at 34 weeks of gestation). All women were offered treatment with HIG (200 UI per kilogram of maternal weight). In case of late infection (Group 2), were not performed amniocentesis and HIG therapy, but they were subjected to the same instrumental management of Group 1. Fetal biometry, fetal well-being and placental thickness were evaluated. In this study we considered the scans performed between 30-35 weeks. The neonatal infection was verified by urine analysis at birth

### RISULTATI

Of the 14 women with primary CMV infection, amniocentesis for CMV DNA detection was performed in 8 patients with early infection, and all amniotic fluid were positive. Six patients did not perform amniocentesis. HIG was administered only to all Group 1 patients. At the ultrasound scan performed at 30 weeks, head circumference ( $p$  0.01), abdominal circumference ( $p$  0.01) and estimated fetal weight were significantly lower in the Group 1 ( $p$  0.04). Only in the Group 1 there were 3 cases of intrauterine growth restriction and 1 case in Group 2. The placental thickness at 34 weeks was significantly lower in the Group 1 (39.5 mm versus 63.75 mm,  $p$  < 0.0001). Whether fetal MRI performed at the diagnosis of CMV seroconversion was negative in both groups, at 34 weeks it showed intracranial abnormalities, two in the Group 2 (alteration of the white matter, ventriculomegaly) and 1 in the Group 1 (intracranial cysts)

### CONCLUSIONI

In this study HIG treatment did not improved the fetal growth in presence of CMV infection but seems to influenced placental thickness. The presence of structural abnormalities were indicative of fetal CMV infection but, considering the number of patients, were less in HIG group

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## **32. FETAL HYDROTHORAX & CAPILLARY MALFORMATION: CASE REPORT**

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### **INTRODUZIONE**

Fetal pleural effusion (hydrothorax) is a rare condition that carries a high rate of perinatal morbidity and mortality, especially in the presence of hydrops fetalis and premature delivery. It can be primary (chylothorax by an abnormal circulation of chyle into the thoracic duct) or secondary (non-immune hydrops as fetal infections, chromosomal anomalies, cardio-thoracic malformations, etc.). Capillary malformation (CM) is defined as a pink to dark red macular stain first evident at or recently after birth; it can be isolated or associate to complex syndromes. We present a case report about fetal pleural effusion and capillary malformation

### **MATERIALI E METODI**

A 33 years old pregnant women was referred for a report of left pleural effusion on routine fetal ultrasonography. Obstetrical history was uneventful, Left hydrothorax was confirmed and followed up. Fetal anemia was ruled out by checking and demonstrating a normal peak systolic velocity of middle cerebral artery (MCA-PSV). Congenital heart defects, other structural anomalies and immunological profile were checked as well and no anomaly was found. According to international guidelines, due to mediastinal shift fetal, the pleural effusion was drained at 34 weeks of gestation under ultrasound guidance, in order to improve respiratory fetal-neonatal outcome

### **RISULTATI**

After 4 days, the hydrothorax formed again, improving and deteriorating day by day, so at 35+4/7 weeks of gestation a mediastinal shift was evident again, a second attempt of drainage was unsuccessful cause fetal movement and a Cesarean Section was performed. A male baby was delivered (3000 g weight, 90° C). On physical examination, there were erythematous-purplish stains, with a narrow network morphology and with a diffuse distribution involving the skin overlying the trunk, both anterior and posterior, the limbs, especially the right arm and the left leg spreading along the plantar surface. During the admission in NICU, the hydrothorax was always present and chylothorax was diagnosed. It didn't disappeared, nevertheless after shunting and specific milk regimen. Nowadays, the baby is fine (three month old), but with enlarged right limb and hallux and DCM

### **CONCLUSIONI**

We describe a rare association, fetal hydrothorax and DCM, with newborn wellbeing



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## **33. FETAL VENTRICULOMEGALY: COMPARISON BETWEEN ULTRASOUND EXAMINATION AND MAGNETIC RESONANCE IMAGING**

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### **INTRODUZIONE**

To evaluate the role of prenatal Magnetic Resonance Imaging (MRI) in fetal ventriculomegaly (VM) detected at ultrasound (US) for the pregnancy management and counseling

### **MATERIALI E METODI**

A retrospective study of all fetuses with a ultrasound diagnosis of VM in the years 2002–2014 was performed. Our analysis focused on cases that underwent MRI, as further diagnostic step. The population was divided into 2 groups: the first based on the presence or absence of other central nervous system (CNS) abnormalities (isolated/associated VM) and the second based on the ventricular width (severe VM  $\geq 15$  mm). Data on neonatal outcome were collected through a telephone interview. Fisher's exact test was used for statistical analysis with  $p < 0.05$  considered significant

### **RISULTATI**

37 fetuses with VM detected at US received also MRI. Mean gestational age (GA) at US was 26.4 weeks and mean GA at MRI was 29.1 weeks. MRI showed additional CNS findings not shown by ultrasound in 5/9 (55.56%) fetuses with isolated VM and in 21/28 (75%) fetuses with associated VM but there was no statistically significant relationship ( $p = .404$ ). MRI provided additional information in all severe VM ( $p = .018$ ). Postnatal outcome was normal in 12/30 (40%) infants. When the two prenatal methods agreed (24/30) all fetuses with isolated VM (4) had a good prognosis whereas associated VM was statistically (15/20, 75%,  $p = .012$ ) associated with abnormal postnatal neurodevelopmental especially if the ventricular atrial exceed 12 mm. Among 6/30 fetuses with not coincident diagnosis, a good prognosis was associated with an atrial size  $< 12$  mm, a symmetrical VM and a regression of the condition in uterus

### **CONCLUSIONI**

Our study confirms the usefulness of MRI in the diagnosis of fetal VM; ultrasound and MRI are complementary to define fetal VM and so for the pregnancy management and counseling. Serial ultrasounds appears to be important in order to better define the fetal prognosis

## **34. FIRST TRIMESTER COMBINED SCREENING FOR FETAL ANEUPLOIDIES: A TWO YEARS EVALUATION SINCE ITS INTRODUCTION AT SAN GERARDO HOSPITAL - MBBM FOUNDATION**

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### **INTRODUZIONE**

First trimester screening using a combination of maternal age, fetal nuchal translucency (NT) thickness, maternal free beta-human chorionic gonadotropin ( $\beta$ -hCG) and pregnancy-associated plasma protein-A (PAPP-A) at 11+0-13+6 weeks of gestation is now established as an effective screening program with a reported detection rate of approximately 90% for a 5% false-positive rate. The principal aim of the paper is to assess the performance of a combined first trimester screening for the most common trisomies in an unselected population referred to a specialized private centre for prenatal medicine. Secondly, we evaluate neonatal outcome and developed comorbidity in false positive tests and lastly we relate pregnancy's outcomes with a nuchal translucency above 95<sup>o</sup> percentile and a PAPP-A beyond 5<sup>o</sup> percentile

### **MATERIALI E METODI**

An observational retrospective study on an unselected Italian population of Obstetrics and Gynaecology Clinic at San Gerardo hospital in Monza, between October 2012 and October 2014. Measurements of nuchal translucency were performed on fetuses with a crown-rump length between 45-84 mm. The Fetal Medicine Foundation's software, Astraia 1.23.6, was used to calculate the risk of chromosomal abnormalities. The test result was considered positive if the risk was above 1:250 for trisomy 21 and 1:50 for trisomy 18 and 13. Not all the pregnancies underwent amniocentesis and CVS to establish the karyotype. For this reason after-born clinical evaluation integrates the karyotype evaluation to recognise affected newborns. A 95<sup>o</sup> and 5<sup>o</sup> percentile cut off were used to define the subpopulation with an increased NT and a reduced PAPP-A respectively

### **RISULTATI**

Among the 898 pregnancies included in the study, we had a complete follow up on 863. Ten fetuses with trisomy were detected; six trisomies of 21, two trisomies of 18 and two trisomies of 13. The detection rate in our centre was 100% for a 6.08% false positive rate. The subpopulation of false positives (54 fetuses, 6% of the total) were pregnancy with an increased association with fetal death, malformation and development of gestational hypertension. On the other hand, the group with a reduced level of PAPP-A among the unaffected fetuses (4.5% of the total) resulted to be associated with SGA newborns and late preterm infants (born between 34<sup>o</sup>-37<sup>o</sup> gestational week). The sub-population of the unaffected fetuses with an increased NT (2.5% of the total) had an augmented incidence of fetal death and malformations

### **CONCLUSIONI**

The detection rate of our test results higher than the established one, but with a higher false positive rate. We found an increased risk for adverse pregnancy outcome in gestation with positive test but normal karyotype. Finally, we could confirm that the detection of a low PAPP-A level and a high NT measurement was associated with a greater risk for pregnancy

## 35. GESTATIONAL WEIGHT GAIN AND FETAL GROWTH IN UNDERWEIGHT WOMEN

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### INTRODUZIONE

Despite the current epidemic of obesity, maternal underweight remains a common occurrence with potential adverse perinatal outcomes. We aimed to investigate the relationship between weight gain during pregnancy and fetal growth in underweight women

### MATERIALI E METODI

Maternal and neonatal data were prospectively collected on the maternity ward of Policlinico Abano Terme, Abano Terme (Italy), from January 2014 to June 2015. The hospital is located in an industrialized area supporting advanced educational levels, good socio-economic status, and low and late fertility. Women were categorized according to both pre-pregnancy body mass index (BMI), as underweight (BMI < 18.5 kg/m<sup>2</sup>), normal (BMI ≥ 18.5 and < 25 kg/m<sup>2</sup>), overweight (BMI ≥ 25 and < 30 kg/m<sup>2</sup>), and obese (BMI ≥ 30 kg/m<sup>2</sup>), and guidelines for 'optimal' gestational weight gain (GWG), according to the Institute of Medicine (IOM), 2009 classification. Neonatal birth weight, length, and head circumference were also collected

### RISULTATI

Among 792 consecutive women included in this analysis, 96 (12.1%) were categorized as underweight, 551 (69.5%) as normal weight, 127 (13.5%) as overweight, and 39 (4.9%) as obese, respectively. Underweight women were 33.0 ± 4.9 years old, 57.1% were nulliparae, most completed high school (51.1%) or graduated (20.7%), and 85.4% were employed. Their (Mean ± SD) BMI was 17.6 ± 0.7 and their GWG was within the range recommended by IOM guidelines (12.8 ± 3.9 kg). Pre-pregnancy BMI was by far the strongest predictor of the neonatal fetal growth. Offspring of underweight women were comparable in size at birth to neonates of normal weight women (birth weight 3,239.2 ± 423.5 kg vs. 3,264.0 ± 421.9 kg, length 49.5 ± 1.9 vs. 49.9 ± 1.9 cm, and head circumference 33.8 ± 1.3 vs. 34.1 ± 1.7 cm), but they resulted significantly lighter to offspring of both overweight [(birth weight 3,239.2 ± 423.5 vs. 3,422.7 ± 471.2 kg, p < 0.001, length (49.5 ± 1.9 vs. 50.0 ± 2.9 cm, p < 0.001, and head circumference 33.8 ± 1.3 vs. 34.5 ± 2.5 cm, p < 0.02) and obese women (birth weight 3,239.2 ± 423.5 vs. 3,458.6 ± 414.1 kg, p < 0.001, length (49.5 ± 1.9 vs. 50.8 ± 1.7 cm, p < 0.003, and head circumference 33.8 ± 1.3 vs. 34.5 ± 1.8 cm, p < 0.02). Conversely, GWG was higher when pre-pregnancy BMI was lower and within the range recommended by 2009 IOM guidelines (normal women 12.3 ± 6.7 kg, overweight women 11.0 ± 4.7 kg, and obese women 5.8 ± 6.1 kg). In addition, while LBW occurrence was unaffected, underweight women presented almost a 50% reduction in LGA (2.0 vs. 5.9%) as well as in operative delivery: caesarean section (7.2 vs. 14.3%) and vacuum extractor use (2.5 vs. 4.7%) in comparison to normal weight women while this reduction is more enhanced in the comparison to overweight and obese women

### CONCLUSIONI

Pre-pregnancy underweight does not impact on birth weight of term neonates in presence of normal GWG. It can be supposed that medical or personal efforts for reach 'optimal' GWG could be a leading choice for many women living in industrialized and in low-income countries

## 36. HEALTH FOR PROJECT: SURVEY ON FOOD CONSUMPTION AMONG PREGNANT IMMIGRANTS IN ITALY

### LISTA AUTORI

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### INTRODUZIONE

Several studies have shown that changes from traditional food habits and recipes toward Western dietary patterns generally occur in immigrants through the "Dietary Acculturation" process. This departure seems to affect diet quality and body composition in a manner detrimental to health. It is reasonable to expect some effects on pregnancy outcome, too, as nutrition during pregnancy might have long-lasting effects on the well-being of the mother and the fetus.

Despite immigrant populations are dramatically growing in Italy, there is a lack of evidence about their eating habits and health-related problems. Thus, in line with 2015-EXPO goals, the Italian Society of Perinatal Medicine, financially supported by "Bracco Foundation", has launched the HEALTH\_FOR (Habitual EAting Linked To Health in Foreigner Obstetric Research) Project aiming to investigate eating customs and lifestyle during pregnancy among immigrants from China and Arab Countries. To this purpose, a Food Frequency Questionnaire (FFQ) to assess food intake has been specifically developed to tailor each population

### MATERIALI E METODI

This on-going one-year project, starting in April this year, is a multi-centre study comprising the Hospital "L. Sacco", Milano, the Hospital "Careggi", Firenze, and the Hospital "Buccheri La Ferla-Fatebenefratelli", Palermo.

Population:

Healthy women from Arab Countries (Arab refers to a person who speaks Arabic and shares

the values and believes of Arabs culture) and China are invited to participate in the survey. The following inclusion criteria are considered:

- between the 20th week of gestation and 40 days after delivery
- born in their Country of origin but currently living in Italy
- aged  $\geq 18$  years
- normal singleton pregnancy
- not on special diets (e.g. celiac disease, vegan etc)
- given informed consent.

The study is conducted in accordance with the guidelines laid down in the Declaration of Helsinki.

Study Design:

Women are recruited during their regular visits at the public antenatal clinic. After informed consent, maternal basic information, routine clinical-obstetric data and anthropometric measurements are collected at the interview. Data on birth outcomes are also recorded at delivery.

Women are asked questions from a specifically developed three-sections questionnaire, regarding:

1. Socio-demographic information and proficiency of Italian language
2. Lifestyle
3. General eating behavior during pregnancy, including frequency of food consumption, eating patterns, food choices and preferences (along with influencing factors).

A Chinese mediator and an Arab cultural mediator support the investigator.

Food-section design:

Food section has been purposely designed to tailor pregnant immigrants from China and Arab Countries, respectively, by adapting existing questionnaires. In particular, a semi-quantitative FFQ validated on Italian adults has been modified by the means of questionnaires used to assess the "Dietary Acculturation" among the focused cultural groups in other Countries. To this aim, for each culturally-based FFQ the list of food items has been assembled in order to include traditional and ethnic foods by referring to scientific literature, books/articles on ethnic recipes and cuisine, comments from the cultural mediators. Respondents are asked to report how often (never; per day, week, and month), on average, they had consumed a standard portion of each food from the list during the last 3-months.

Analysis of data:

Mean  $\pm$  Standard Deviation were calculated

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## RISULTATI

Currently, 28 Arab immigrants and 49 Chinese immigrants have been interviewed.

Eating habits:

Results are reported in table 1.

Food consumption frequency during pregnancy among Chinese immigrants:

Due to the small size of the Arab sample, only results about critical foods from Chinese women are shown.

Participants ate:

2.9 ( $\pm$  1.6) servings/day of "Fruit";

1.6 ( $\pm$  0.7) servings/day of "Vegetables";

1.6 ( $\pm$  0.7) servings/day of "Rice and Rice-noodles" corresponding to 81% of the total consumption of "Pasta and Grains";

0.9 ( $\pm$  0.8) servings/day of "Cakes, Biscuits, Croissants, Breakfast Cereals"; 4.8 ( $\pm$  5.2) servings/week of "Sweet products and substitutes" (including ice-creams, jam, honey, desserts etc);

2.5 ( $\pm$  1.5) servings/week of "Fish" and 2.4 ( $\pm$  2.2) servings/week of "Seafood";

3.6 ( $\pm$  2.7) servings/week of "Legume" with "Soy and soy product" the most frequently consumed (54%)

## CONCLUSIONI

Even if preliminary, our results provide some information about eating behavior during pregnancy among immigrants living in Italy.

Eating habits:

Most women in both populations ate at least 1 snack daily in line with nutritional guidelines to pregnant women to have snacks between meals (possibly fruit, yogurt, bread).

Predominantly, both populations maintained the bond with their native foods and traditional diet. However, about 1/5 women in each group indicated to have most commonly adopted Italian foods. Moreover, about 1/5 women in each group reported to have never had shopping in culturally-based food shops to witness the overall availability of multi-cultural foods on Italian market.

Some differences between the two populations have been detected. Chinese women tended to prefer supermarkets with respect to Chinese shops whereas Arab women reported to buy foods equally from both supermarkets and Islam shops to suggest a religious beliefs' effect on food choices as also confirmed by our data. In fact, at statement "Avoid eating certain food and beverages because of religious beliefs" most of Arabs replied "Always" whereas all Chinese replied "Never".

Food consumption frequency during pregnancy among Chinese immigrants:

As expected, we found a high frequency of consumption of "Rice" (the main staple food in the traditional Chinese cuisine which is often eaten at breakfast, too), "Soy and Soy products", "Sea Foods" all typical Chinese food-items to indicate an on-going tie to native foods.

The frequency of consumption of key-foods was likely in line with nutritional recommendations and guidelines for pregnant women, to suggest adequate intakes of micronutrients, dietary fiber, antioxidants, unsaturated fatty acids crucial to prevent risks of pregnancy pathologies.

However, the frequency of consumption of sugar-containing products (i.e. Cakes, Pastries, Biscuits, Croissants, and other Sweet products and substitutes) surpassing the recommendations points out, along with the high frequency of "Rice" consumption, a high presence of high Glycemic Index foods in Chinese diet which may represent a risk factor for gestational-diabetes



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## **37. HEMATOLOGIC PROFILE AND DOPPLER ABNORMALITIES IN NEONATES WITH INTRAUTERINE GROWTH RESTRICTION**

### **LISTA AUTORI**

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### **INTRODUZIONE**

In fetuses with intrauterine growth restriction (IUGR), the severity of cardiovascular deterioration is related to increasing blood flow resistance in the umbilical arteries and villous vascular abnormalities, predisposing the fetuses to intra-placental platelet activation, microthrombosis and lower platelet counts at birth.

Aim: to analyze the relationship between hematologic parameters at birth, Doppler abnormalities and vascular markers of fetal endothelial dysfunction

### **MATERIALI E METODI**

This was a prospective study conducted between April 2013 and June 2015. One hundred singleton pregnancies were enrolled during the third trimester routine scan or for suspected growth retardation; 50 presented diagnosis of IUGR and 50 were controls. IUGR fetuses were divided in Group 1 (estimated fetal weight (EFW) below the 10th percentile with umbilical artery Doppler abnormalities, above 2 standard deviations) and Group 2 (EFW below the 3th percentile and normal fetal Doppler velocimetry for gestational age). Controls were those with an EFW between the 10th and the 90th percentile. All newborns were recovered in NICU for preterm delivery. For both groups, a complete blood count was performed at birth

### **RISULTATI**

There were no differences among the groups about maternal age, ethnicity, parity and gestational age at delivery. Birthweight was lower in IUGR Group 1 and 2 than controls. Whether leukocytes, neutrophil and platelet count were statistically decreased, hemoglobin, hematocrit, erythroblasts, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCV) and red cell distribution width (RDW) were increased than controls. The hematologic profile of IUGR Group 1 showed a lower count of leukocytes and platelets than IUGR Group 2, while hemoglobin, hematocrit and erythroblasts were increased. Finally, erythroblasts count presented a positive correlation with the pulsatility index of umbilical artery ( $p < 0.001$ ) and a negative correlation with platelet count ( $p < 0.02$ )

### **CONCLUSIONI**

Our results suggest a relationship between the severity of IUGR and hematologic abnormalities at birth. The hypoxic insult, that progressively affects the fetus with restrictions, might stimulate the erythropoiesis, reactivating the extramedullary hematopoiesis and inhibiting the maturation of white blood cells and megakaryocytes. The decrease blood platelet count could be explained by placental consumption or dysfunctional erythropoiesis and thrombopoiesis

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## 38. HIGH FREQUENCY OF PREVIOUS VIRAL INFECTIONS IN PREGNANT WOMEN WITH AUTOIMMUNE DISEASE

### LISTA AUTORI

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### INTRODUZIONE

Our aims were to assess the serological profile of different viruses in pregnant women with autoimmune disease (cases) and in healthy women (controls)

### MATERIALI E METODI

Data from 36 pregnancies in patients with autoimmune disease and 39 pregnancies in healthy women were collected. Each woman in both groups was screened for Epstein Barr Virus (anti-EBNA IgG, anti-VCA IgG and IgM) and Parvovirus B19 (anti-PV B19 IgG and IgM). Every effort was performed in order to identify primary infection or false positivity

### RISULTATI

As showed in figure 1, an higher rate of positive IgG for EBV and PV B19 was found in cases in comparison with controls. In particular, the difference was statistically significantly for positive anti-EBNA IgG, observed in pregnancies complicated by autoimmune disease

### CONCLUSIONI

The relationship between autoimmune disease and infections is an interesting and complex issue. Infections may be considered as a trigger factor of the beginning or exacerbation of autoimmune disease, inducing a non-specific activation of immune system. In predisposed subjects, antigenic similarity between infectious agents and host tissues might result, by a mechanism of molecular mimicry, in an immune response to shared determinants, resulting in disease. Moreover, viruses, integrating genetic material in the host cell, may induce a cellular activation and proliferation: our results, despite the small sample sizes, confirm the central role of viral infections in the mosaic of autoimmune disease



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## 39. IL CONTROLLO DEL DOLORE DURANTE IL TRAVAGLIO DI PARTO: UMANIZZAZIONE, MEDICALIZZAZIONE E IATROGENICITÀ

### LISTA AUTORI

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### INTRODUZIONE

Il dolore in travaglio è classificato nella parte superiore della scala del dolore, tra il dolore da cancro e il dolore da amputazione di un dito.

Nel 2002 l'ACOG ha affermato che "non ci sono altri casi nei quali viene considerato accettabile che un individuo debba sopportare un dolore severo, senza trattamento, quando è possibile invece intervenire in modo sicuro sotto controllo medico. In assenza di una controindicazione medica la richiesta della madre è di per sé una indicazione sufficiente per alleviare il dolore durante il travaglio".

Il Comitato di Bioetica il 30 marzo 2001 ha redatto un documento dal titolo "La terapia del dolore: orientamenti bioetici". Ivi afferma che "i processi culturali fra le donne sono orientati sia contro la medicalizzazione di un evento naturale come il parto, che ad evitare il dolore tramite i trattamenti analgesici; per quest'ultima categoria di donne, il dolore del parto è un grosso scoglio da superare, che limita notevolmente la partecipazione piacevole e serena all'evento; quindi ricorrere alla sedazione del dolore non si pone come alternativa al parto naturale, ma come mezzo per compiere una libera scelta e per realizzare con la sedazione del dolore un maggior grado di consapevolezza e di partecipazione all'evento".

Il dolore del travaglio ha due componenti: una sensoriale, relativa alla trasmissione dell'impulso nocicettivo, e una affettiva, che interpreta le sensazioni dolorose attraverso l'interazione di variabili emozionali, sociali, culturali e cognitive. L'analgesia epidurale interviene sulla componente sensoriale e rappresenta la modalità più efficace, flessibile e con minori effetti sulla madre e sul neonato rispetto ad altre procedure farmacologiche.

Ciononostante dati della letteratura relativi agli effetti della peridurale sulla maggiore durata del travaglio, sull'aumentato ricorso all'uso dell'ossitocina e incidenza di parti operativi pongono interrogativi sull'uso/abuso della peridurale in travaglio di parto

### MATERIALI E METODI

Abbiamo analizzato i parti verificatisi nell'UOC di Clinica Ostetrica e Ginecologia dell'AOU di Cagliari nel 2014. Nel nostro punto nascita la peridurale viene offerta gratuitamente a tutte le donne che ne facciano richiesta previa adesione a protocollo operativo dal 2008. Tale protocollo prevede la partecipazione ad un incontro esplicativo con le gestanti seguito da visita anestesiológica su ogni singola donna al fine di valutare per ogni singolo caso eventuali controindicazioni all'analgesia epidurale, compilare cartella anestesiológica dedicata e ottenere nel contempo il consenso informato alla procedura.

Il totale dei parti, la modalità del parto, il numero di parti in epidurale sono stati rilevati dall'analisi del registro della sala parto.

Per ottenere informazioni relative all'uso di ossitocina durante travagli in gravidanze a termine, ad esordio spontaneo, con ricorso o meno all'analgesia epidurale, abbiamo analizzato un campione di 212 partogrammi

### RISULTATI

Nel 2014 sono stati registrati 1613 parti nel nostro punto nascita, di cui 210 applicazioni di ventosa ostetrica e 578 tagli cesarei, con percentuali rispettivamente del 13% e del 35,8%.

Sono state eseguite 665 analgesie epidurali, pari al 41,2% sul totale dei parti e al 61% dei parti vaginali.

Dei 210 parti vaginali operativi, 180 (85%) si sono verificati in donne in analgesia epidurale, pari al 27% del totale dei travagli su cui è stata eseguita analgesia epidurale, più del doppio di quanto calcolato sul totale dei parti. È risultata molto bassa la quota di tagli cesarei rispetto al tasso di tagli cesarei sul totale dei parti, eseguiti su donne che in travaglio di parto hanno richiesto l'analgesia epidurale, 35/665 (5%). Nei travagli ad esordio spontaneo si è ricorso all'uso di ossitocina durante il travaglio nel 37% dei casi. Valutando solo i travagli ad esordio spontaneo in cui è stata richiesta l'analgesia epidurale l'uso di ossitocina è salito al 51% dei casi esaminati

### CONCLUSIONI

L'analgesia peridurale rappresenta una procedura sicura ed efficace per il controllo del dolore in travaglio di parto. La possibilità di poter usufruire di un servizio dedicato e gratuito rappresenta una grande opportunità per la donna, in particolare in situazioni in cui il dolore può essere difficilmente sopportabile quali l'induzione al travaglio, distocie dinamiche e meccaniche del travaglio, in caso di patologie materne in cui si ritenga opportuno ridurre i rischi da eccessiva produzione di catecolamine (ipertensione, cardiopatie, asma, malattie neurologiche) e/o quando il dolore sia considerato insopportabile dalla donna.



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I nostri risultati confermano le perplessità relative al rischio di medicalizzazione (parti operativi, uso dell'ossitocina) associato all'uso dell'analgesia peridurale sebbene introdotta ed eseguita nel massimo spirito di umanizzazione al fine di offrire alla donna un'esperienza positiva del parto.

Sebbene il dolore consti di una componente sensoriale e di una affettiva una prevalente attenzione alla componente sensoriale può comportare un'inadeguata formazione, attivazione e supporto da parte del personale sanitario alla componente affettiva della sofferenza in travaglio. Questa può essere aggravata di parto dal senso di ansia e paura per sé stesse e il nascituro, il timore della perdita di controllo, componenti emotive e sociali legate al partner, la famiglia, il lavoro.

Sempre maggiori perplessità emergono in relazione all'uso dell'ossitocina, a volte considerato incauto ed esagerato, per le conseguenze ostetriche immediate come ipercinesie, alterazioni cardiotocografiche e per le possibili implicazioni a breve e lungo termine sul processo del bonding e attachment legate all'inibizione della liberazione dell'ossitocina endogena e delle conseguenti azioni sul sistema nervoso centrale.

Pertanto valutare altre metodiche del contenimento del dolore che tengano maggiormente conto della componente emotiva del dolore può risultare efficace nel rivalutare il ruolo attivo dell'ostetrica durante il travaglio e nell'evitare che la medicalizzazione sfoci nella iatrogenicità



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## 40. IL PARTO PRETERMINE: PREVENZIONE E MANAGEMENT DELLE PROBLEMATICHE RESPIRATORIE NELL'AZIENDA OSPEDALIERA DI PERUGIA

### LISTA AUTORI

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### INTRODUZIONE

La nascita pretermine costituisce la principale causa di morte neonatale, sia nei Paesi in via di sviluppo che in quelli industrializzati. Dal punto di vista della Sanità Pubblica, pertanto, uno studio sulla gestione del neonato pretermine può contribuire in termini di miglioramento della qualità assistenziale: il presente lavoro illustra e analizza i risultati riguardo l'assistenza al pretermine nell'Azienda Ospedaliera di Perugia, focalizzando l'attenzione sulla prevenzione e il management delle problematiche respiratorie

### MATERIALI E METODI

La registrazione dei dati relativi ai nati di peso molto basso ( $\leq 1.500$  grammi) è attiva in Umbria su iniziativa della Sezione Sanità Pubblica dell'Università degli Studi di Perugia, con il supporto del Servizio mobilità sanitaria e gestione del sistema informativo sanitario e sociale della Regione Umbria.

Il formato del database è quello proposto dal Vermont Oxford Network (VON).

La registrazione dei dati avviene presso l'Unità di Terapia Intensiva Neonatale (UTIN) dell'Azienda Ospedaliera di Perugia

### RISULTATI

Nel 2014 sono stati assistiti 44 neonati di peso 501-1.500 grammi. Essi costituiscono lo 0,6% dei nati assistiti in Umbria; il tasso di nati-mortalità per questa classe di peso risulta pari all'8,1%.

La profilassi steroidea per la prevenzione della sindrome da distress respiratorio (RDS) è stata effettuata nell'81,1% dei casi, frequenza di poco inferiore al valore medio registrato nel VON (81,7%).

In particolare la profilassi steroidea è stata effettuata:

- nel 100% dei neonati di peso 501-750 grammi;
- nel 75% dei neonati di peso 1251-1500 grammi;
- nel 100% dei neonati con età gestazionale  $\leq 26$  settimane;
- nel 50% dei neonati di età gestazionale  $\leq 32$  settimane.

La frequenza di malattia polmonare cronica nei neonati di età gestazionale  $\leq 32$  settimane è pari al 24,1%.

Lo pneumotorace registra una frequenza pari al 2,7%, con differenze per classi di peso e per classi di età gestazionale:

- 7,7% nella classe 1.251-1.500 grammi;
- 100% nella classe 501-750 grammi;
- 50% nella classe 24-26 settimane;
- 0% nella classe  $\geq 30$  settimane.

Considerando la necessità di supporto alla funzione respiratoria, nell'Azienda Ospedaliera di Perugia si registra una maggiore frequenza di somministrazione di surfactante (73% versus 58,7% VON) e una minore frequenza di assistenza in nCPAP (48,3% versus 57,2% VON), che si contrappone ad un maggiore ricorso alla ventilazione meccanica assistita (62,2% versus 58,8% VON)

### CONCLUSIONI

Il presente studio mette a disposizione informazioni che potranno risultare preziose a tutti coloro che si occupano di assistenza al neonato pretermine. Il riferimento dell'Azienda Ospedaliera di Perugia con il Vermont Oxford Neonatal database (VON) garantisce un benchmarking costante e contribuisce in modo essenziale alla definizione delle priorità su cui intervenire, in particolare in materia di nascita pretermine e conseguenti problematiche respiratorie del neonato

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## 41. IMPATTO DELL'ETÀ MATERNA SUGLI ESITI OSTETRICI E NEONATALI NELLE GRAVIDANZE DA OVODONAZIONE

### LISTA AUTORI

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### INTRODUZIONE

Può l'età materna influenzare gli esiti ostetrici e neonatali delle gravidanze da ovodonazione (OD)?

Le gravidanze da ovodonazione mostrano un maggior tasso di complicanze rispetto alle gravidanze spontanee o derivate da altre tecniche di fecondazione in vitro. Ciò è vero in particolare per quanto riguarda l'incidenza dei disordini ipertensivi. È difficile condurre studi a riguardo in quanto l'età materna nelle gravidanze da OD (avanzata età riproduttiva o menopausa) non è paragonabile a quella delle donne dei gruppi di controllo.

Obiettivo del nostro studio è stato pertanto, per la prima volta, valutare gli esiti ostetrici e neonatali di gravidanze da OD che fossero paragonabili per età materna al gruppo di controllo

### MATERIALI E METODI

Studio retrospettivo sugli outcomes ostetrici e neonatali di due gruppi di donne, distinte per fasce di età (104 donne con età < 44 aa vs 102 donne con età > 44 aa; età minima 29 aa, massima 55 aa), con gravidanze singole o gemellari, seguite presso l'Ospedale Sant'Anna (Città della Scienza e della Salute, Torino), tra il 2008 e il 2013. Per ogni donna sono stati raccolti dati relativi ad anamnesi, BMI, decorso della gravidanza, esiti del parto sia materni che neonatali

### RISULTATI

I gruppi analizzati sono paragonabili per età, BMI pregravidico e prevalenza di ipertensione cronica.

Non è stata rilevata nessuna differenza nell'incidenza di pre-eclampsia (PE), ipertensione indotta dalla gravidanza (PIH), diabete gestazionale (GDM) e taglio cesareo (TC) nei diversi sottogruppi analizzati. Nelle gravidanze gemellari, è stata riportata una maggiore incidenza di parto pretermine, di feti SGA (small for gestational age) e di feti con basso peso alla nascita, se paragonate alle gravidanze singole

### CONCLUSIONI

Sulla base dei nostri dati, nelle gravidanze da ovodonazione, l'età della ricevente sembrerebbe svolgere un ruolo marginale nell'aumento dei rischi ostetrici e neonatali, almeno per quanto riguarda le fasce di età da noi prese in considerazione. La gemellarità sembrerebbe invece essere il maggiore fattore di rischio e pertanto è tale condizione a richiedere una adeguata e più intensiva gestione clinica



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## 42. INCREASED INFLAMMATION AND ANTIOXIDANT LEVELS IN SALIVA OF OBESE PREGNANT WOMEN

### LISTA AUTORI

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### INTRODUZIONE

Obesity is associated with inflammation and higher gestational risks. Periodontal diseases (PD), i.e. gingivitis and periodontitis also represent a distant source of low-grade systemic inflammation. We previously reported increased PD in obese (OB) vs normal weight (NW) pregnant women. Few studies investigated biomarkers in saliva (S) of pregnant women. The aims of our work were to analyze C-reactive protein (CRP) concentrations and total antioxidant capacity (TAC) in S of OB vs NW pregnant women and their association with plasma CRP and with P

### MATERIALI E METODI

53 singleton pregnancies (13 NW, BMI 18-24.9; 40 OB, BMI  $\geq 30$ ) were studied at 3rd trimester. Periodontal status was assessed by oral clinical examination. Periodontitis (P) was defined as the presence of at least 4 teeth with pockets  $\geq 4$  mm. Gingivitis (G) was defined as the presence of soft and/or calcified bacterial plaque and/or gingival bleeding in 4 or more teeth.

Unstimulated samples of S were collected and processed for the analysis of CRP (ELISA) and TAC (AntiOxidant Assay). CRP levels were also measured in plasma samples (ELISA)

### RISULTATI

S-CRP levels were significantly related with maternal BMI ( $p=0.04$ ;  $R=0.42$ ). S-TAC was significantly higher in OB vs NW ( $p=0.01$ ) and significantly related with S-CRP ( $p=0.00$ ;  $R=0.70$ ). CRP levels in plasma were significantly increased in OB vs NW ( $p=0.00$ ), correlating with both S-CRP ( $p=0.00$ ;  $R=0.85$ ) and S-TAC ( $p=0.01$ ;  $R=0.52$ ).

90% OB and 38% NW had PD (P and/or G). PD in healthy-NW did not increase CRP and/or TAC, while in OB the presence of PD was associated with increased plasma CRP ( $p=0.017$ ) and with a non significant increase in S-CRP/TAC vs healthy NW

### CONCLUSIONI

In our population, higher maternal plasma CRP levels confirm that obesity is associated with systemic inflammation. Moreover, salivary CRP levels, potentially reflecting local inflammation, were significantly associated with maternal BMI.

Both salivary and plasma CRP correlated with S-TAC, which was significantly increased in OB. This might suggest the induction of a compensatory antioxidant response detectable in S of OB. Periodontal disease was more frequent in OB vs NW and this might represent a further local stimulus to inflammation and to an antioxidant response.

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## **43. INTERPRETATION OF FETAL HEART RATE DURING LABOR: COMPARISON OF ABDOMINAL FETAL ELECTROCARDIOGRAPHY AND DOPPLER CARDIOTOCOGRAPHY**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Doppler cardiotocography (CTG) still remains the main way to assess fetal heart rate (FHR) and wellbeing during labor, thanks to its non-invasivity. Among its limits, intra- and inter-observers variability is still consistent even after attempts to improve it through the spread of standardized systems of CTG trace classification and through the invention of softwares for computerized CTG trace analysis. Besides this, it is well known that cardiotocography is often affected by poor quality of recording, mainly signal loss and maternal - fetal ambiguity, leading to difficulties in its interpretation. Monica AN24 is a recent non-invasive electronic fetal monitoring technique which is able to monitor both FHR by abdominal fetal ECG (abfECG) and uterine activity by electrosterography (EHG).

The aim of the study was to assess whether inter-observer variability may be influenced by the type of FHR recording technique

### **MATERIALI E METODI**

Twenty-eight pregnant women at term undergoing fetal monitoring during labor using both Doppler CTG and AN24 for more than 30 minutes were included in the study. 92 tracks lasting 30 minutes obtained by CTG and AN24 were independently evaluated by four obstetrics consultants, blinded to patient identity, mode of delivery and neonatal outcomes. Operators were defined junior, with experience < 5 years, and senior, with experience > 5 years, and classified FHR tracings according to ACOG criteria. We assessed intra- and inter-observer variability by calculating the percentage of agreement for both monitoring techniques

### **RISULTATI**

Overall percentage of agreement was higher using AN24 than using Doppler CTG (47.8% vs. 39.1%). Agreement between juniors was higher than between senior for both methods (CTG: 69,6% vs. 65,2%; AN24: 76,1% vs. 69,6%). Percentage of FHR traces classified in ACOG 1 category was higher with AN24 (48.4% vs. 40.8%), whilst the percentage of ACOG 2, 3 and unclassified was lower (ACOG 2: 46,2% vs. 48,9%; ACOG 3: 4,9% vs. 6,5%; NC: 0,5% vs. 3,8%). Intra-observer variability between the two methods was on average 64.1%

### **CONCLUSIONI**

Our study suggest that abdominal fetal ECG is associated to a trend of lower inter-observer variability. Moreover, recordings obtained with this method seem to be more reassuring, probably thanks to a better quality of signal

## **44. KIDNEY TRANSPLANTATION AND PREGNANCY: JUST ANOTHER FORM OF CHRONIC KIDNEY DISEASE? OUTCOMES OF PREGNANCIES AFTER KIDNEY TRANSPLANTATION AND IN NON TRANSPLANTED CKD AS COMPARED WITH LOW-RISK PREGNANCIES: PATHOPHYSIOLOGIC AND DIAGNOSTIC CLUES**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Although fertility is at least partly restored in kidney transplantation (KT), the reasons why materno-foetal outcomes are still inferior to those of the overall population are partially known. No study was aimed at comparing pregnancy after KT with a chronic kidney disease (CKD) population with a comparable degree of renal function impairment; such an analysis may offer some pathophysiologic insights and suggestions for counselling.

Aim of this study was to analyse the outcomes of pregnancy after KT in a nationwide Italian cohort, compared with a large population of non-transplanted CKD patients and with low-risk control pregnancies

### **MATERIALI E METODI**

Sources of data: KT: Database of the Italian study group of kidney in pregnancy, with a national coverage of about 80% of pregnancies in KT in Italy (2000-2013: 121 live-born singletons, with baseline and delivery data). CKD patients were observed in the two Italian Centers with the largest recruitment (610 live-born singletons in 2000-2014). Low-risk controls were gathered in the same Centers in the same period (1418 live-born singletons).

The following outcomes were considered: preterm delivery (<37 gestational weeks); early preterm delivery (<34 weeks); small for gestational age (SGA); doubling of serum creatinine or shift of CKD stage; death; malformations. Data were analysed according to kidney disease, renal function (staging according to CKD-EPI), hypertension, maternal age, KT versus CKD

### **RISULTATI**

Materno-foetal outcomes are less favourable in KT and CKD as compared with the low-risk population, for SGA, preterm, and early preterm delivery. CKD-stage and hypertension are important determinants of results. No significant difference is found in materno-foetal outcomes between CKD stage 2-5 and KT patients with comparable kidney function. KT patients with normal kidney function are at higher risk for adverse pregnancy related outcomes compared with CKD stage 1 patients; however, the differences disappear when KT are compared with CKD patients affected by "potentially progressive" kidney diseases (glomerulonephritis or systemic diseases)

### **CONCLUSIONI**

The materno-foetal outcomes in patients with KT are comparable with those of non-transplanted CKD patients with similar levels of kidney function impairment or with "potentially progressive" kidney disease

## **45. LIMITED IMPACT OF A NEONATAL REANIMATION COURSE IN CLINICAL PRACTICE IN A LOW RESOURCE SETTING: THE MIDWIVES' PERSPECTIVE**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Under 5 year mortality is highly influenced by neonatal mortality (44%). About a quarter of neonatal mortality is related to events during the delivery. Training the personnel involved in neonatal resuscitation (NR) is crucial during this phase. Previous studies have shown that a course on NR had limited impact on clinical practice. The reasons of such a failure are unknown.

Objectives: understanding the opinion of the personnel involved in the resuscitation of the newborn in the delivery room on the causes of failure of a NR course in a low-resources setting

### **MATERIALI E METODI**

A questionnaire administered to 13 midwives six months after a NR course performed in the Beira's Central Hospital. Mozambique. The questionnaire was made up of two parts: a first part with a self-assessment of the midwives on the level of their theoretical and practical knowledge. We then showed the midwives a videotape demonstrating the low impact of the NR course and their low performances in NR. The second part of the questionnaire was administered after the video, asking to identify the problems related to the failure to apply the theoretical knowledge in clinical practice. Each question had a score from 0 (= bad) to 5 (= excellent)

### **RISULTATI**

All the midwives filled the questionnaires. Seventy-seven percent of the participants evaluated their own preparation on NR as good-excellent; the majority of them considered their performance on NR as well performed (54% with manikins and 85% with newborns). The three major causes accountable for the lack of application of the theoretical knowledge in clinical practice were: lack of qualified personnel (85%), newborn's fate independent from the resuscitative intervention (77%), discrepancy between the knowledge acquired at the course from the ones learned at nurse school (62%)

### **CONCLUSIONI**

Our study shows that, although the rate of application in the clinical practice of the theoretical knowledge acquired is low, the self-esteem of the midwives on their core competencies is high. The lack of application of the knowledges acquired during the theoretical course in the clinical practice can be attributed to the lack of qualified personnel with whom cooperate, fatalism and difficulty in accepting training proposal other than the normal ones. Improving the knowledge of these aspects could improve the application of theoretical knowledge in clinical practice in a low-resource country

## **46. MATERNAL PERICONCEPTIONAL DIETARY PATTERNS AND FIRST TRIMESTER EMBRYONIC GROWTH: THE ROTTERDAM PERICONCEPTIONAL COHORT (PREDICT STUDY)**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Maternal nutrition, the main determinant of fetal nutrition, is known to influence pregnancy outcomes, as well as future life of the offspring. Despite great attention given to the association between maternal nutrition and pregnancy outcomes, data are scarce about the influence of maternal diet on first trimester embryonic growth, assumed to be homogeneous and independent by environmental factors until few years ago.

Our aim is to investigate the association between maternal periconceptional dietary patterns and first trimester embryonic growth trajectories

### **MATERIALI E METODI**

In a prospective periconceptional cohort study, 135 women with singleton ongoing spontaneous pregnancies, known last menstrual period, regular cycle and corresponding crown-rump length (CRL) underwent weekly transvaginal three-dimensional ultrasound (3D-US) scans from 6+0 up to 12+6 weeks of gestation. Embryonic CRL and volume (EV) were determined using virtual reality (V-Scope software program, BARCO I-Space). At enrollment, dietary intakes were collected via food frequency questionnaires (FFQ) and a principal component analysis (PCA) was performed to identify maternal dietary patterns. Associations between maternal dietary patterns and CRL and EV trajectories were assessed using linear mixed models adjusted for potential confounders (parity, alcohol use, smoking habit, folic acid use, maternal age, BMI and comorbidity, fetal gender)

### **RISULTATI**

We performed a median of five 3D-US scans per patient. 619 out of 748 datasets were of sufficient quality to perform CRL measurements (82.8%) and 559 to perform EV measurements (74.7%). A 'fish-related dietary pattern', comprising a high intake of fish, olive oil and vegetables, and low intake of meat was identified. The adherence to this pattern was related to increased CRL (+14.6% at 7 weeks, +6.9% at 11 weeks; figure 1) and EV (+20.4% at 7 weeks, +14.4% at 11 weeks) measurements in the fully adjusted model

### **CONCLUSIONI**

This study suggests that maternal periconceptional adherence to a fish-related dietary pattern is positively associated with embryonic growth trajectories, depicted by longitudinal CRL and EV measurements, in spontaneously conceived pregnancies.

Our data confirm that periconceptional factors are able to modulate fetal growth already in early stages. Moreover, since previous research showed an association between first trimester CRL and pregnancy outcomes (birth weight, preterm birth and small for gestational age babies), first trimester care represents a challenge in order to prevent subsequent adverse pregnancy outcomes

## 47. **MAY UNDERDIAGNOSED NUTRITION IMBALANCES BE RESPONSIBLE FOR A PORTION OF SO CALLED UNEXPLAINED INFERTILITY? FROM DIAGNOSIS TO POTENTIAL TREATMENT OPTIONS**

### LISTA AUTORI

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### INTRODUZIONE

In the majority of developed Countries the percentage of couples suffering from infertility which turn to assisted reproduction techniques (ARTs) is drastically increased in the last decade. When stratified according to pathogenesis, the absence of a definable cause (unexplained/idiopathic infertility) is observed in 15-30% of infertile couples. Since the inability to define the reasons does not mean that there is no cause for the disorder, extensive research should be conducted on other possible causes of failed conception rather than immediately recommending ART. Though it is universally accepted that nutrition and lifestyle factors (diet, exercise, obesity) may affect reproductive performance, preconception nutritional care is often inadequate. Nonetheless, during ART there are few structured clinical initiatives aimed at offering couples preconceptional counselling. Investigation into a potential association between diet and unexplained infertility represents a great challenge in clinical practice. The evaluation of dietary status in patients with "apparent" idiopathic infertility may potentially solve the diagnostic dilemma and restore spontaneous fertility or at least improve success rate of ART. We conducted this study with the aim of investigating whether asymptomatic dietary imbalances negatively affecting fertility may be present in women belonging to this cohort. Secondly we investigated whether different degrees of abnormalities in macro- and micronutrient intake may benefit from different periconceptional non pharmacological dietary supplementations, evaluating the most effective protocol in improving pregnancy rate after IVF

### MATERIALI E METODI

We conducted an epidemiological survey followed by a prospective semi-randomized interventional study on Italian women affected by unexplained infertility and scheduled for fresh non-donor IVF treatment at the Assisted Reproduction Unit of Padua University (January 2012-October 2014). The first step of the study was to conduct an epidemiological survey on separate cohorts of patients (Group-A and Group-B) in order to investigate their dietary status. We distinguished women without dietary abnormalities (cohort\_1) as opposed to those with abnormalities exclusively in micronutrient intake (cohort\_2) or combined abnormalities in both micro- and macronutrient intake associated with obesity (cohort\_3). In detail, Group-A (case group) was composed of healthy Italian women aged between 18 and 40 years affected by unexplained infertility while Group-B (control group) was comprised of healthy nulliparous women in the first trimester of singleton pregnancy (spontaneously onset). Cases and controls were matched for age. Women admitted to the control group were recruited from the Obstetrics Clinic of University of Padua. In the second step of the study, regardless of the outcome of the dietary investigation, to all women included in Group-A was offered the opportunity to receive a prescription for one of the following schemes comprised of a three-month daily dietary supplementation before IVF treatment: i) Supplementation with iron (7 mg) and folic acid (400 µg) (SubGroup-A1); ii) Supplementation with iron (30 mg), folic acid (400 µg), lactoferrin (75 mg), fluorine (1 mg), docosahexaenoic acid (150 mg), Zinc (7.5 mg), Copper (1.2 mg), calcium (400 mg), magnesium (100 mg), manganese (2.5 mg), iodine (150 µg), vitamin D3 (10 µg), vitamin B6 (1.4 mg), vitamin B12 (2.5 µg) and vitamin C (60 mg) (SubGroup-A2); iii) Supplementation similar to the SubGroup-A2 plus inositol (Myo-Inositol 550 mg, D-chiro-Inositol 13.8 mg) (SubGroup-A3). At recruitment, patients of both groups underwent dietary evaluation using Recall 24-hour questionnaire. Simultaneously all patients received ad-hoc "one week dietary diary" to be completed in the following week and underwent body weight and height measurements. Waist circumference was measured at the midpoint between the lowest rib and the iliac crest during minimal respiration. Abnormalities in macronutrient and/or micronutrient intake were evaluated by validated electronic software (METADIETA®) for diet evaluation in comparison with standard values reported as normal for the Italian population -LARN- (standard measure discriminating for sex, age, weight, physical activities, and physiological status such as pregnancy, breastfeeding, menopause). Patients in Group-A participating in the second phase of the study, following one of the above mentioned 3-month dietary supplementation schemes, were scheduled for IVF treatments by standard long agonist protocol. All oocytes were fertilized by FIVET/ICSI technique depending on semen parameters. Double-embryo transfer was performed 3 days later in all patients (after morphological assessment). All patients received high dose progesterone supplementation. Clinical pregnancy (CP) was confirmed by positive serum  $\beta$ -hCG test 2 weeks after embryo-transfer and ongoing pregnancy (OP) was defined as an uncomplicated pregnancy over 12 gestational weeks. For all patients we collected data regarding general features (age, height, weight, BMI, waist circumference, daily physical activity, occupational status). To overcome potential differences between Group\_A and Group\_B, which may emerge by the entry of general features in the software (according to the suggestion of LARN 2012) we

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calculated the recommended average daily energy intake (estimated as kcal) for each individual woman according to basal metabolism and physical activities. For each patient, in both Group\_A and Group\_B, we calculated the daily energy intake comparing them with the estimated 50th, 25th and 75th centiles of the recommended energy intake charts. Furthermore, we calculated T variation of calories truly introduced compared with what is estimated as adequate considering as minor dietary alterations calorie intake within the 25th and the 75th centiles and as major those over or under this range. For all patients we evaluated the number of meals and snacks per day and relative percentage of calorie distribution as well as the percentage of calories produced by each class of macronutrients (carbohydrates considering the percentage of simple sugars, lipids considering the percentage of n-6 and n-3 polyunsaturated fatty acids, and proteins). Regarding micronutrients, we estimated the daily intake and compared this value to the suggested standard for the population. Primary endpoint of the study was to compare Group-A versus Group-B in terms of nutritional status. Secondary endpoint was to evaluate the outcome of IVF in the different subGroups of dietary supplementation schemes stratifying data according to initial dietary abnormalities

## RISULTATI

198 women were assigned to Group-A and 59 to Group-B. The average value of daily calories was significantly different between groups ( $p < 0.001$ ). They showed significant differences in terms of T variation of calories compared to recommended values ( $p < 0.001$ ). Comparing groups we found that 43% (Group-A) vs 25.4% (Group-B) had minor dietary alterations ( $p < 0.05$ ) while 30.8% vs 3.4% had severe alterations ( $p < 0.001$ ). Interestingly the daily distribution of calories resulted significantly different ( $p < 0.05$ ). Regarding macronutrients intake, Group-A showed a significantly lower intake of carbohydrates ( $p < 0.001$ ) and a significantly higher lipid intake ( $p < 0.001$ ). Regarding vitamin intake, differences between the two groups were found concerning vitamin C, B1, B2, B3, B12, A, D, folic acid ( $p < 0.05$ ), while no differences were found in terms of vitamin B6. We found that Group-A was under the recommended daily dose for all the considered vitamins with the exception of B6. Regarding trace minerals, Group-A showed a significantly lower intake of calcium, iron, magnesium and zinc ( $p < 0.01$ ) and a significantly higher intake of copper and selenium ( $p < 0.001$ ). Only 122 patients of Group\_A were eligible for second phase of the study (41, subgroup\_A1; 43, subgroup\_A2; 38, subgroup\_A3). We found that more than 40% of patients were affected by micronutrient abnormalities (cohort\_2), followed by severe dietary imbalances (cohort\_3). Only the 25% of women were free of dietary abnormalities (cohort\_1). We found within all subgroups a significant association between years of infertility and severity of dietary abnormalities ( $p < 0.001$ ). Regarding CP, statistical differences were found between subgroups (19.5% vs 25.5% vs 13.1%) ( $p < 0.05$ ). When patients were stratified according to dietary cohort, we found that the best outcomes was obtained in patients without dietary abnormalities only in subgroup\_A1 and subgroup\_A2 ( $p < 0.01$ ). Regarding patients with abnormalities in micronutrient, we found a good outcome in subgroup\_A2, an intermediate outcome in subgroup\_A1 and a poor outcome in subgroup\_A3 ( $p < 0.05$ ). Regarding the cohort with severe dietary abnormalities, the outcome was poor in all subgroups despite a significant trend was observed: 0% in subgroup\_A1 vs 7.1% in subgroup\_A2 vs 15.3% in subgroup\_A3 ( $p < 0.05$ ).

## CONCLUSIONI

In conclusion, our results allowed us to postulate that, when compared with fertile women, patients suffering from unexplained infertility showed significant abnormalities in dietary habits. These differences ranged from minimal micronutrient imbalances (potentially avoidable with dietary supplementation) till severe combined macro- and micronutrient imbalances frequently associated with obesity (partially amendable by inositol supplementation and frequently requiring long term dietary education before establishment of fertility). Despite the above mentioned limitations and difficulties encountered in introducing nutritional screening and counselling into infertility care, it could not be excluded that nutritional investigation and treatment may explain and solve a percentage of cases of infertility currently included in the category of infertility "without apparently cause" and frequently subjected to empiric "over or under ineffective treatments"



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## **48. NEONATAL HYPOGLYCEMIA CONTINUOUS GLUCOSE MONITORING: A RANDOMIZED CONTROLLED TRIAL IN PRETERM INFANTS**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Background. Neonatal hypoglycemia is associated with brain injury and impaired neurodevelopmental outcomes in very low birth weight infants (VLBWI). Glycemic monitoring is usually performed by capillary or central line sampling but does not identify up to 81% of hypoglycemic episodes in preterm newborns. We aim to assess if a continuous glucose monitor (CGM) can be used without undo pain to increase time-in-range for glycemia (77-144mg/dl according to the suggested range of NIRTURE consort), reducing hypoglycemia

### **MATERIALI E METODI**

Newborns  $\leq 32$  weeks gestational age and/or of birthweight  $\leq 1500$  g were randomized to receive glucose control (target glucose 72-144 mg/dl) during the first 7 days of life using a Dexcom-G4-Platinum-CGM vs standard care practice. CGM-monitored patients had glucose infusion rates (GIR) adjusted every 3 hours using a glucose-control algorithm that incorporated CGM values, as well as CGM hypoglycemic alarms. Patients receiving standard care wore blinded CGMS without alarms, and GIR was modified according to 2-3 daily capillary glucose levels. Pain at insertion was evaluated with the validated Premature Infant Pain Profile (PIPP) scale

### **RISULTATI**

We report preliminary results on 15 patients. Mean $\pm$ SD gestational age was  $28\pm 1$  wks and birthweight was  $1140\pm 144$ g. Mean Absolute Relative Difference CGM v. HeelPrick was 16.9%. Sensor insertion was not more painful than HeelPrick (PIPP median (range), 4 (3-15) v. 6 (3-18) respectively). No complications were observed  
Time in range of the open group was (mean (SD)) 86%(5) vs 74%(19) of the blinded group. Such data will have to be evaluated at the term of the enrollment (50 patients)

### **CONCLUSIONI**

CGM can be efficacious and safe in NICU for improving glycemic control and avoid hypoglycemia in VLBWI

## **49. OBESITY AND PREGNANCY COMPLICATIONS: THE EMERGING PROBLEM OF GROWTH RESTRICTION APPLYING GARDOSI CUSTOMIZED GROWTH CURVES**

### **LISTA AUTORI**

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### **INTRODUZIONE**

As known from the literature, obesity in pregnancy is associated with a higher incidence of obstetric complications. The most likely complications are fetal macrosomia, metabolic dysfunctions, hypertensive disorders and complications in labour. Because the epidemic of obesity is growing all over the world, we wanted to analyze this phenomenon in our population of pregnant women

### **MATERIALI E METODI**

We performed a retrospective study over the past four years (January 2010 – June 2014) on 14,629 women who delivered in our hospital. Of these, 678 were found with a prepregnancy body mass index (BMI) > 30 Kg/m<sup>2</sup>, of which 621 were singleton pregnancies and constituted the study group. The obstetric outcomes of the patients in the study group were compared to those of a sample of normal prepregnancy BMI, singleton, pregnant women (1310 patients)

### **RISULTATI**

The obese pregnant women represented 4.6% of our population. By analyzing the distribution of complications, we confirmed a higher incidence of gestational diabetes (25.3% vs 9.7%;  $p < 0.001$ ), hypertensive disorders (11.0% vs 1.6%;  $p > 0.001$ ), macrosomia (9.2% vs 5.6%;  $p = 0.004$ ), preterm delivery (11.1% vs 5.5%  $p < 0.001$ ) and cesarean section (45.2% vs 27.9%;  $p < 0.001$ ).

Applying the Gardosi customized curves to evaluate the growth of the neonates, we unexpectedly found a higher incidence of small for gestational age (SGA) newborns below the 10th (22.1% vs 14.4%;  $p < 0.001$ ) and the 5th percentile (13.8% vs 7.7%;  $p < 0.001$ ) in the study group with respect to the control group, that was not previously highlighted using standard population curves

### **CONCLUSIONI**

An increasing body of literature has recently focused on placental damage associated with obesity in pregnancy. Even though this could, in part, explain fetal growth restriction (FGR), evidence in literature on the correlation between placental damage in obese patients and FGR is lacking.

It is possible that FGR is not recognized in other studies because Gardosi customized curves for the evaluation of fetal growth do not apply, but we assume that the best evaluation of optimal fetal growth of obese pregnant women should be that which takes into account the genetic contribution that is transmitted from the mother to the fetus

## 50. OBESITY, DIABETES AND MACROSOMIA

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### INTRODUZIONE

During pregnancy, many women gain excessive weight and gestational weight gain (GWG) is related to adverse maternal and neonatal outcomes. Obesity has increased dramatically in the development countries over the last several decades. The obesity affects the pregnant population, with 40% of women qualifying as either overweight or obese, and 28% of pregnant women qualifying as obese. Obesity is defined as having a body mass index (BMI) of 30.0 kg/m<sup>2</sup> or greater, whereas overweight is defined as having a BMI of 25.0 to 29.9 kg/m<sup>2</sup>. Obese women with low gestational weight gain have a decreased risk for preeclampsia, cesarean section, and large for gestational age (LGA) infants. There are few studies of the relationship between early gestational weight gain and gestational diabetes mellitus (GDM) and gestational weight gain prior to glycemic screening and maternal hyperglycemia. Gestational diabetes mellitus (GDM) is a common complication of pregnancy. The prevalence of GDM has been reported to be as high as 16.1 %, and this rate is increasing worldwide. A higher body mass index (BMI) before or in the first trimester of pregnancy and excessive gestational weight gain (GWG) during early and mid-pregnancy are both considered prominent early markers of GDM. In women with both high pre-pregnancy BMI and excessive GWG, the risk of GDM increases by 2.2–5.9 fold.

The aim of the study was to evaluate in patients with gestational diabetes the relationship between maternal weight, treatment for glycemic control and pregnancy outcomes, including macrosomia (fetal birth weight  $\geq$  4000 g)

### MATERIALI E METODI

From January 2013 to December 2014, 80 pregnant women were enrolled in this observational prospective study conducted at the Reproductive Medicine Unit of the University of Naples Federico II.

Inclusion criteria were: maternal age >18 years, healthy women, spontaneous pregnancy, first pregnancy with Diagnosis of gestational diabetes.

Gestational diabetes is diagnosed with an oral glucose tolerance test (OGTT) performed between the 24th and the 28th week of gestation. The OGTT was performed with 75 grams of glucose and venous samples were performed at the time 0', 60' and 120' for the determination of blood glucose in plasma. Gestational diabetes is diagnosed when one or more values are equal or higher than the threshold.

We divided participants into the following two groups according to the treatment (Group A: diet; Group B: diet and insulin) and BMI (normal weight; overweight/obese). Because pregnant women with GDM should also receive dietary intervention during pregnancy, we further divided participants into subgroups to separately evaluate the role of insulin therapy and dietary intervention.

The subgroups were the following: normal weight pregnant women with GDM (A1 Group) and overweight/obesity pregnant women with GDM (A2 Group) treated with dietary intervention; normal weight pregnant women with GDM (B1 Group) and overweight/obesity pregnant women with GDM (B2 Group) treated with both dietary and insulin therapy.

In A Group, we selected 25 patients with normal weight (A1 Group) and 15 obese/overweight patients (A2 Group). In B Group, we selected 7 normal-weight patients (B1 Group) and 33 overweight/obese patients (B2 Group).

Caloric restriction has been prescribed to overweight/obese patients (25 kcal/kg) and normal-weight patients (35 Kcal/Kg). Dietary compliance was assessed on the basis of a weekly clinical control. Patients who did not achieve adequate glycemic control with diet alone, started insulin therapy within two weeks of dietary failure. All women had a glycemic profile seven times daily, by measuring capillary blood glucose before and 2 hours after meals and before going to bed.

Student's t-test was used to compare continuous variables (maternal age, gestational age at delivery, glycemic profile) and the chi-squared test was used to compare the incidence of fetal macrosomia in the two study groups

### RISULTATI

In A group, the overweight/obese patients showed a risk of macrosomia about 3 fold higher than normal-weight patients with p 0.0022 (A2 Group: 73% versus A1 Group: 24%). In B group, the overweight/obese patients showed the same incidence of macrosomia than normal-weight patients (B1 Group: 24% versus B2 Group: 28%).

The overweight/obese patients with GDM treated with insulin therapy, had the same risk of fetal macrosomia than normal-weight women with GDM treated with insulin. In contrast, overweight/obese patients with GDM who did not receive insulin had worse outcomes (macrosomia) compared with normal-weight patients with GDM who do not receive insulin. We found that obesity alone was a risk factor for adverse pregnancy outcomes. However, new studies are needed for an exact quantification of such correlations

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## CONCLUSIONI

Maternal overweight status and obesity, excessive GWG and GDM are all independently associated with an increased risk of adverse pregnancy outcomes, such as preterm birth, macrosomia and caesarean delivery, particularly when these three factors occur simultaneously.

Thus, we hypothesize that targeting excessive GWG, which is a modifiable risk factor during pregnancy, would contribute to improving adverse GDM related pregnancy outcomes. All maternal fuels play a role in pregnancy outcomes, but tight glycemic control remains the primary management strategy in pregnancies affected by diabetes. The current glucose targets reduce LGA/macrosomia and improve perinatal outcomes



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## 51. OOCYTE DONATION PREGNANCIES: MATERNAL AND FETAL OUTCOMES

### LISTA AUTORI

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### INTRODUZIONE

Since the first successful use of donated oocytes in 1984, the number of oocyte donation (OD) cycles in Europe and United States has dramatically increased, becoming nowadays a common treatment option, especially to overcome infertility due to advanced age. Oocyte donation pregnancies address specific issues, due to the separation between the "oocyte age" of the conceptus and the "uterine compartment age" of the mother. Consequently, there has been increasing interest in the impact of OD on several aspects, especially maternal and fetal outcomes

### MATERIALI E METODI

We performed a retrospective study to analyze obstetrical and neonatal outcome of singleton oocyte donation pregnancies. Data relative to pregnant women who underwent their first trimester screening for aneuploidies between January 2005 and June 2013 were collected. 158 patients with singleton oocyte donation pregnancies were eligible for the study. 60 patients were not reachable at the time of telephone interview. 98 patients were enrolled for the study and were contacted by telephone interview to collect maternal and neonatal outcomes

### RISULTATI

Population: the mean maternal age of oocyte donation recipients was 43 years (range 30-54 years), while the mean age of oocyte donors was 26 years (range 18-36 years). Mean maternal pre-pregnancy BMI of recipients was 22.7 kg/m<sup>2</sup> ( $\pm$  3,51). 88.8% of patients were nulliparous. 40.8% of pregnant women had a Bachelor Degree.

Obstetrical and neonatal outcome: 89% of women delivered by Cesarean Section and 78% of these were elective C-section by maternal request. 86.6% of patients (n=84) delivered at term ( $\geq$ 37 weeks) while 13.4% of deliveries (n=13) were preterm ( $<$ 37 weeks). 1 pregnancy terminated with therapeutic abortion due to congenital malformation of genito-urinary tract of the fetus. Hypertensive disorders of pregnancies (pregnancy-induced hypertension and preeclampsia) complicated 19.3% of pregnancies. 7.1% of patients were affected by gestational diabetes. Less frequent complications reported were threatened abortion (4.1%), pPROM (3.1%), intrauterine growth restriction (1%) and post-partum hemorrhage (1%). 48 males (50%) and 48 females (50%) were born in our cohort. Mean birthweight of male neonates was 3175 g ( $\pm$  490 g), with a minimum birthweight reported of 1915 g and a maximum of 4400 g (Q1= 2980 g; Q2= 3100 g; Q3= 3412 g.). Mean birthweight of female neonates was 2959 g ( $\pm$  502 g), (range 1480- 3700 g; Q1= 2852 g; Q2= 3000 g; Q3= 3212 g). The birthweight of neonates from oocyte donation pregnancies resulted significantly distributed under 50<sup>o</sup> percentile of standard reference percentile curves of spontaneous pregnancies

### CONCLUSIONI

In our cohort, oocyte donation pregnancies are associated with a high incidence of hypertensive disorders of pregnancies. Furthermore, birthweight of neonates from oocyte donation pregnancies results significantly distributed under 50<sup>o</sup> percentile of standard reference gestation-specific curves of spontaneous pregnancies. These findings are in agreement with previous studies which also reported a higher incidence of pregnancy-induced hypertension, preeclampsia and placental pathology in oocyte donation pregnancies. In this light, the recognition of risks associated with oocyte donation pregnancies, should lead obstetricians to consider tailored clinical surveillance and, possibly, preventive strategies and appropriate screening

## 52. ORAL AND SYSTEMIC INFLAMMATION IN OBESE PREGNANT WOMEN. A LONGITUDINAL EXPERIMENTAL STUDY

### LISTA AUTORI

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### INTRODUZIONE

Pregnancy is characterized by a physiological upgrade of the inflammatory state. Some maternal conditions as obesity and parodontitis may be able to further increase this natural condition, promoting the development of obstetric syndromes like preeclampsia, gestational diabetes and preterm birth.

In the last years the prevalence of obesity has significantly increased in the general population especially in women of childbearing age; similarly in this population periodontal disease is a common finding.

The aim of this study is to investigate the inflammatory status, both oral and systemic, in relation to BMI and to outcome of pregnancies

### MATERIALI E METODI

We enrolled 72 obese (BMI > 30), and 33 normal weight (18-25) pregnant women. Obese patients were given a balanced diet and nutritional counseling and provided indications on the recommended weight gain according to the Institute of Medicine (IOM) guidelines. At each visit we evaluated maternal blood pressure, maternal weight gain, US fetal growth and noted any pathological event, such as hypertensive disorders and gestational diabetes. In a subset of patients, blood samples were collected in the third trimester for evaluation of hepcidin and CRP (C reactive protein). Hepcidin is a peptide hormone of low molecular weight produced by the liver and it's a key regulator of iron homeostasis and bioavailability. Both proteins increase during inflammation.

A subset of patients in both groups received a complete periodontal clinical exam to define the bleeding on probing (BOP), the plaque index (PI) and periodontal probing depths (PPD).

At birth, data on gestational age, mode of delivery, neonatal birth weight, Apgar score and pH of the umbilical artery were collected from all patients

### RISULTATI

Obese were significantly older than normal weight women; parity was also significantly higher in obese. This can be explained by the fact that a previous pregnancy is a well known risk factor for the development of obesity. Obese women had a significantly lower weight gain ( $8.18 \pm 6.58$  kg) than normal weight women ( $14.34 \pm 4.99$  kg), although only 57% had respected IOM suggested limits against 78% of normal-weight controls.

Gestational age at birth was not significantly different between the two groups. 39 (54%) obese mothers underwent caesarean section but only 16 of them for intercurrent medical issues; of these, 23 had a previous CS. In normal weight women the rate of CS was 21%. In the obese group there were 4 late preterm births and 2 cases of late pre-eclampsia.

Concentration of plasma hepcidin was significantly higher in obese ( $8.0 \pm 3.3$  ng / mL) compared to normal weight ( $4.7 \pm 1.6$  ng / mL) ( $p=0.01$ ) subjects and it showed a significant and positive correlation with pre-pregnancy BMI [Pearson correlation  $R=0.514$ ;  $p=0.017$ ]. A significant negative correlation was found between maternal plasma hepcidin concentrations and weight gain during pregnancy [Pearson correlation:  $R=-0.460$ ;  $p=0.04$ ].

Similarly, the levels of CRP of obese women were significantly higher than those of normal weight women ( $0.83\text{mg/dl} \pm 0.66$  vs  $0.33\text{mg/dl} \pm 0.14$ ).

Regarding oral analysis both the Plaque Index and Bleeding On Probing index were significantly higher in obese women versus normal weight women (PI 58.4% vs 30.2 %  $p=0.018$ ; BOP 57% vs 39.9%  $p=0.084$ ). Also the PPD values were significantly different (obese 2.7 mm vs normal weight 2.3 mm,  $p=0.065$ ). Overall, obese women had a worst periodontal status compared with normal weight patients

### CONCLUSIONI

In our population of obese pregnant women, clinical and nutritional counseling was associated with a significantly lower gestational weight gain when compared to normal weight women. This has allowed a better pregnancy outcome when compared with previously reported data. Nevertheless in these patients levels of inflammation, both systemic and local, are significantly increased, and correlate with BMI and gestational weight gain. Further studies are needed to evaluate if preventive strategies like oral care and target diet, both before conception and during pregnancy, may reduce the inflammatory status and improve pregnancy outcomes

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## 53. PERICONCEPTIONAL AND PERINATAL COUNSELLING IN WOMEN WITH HEART DISEASE

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### INTRODUZIONE

Over the years, the prevalence of cardiovascular diseases in pregnancy has been increased, related to the improvement of paediatric heart surgery (congenital heart disease), to the grown of cardiovascular risk factors and to the immigration (acquired heart disease), achieving 0.2-4% of all pregnancies. The risk of maternal complications in pregnancy is determined by the different impact of heart diseases on the physiological changes during pregnancy and to the type and severity of heart disease.

During the pregestational visit, the use and need of drugs should be evaluated and some diagnostic exams have to be performed (exercise electrocardiogram and echocardiogram, RM or TC, cardiac catheterization or intracardiac electrophysiology study). These exams should also be scheduled during the pregnancy, with different timetable, according to the type of heart disease.

Based on the severity and the type of heart disease, but also on the functional class, on the left ventricular function, on the presence of cyanosis and pulmonary hypertension, the women were classified into four- risk class (WHO: World health organization). During the pregnancy and the labour it is necessary to balance the maternal clinical status and fetal risks (abortion, prematurity, low weight at birth and incidence of small for gestational age, neonatal morbidity and congenital heart disease recurrence), related to maternal heart disease, to the use of drugs during pregnancy, to the diagnostic and therapeutic procedures during the pregnancy and to the labour.

The pregnancies of women with heart diseases have a higher risk of complications compared to the general population; the management of these patients requires a multidisciplinary evaluation, starting from pregestational counselling and continuing until the labour.

The aim of this project was to evaluate the maternal and fetal outcomes of women with heart disease, followed by a multidisciplinary approach

### MATERIALI E METODI

This is a prospective, monocentric analysis that involved all women with heart disease followed by multidisciplinary team, in the Obstetrics and Gynaecological Department, at Sant'Anna Hospital in Turin, from February 2014 to April 2015. The team included a cardiologist, an obstetrician, an anaesthesiologist and an internist. Cardiac (electrocardiogram and echocardiogram) and obstetrical evaluation (routine visit, blood samples and obstetric ultrasound) were performed every visit, according to the maternal heart disease and the obstetric schedule.

For each woman we collected some cardiologic (main heart disease, presence of comorbidity, previous and current therapy, smoke, recovery for cardiologic reasons) and obstetric data (parity, obstetrics complications and/or recovery for obstetric reasons, modality of labour and modality of delivery, gestational age at delivery, use of analgesia, maternal complication after delivery and neonatal characteristics).

Furthermore, a retrospective review of medical records of all women with heart disease that deliver in Sant'Anna Hospital between 2009 and 2013 was performed.

These are the results of an interim analysis ended on April 2015

### RISULTATI

From February 2014 to April 2015, among 81 women with heart disease, 15 were just pregnancy consultation, 8 patients were only preconceptional counselling and we followed 58 pregnancies. Twenty one women had congenital heart disease, instead 35 women had acquired heart disease and 2 women had both. The mean age of patients was 33.3 years. We classified women according to WHO risk class: 22.4% in class I, 48.3% in class II, 25.9% in class III and 3.4% in class IV.

33 women (56.9%) have taken some medication during pregnancy and 19 of them have taken beta- blockers.

During pregnancy, 27.5% of women (16 out of 58 cases) were recovery; 7 of them for obstetrics reasons and 9 of them for cardiologic ones. 44 women gave birth. Vaginal delivery occurred in 54.5% of women, instead caesarean delivery occurred in 45.5% of cases. Among vaginal delivery, 79% of women did epidural analgesia



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Mean gestational age (GA) of the babies was 37 weeks + 5 days, the mean birth weight was 2823 gr and among them 13.3% was small for gestational age (SGA). 20.4% of deliveries occurred before 37 weeks of gestation and there was only one case (2.7%) of neonatal death for placental abruption at 37 weeks of gestation. No women died during or after the pregnancy. Regarding oral analysis both the Plaque Index and Bleeding On Probing index were significantly higher in obese women versus normal weight women (PI 58.4% vs 30.2 %  $p=0.018$ ; BOP 57% vs 39.9%  $p=0.084$ ). Also the PPD values were significantly different (obese 2.7 mm vs normal weight 2.3 mm,  $p=0.065$ ). Overall, obese women had a worst periodontal status compared with normal weight patients.

## CONCLUSIONI

Our data have been compared to the data collected retrospectively from 2009 to 2013, which included 134 women with heart disease. The rate of vaginal delivery increases (47% vs. 54%), thanks to the use of epidural analgesia that became more common (32% vs. 79%) and to the correct multidisciplinary planning of the delivery timing. Some complications like the low birth weight was not reduced by this teamwork: the neonatal weight at delivery was lower (2823 g) than the mean weight at the same gestational age (3037-3160 g) with no significant differences from our control group. We suppose it depends on the use of beta-blockers during pregnancy, as supported by literature.

The management of pregnancy in women with heart disease based on a multidisciplinary approach has become essential. The team should include cardiologists, obstetricians, anaesthesiologists, internists and, when needed, heart surgeons. They should monitor the women, starting before the conception and during the whole pregnancy, at the delivery and during the postpartum period. This approach could improve the management of pregnancy and the maternal and fetal outcomes.



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## **54. PERINATAL DEPRESSION: SCREENING AND CLINICAL OUTCOMES. THE ITALIAN EXPERIENCE OF A INTER-UNIVERSITY ROMAN GROUP**

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### **INTRODUZIONE**

Perinatal depression (PND) is a global epidemic with adverse life-long consequences for the mother, the partner and the offspring. Despite the high prevalence of PND most cases remain undetected leading to an increased burden of the disease.

The need and the modality to perform screening programs in order to prevent and reduce the negative impact of PND are still a matter of controversy.

International guidelines highlight the failure of the screening plans when they are not linked to treatment options.

Moreover a growing number of researches have recently focused on perinatal anxiety disorders (PAD), either alone or associated with PND. Nevertheless the results of the studies concerning PAD are still inconsistent.

The authors on behalf of a Inter-University Roman Group, present the protocol of a multicenter prospective clinical trial designed to find an answer to these issues

### **MATERIALI E METODI**

The sample of the study consisted of 434 pregnant women at the third trimester.

All participants completed a clinical information sheet including sociodemographic, gynaecological, obstetrical and psychiatric data. Screening for PND and PAD was performed using Edinburgh Postnatal Depression Scale (EPDS).

At baseline we also performed the Big Five Inventory (BFI), the Experiences in Close Relationships Scale (ECR), the Mood Disorder Questionnaire (MDQ) and the Highs Questionnaire (HQ).

After delivery EPDS was further administered by telephone at 1, 6 and 12 months

### **CONCLUSIONI**

The study is currently ongoing and will be closed in three months.

All data will be included in a prospective database and statistically analyzed.

The final results will be available in the early 2016

## 55. PERINATAL HOSPICE: THE EXPERIENCE OF VERONA

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### INTRODUZIONE

A prenatal diagnosis of "incompatible with long-term survival fetus" involves the need to support the couple in the difficult choices that they will have to take during pregnancy and especially after delivery. Perinatal Hospice, through the "Therapy of Embrace" ("Terapia dell'Accoglienza") [1], is a type of service that aims to provide support to those families and to the unborn child who carries a poor prognosis.

More than 170 hospitals and clinics around the world are committed to ensure such support; the first similar reality in Italy was organized by "Quercia Millenaria" [2], a non-profit association which is headquartered at "Ospedale Gemelli" in Rome.

With the aim to introduce and implement this kind of support, the Department of Gynaecology and Obstetrics of Verona, in collaboration with "Quercia Millenaria", has developed a project for the training of operators [3]. A dedicated multidisciplinary team was created with the aim of developing a specific guideline that was applied to a "pilot" case to see the benefits of this approach and identify any critical areas for improvement

### MATERIALI E METODI

The clinical case of Mrs. R.I., at 24 gestational weeks, with a fetus affected by trisomy 22 and a large diaphragmatic hernia was identified. This chromosomal abnormality is incompatible with long-term survival. It was due to a balanced translocation of chromosomes 11:22, and karyotype analysis revealed that the mother was the carrier of this chromosomal aberration. The case was taken over by the dedicated multidisciplinary team consisting of an obstetrician, a sonographer, a midwife, a neonatologist and a psychologist. A "birth plan" (Fig. 1) was designed and the couple could express preferences about ante-partum and intra-partum care, the post-natal care of the fetus, compassionate care and also religious and funeral aspects. This document, along with a clinical report, was diffused to all the Department in order to share the case with the staff

### RISULTATI

During pregnancy, psychological interviews were conducted weekly, integrated with monthly visits and counselling with members of the dedicated team.

During childbirth, which happened at term after a spontaneous vaginal labor, all the requests expressed by the couple in the "birth plan" about the newborn care, who died 32 minutes after birth, were guaranteed. In particular, the baby was given a name, was washed, was dressed, and held by the parents for the desired time; religious support was present for baptism with the spiritual guide of reference.

The staff of the delivery room collected concrete memories of the child, such as a few pictures, the ID bracelet, the imprint of the hands and feet, a lock of hair, and placed them in the "Memory Box" specially prepared by the parents for the event (fig. 2).

After delivery, hospitalization, as established in the "birth plan", took place in a protected environment (a room previously designated), where the couple could stay together. It was granted an early discharge and a planned psychological interview a week later. On that occasion, the couple decided to bring home the "Memory Box" previously described.

A month after giving birth, during the gynaecological visit, it was possible to know the couple's experience and feedback about the care model that was adopted.

What the patient R.I. reported is that she had opened several times the "Memory Box" to touch the footprints and handprints and view the photos, and she appreciated very much the opportunity to do so.

The couple has also repeatedly emphasized the feeling of security derived from the knowledge that all members of the department were aware of their case and of their "birth plan"

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## CONCLUSIONI

The decision to offer a multidisciplinary supporting care to the couple after a diagnosis that has defined their own son as “terminal”, allowed them to overcome over time this difficult situation and to find appropriate coping strategies to support it. During meetings with various members of the team, the couple was able to express their preferences, make questions, anticipate (when possible) events and prepare for them. The personalized assistance during childbirth and the postpartum, helped them to reach a more peaceful acceptance of the death of their offspring.

This approach finds widespread supporting in literature.

In case of fetal or neonatal death, for a better emotional and psychological recovery, it has been proven the value of contact with the child after giving birth; in women who have had a chance to take care of him and hold him a reduction of anxiety and depression longtime has been shown [4].

As a matter of fact, in our experience, it was important for the couple be able to caress the child, count the number of fingers, feel its weight, touch his hair.

In addition, the collection of concrete memories, identified in the “Memory Box”, is designed to accompany the parents in the mourning process in the long term. As indicated by the latest guidelines RCOG 2010 [5], the parents should always be offered this opportunity, without any persuasion, leaving them free to choose.

Moreover, this testimony confirms that the creation of a dedicated multidisciplinary team is a necessary condition to make a similar project feasible and practical.

The precious testimony of these parents has confirmed the need for the Therapy of Embrace at our Department. Through the establishment of a specific “birth plan” as an operating procedure, training and sensitization of staff, it has been possible to create an increasingly functional and structured Perinatal Hospice for the benefit of other couples that have subsequently faced a similar experience



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## 56. PLACENTA LOCATION AND SPONTANEOUS PRETERM BIRTH: IS THERE ANY CORRELATION?

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### INTRODUZIONE

Human placenta plays a key role during gestation and, through the ideal position at the interface between mother and fetus, it is the major determinant of pregnancy maintenance and labor onset. Previous observations suggested that placental location is instrumental in triggering the normal impulse for initiation and progress of labor. In term pregnancies, anterior location of placenta is associated with a later onset of labor, a higher rate of induction and cesarean section for failure to progress, with higher incidence of postpartum complications. On the contrary, an increased incidence of prelabor rupture of membranes at term is observed in posterior placenta. Thus, placenta location seems to play a role in the activation of labor, through a direct or indirect influence on uterine contractility, mediated by both mechanical and hormonal mechanisms. The aim of the present study is to evaluate whether the placenta location influences the mechanisms underlying spontaneous preterm birth or preterm premature rupture of membranes

### MATERIALI E METODI

A total of 320 preterm deliveries, from 1 January 2013 to 31 December 2014, were subjected to retrospective analysis. Information about placenta location were collected from ultrasound report performed at admission. Indicated preterm births and multiple pregnancies were excluded. Maternal characteristics and delivery outcome such as premature rupture of membranes (pPROM), induction of labor, mode and gestational age at delivery, labor length, postpartum hemorrhage (PPH) and manual removal of placenta were correlated with anterior or posterior or fundal placental locations

### RISULTATI

A total of 150 preterm births were included in study population and they were divided into 2 group according to placenta location: Group A (n=75) with anterior location and Group B (n=75) with posterior placenta. No statistical significant differences were showed between placenta location and labor outcomes, such as early vs late preterm births, pPROM, induction of labor, labor length and mode of delivery. Similarly, any difference was found between placenta location and postpartum outcomes in preterm births

### CONCLUSIONI

The present study failed to show any influences of placenta location on preterm onset and progress of labor, nor on postpartum outcomes. Differently from term labor, placenta location is not implicated in preterm uterine contractility and rupture of membranes where other mechanisms, related to inflammatory and hormonal pathways, seem to play a major role

## 57. PLACENTAL MTDNA CONTENT AND MATERNAL PLASMATIC HEPcidIN LEVELS IN PREGNANCIES WITH MATERNAL OBESITY AND GESTATIONAL DIABETES

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### INTRODUZIONE

The number of pregnancies complicated by obesity has increased in the past 20 years [Stuebe et al., Am J Obstet Gynecol 2012]. A higher risk (up to five times) of intrauterine death and infant mortality is recorded in obese women [Nohr et al., Obstet Gynecol. 2005]. Barker's hypothesis suggests that the maternal nutritional environment may affect offspring metabolism in later life [Cetin et al., Nutr Metab Care 2013; Barker, J Intern Med. 2007].

Obesity is due to incorrect nutrition based on energy imbalance between calories intake/consumption and on excess of macro-opposite to low micro-nutrients. In pregnancy, obesity causes systemic and placental lipotoxicity and a low-grade inflammation and oxidative stress (OxS) [Marseglia et al., Int J Mol Sci. 2014; Rupérez et al., Int J Mol Sci. 2014].

Mitochondria (mt) are source of Reactive Oxygen Species (ROS). Increased intracellular lipids may alter mt structure and function, leading to increased OxS exacerbating the ongoing inflammation. Chronic low-grade inflammation and mt dysfunction are reported in many tissues [Robker et al, Repr Immun 2011], but little is known about the effect of obesity on placental mt. We recently presented data showing higher mt content in healthy OB placentas [Mandò et al., Repr Sc Suppl.- SRI 2015].

Mt metabolism is strongly conditioned by the cell iron status. Hpcidin is a peptide hormone regulating iron homeostasis. During pregnancy hpcidin physiological levels decrease to maximize iron transport from the mother to the fetus. Moreover, hpcidin is a positive mediator of acute inflammation [Rehu et al, Eur J Haematol. 2010].

Here we studied placental mtDNA levels (mt content) and maternal plasmatic hpcidin levels in obese pregnant women (OB) in presence of Gestational Diabetes Mellitus (GDM), and in normal weight pregnancies (NW) to better characterize the oxidative and inflammatory status of maternal obesity

### MATERIALI E METODI

37 pregnant women were classified on their pre-pregnancy Body Mass Index (BMI): 17 healthy normal weight (NW:  $18 \leq \text{BMI} \leq 24$ ) and 20 obese (OB:  $\text{BMI} \geq 30$ ) women. Exclusion criteria were: non-Caucasian race, maternal/fetal infections, alcohol/drug abuse, multiple pregnancies or genetic anomalies. Gestational age, maternal (age, BMI, gestational weight gain-GWG, hemoglobin, glycemia) data were collected. Placental area, thickness and efficiency (fetal/placental ratio) were calculated.

Placentas were collected at elective cesarean section (CS). Maternal decidua was discarded, villi sized from different placental disc sites and immediately frozen in liquid nitrogen. Tissue villi were disrupted and added with Tri-Reagent for DNA extraction. mtDNA levels were assessed by relative Real Time PCR normalizing a mt gene (CytB) to a single-copy nuclear gene (RNase P) ( $2^{-\Delta\text{Ct}}$ ).

Maternal vein blood was collected one hour before ECS and centrifuged to obtain plasma. Hpcidin (Hpn25) plasmatic levels were quantified with a competitive ELISA. The addition of streptavidin-peroxidase and its substrate to plasma samples caused a colorimetric reaction measured by a spectrophotometer. The signal intensity was inversely proportional to Hpn25 and its final concentration was calculated based on a standard curve. Placental mtDNA, hpcidin plasmatic levels and clinical data of study population were analyzed with statistical software SPSS (version 22). Data were analyzed using T-Student or Mann-Whitney U test (significance:  $p < 0.05$ )

### RISULTATI

Maternal pre-pregnancy BMI was significantly different between OB with ( $35.6 \pm 4.8$ ) or without GDM ( $36.5 \pm 4.9$ ) and NW women ( $22.1 \pm 1.9$ ) ( $p < 0.001$ ), following group inclusion criteria. Maternal Gestational Weight Gain (GWG) was significantly lower in healthy OB ( $8.3 \pm 3.2$  Kg) compared to NW women ( $11.3 \pm 3.1$  Kg) ( $p < 0.01$ ). OB with GDM gained less weight ( $8.2 \pm 5.4$  Kg) vs NW though not significantly. Hemoglobin levels were similar in all analyzed groups, while glycaemia (at III trimester) was significantly higher in OB with GDM ( $99.2 \pm 8.1$  mg/dL) compared to NW ( $78.7 \pm 5.3$  mg/dL) and OB without GDM ( $81.7 \pm 6.3$  mg/dL) ( $p < 0.001$ ).

Gestational age at CS and both placental and fetal data did not present significant differences among groups, except for placental weight of OB with GDM women ( $562.9 \pm 72.7$  g) which was higher compared to OB ( $465.7 \pm 79.6$  g) and NW ( $466.8 \pm 97.7$  g) women ( $p < 0.05$ ).

mtDNA in OB with GDM ( $181.2 \pm 49.3$ ) placentas was similar to NW ( $191.4 \pm 46.9$ ) [U-Mann-Whitney- OB with GDM:  $p = 0.671$ ] and significantly lower than healthy obese group we previously analysed ( $277.56 \pm 97.51$ ) [U di Mann-Whitney- OB without GDM:  $p = 0.08$ ].

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Maternal hepcidin levels were significantly increased in OB without GDM ( $8,0 \pm 3,3$  ng/mL) [U-Mann-Whitney-  $p=0.01$ ], but not in OB with GDM ( $4,9 \pm 2,0$  ng/mL) [U-Mann-Whitney-  $p=1.00$ ] compared to NW ( $4,7 \pm 1,6$  ng/mL).

No mtDNA/Hepcidin differences were found depending on fetal sex.

In whole analysed population plasmatic hepcidin displayed a significant negative correlation with maternal GWG ( $R=-0.419$ ;  $p=0.041$ ;  $n=24$ ). In our healthy population (NW and OB women without GDM), maternal pre-pregnancy BMI resulted significantly correlated with placental mtDNA content ( $R=0.342$ ;  $p=0.05$ ;  $n=37$ ) and maternal hepcidin ( $R=0.514$ ;  $p=0.017$ ;  $n=21$ )

## CONCLUSIONI

We previously presented altered mt levels in non-diabetic OB women [Mandò et al., Repr Sc Suppl.- SRI 2015], suggesting a placental functional impairment depending on maternal BMI as consequence of an increased lipotoxic OxS.

Here we showed no difference between mtDNA content in OB with GDM compared to NW pregnant women. A different pathogenesis may characterize the two groups. Obesity presents an inflammatory basis, while GDM has a metabolic pathogenesis usually associated with hyperglycemia and insulin resistance. Therefore, diabetic obese pregnant women could adopt alternative molecular mechanisms against lipotoxic OxS in the womb.

Interestingly, hepcidin levels traced mtDNA content resulting increased in OB without GDM, expanding previous data [Garcia-Valdes et al., Int. J.Ob (Lon) 2015]. Although pregnancy physiologically causes a reduction of hepcidin levels, the inflammatory status (systemic and intrauterine) related to obesity may cause an increase in hepcidin biosynthesis. Actually, a recent work shows increased maternal hepcidin in women with an emergency cesarean section characterized by an inflammatory acute response [Rehu et al, Eur J Haem. 2010].

Other studies have associated both higher BMI and excessive GWG with adverse pregnancy outcomes as GDM, preeclampsia and fetal adiposity [Catalano and deMouzon, Int.J.Ob (Lon), 2015]. The lower maternal GWG found in our healthy OB group may be a result of the personalized counselling with dietary advices provided to this group of patients in our clinic and may justify the lack of significant differences in fetal and placental data or pregnancy outcomes in this group.

Further data are needed to investigate if obesity could trigger some molecular systemic and placental alterations and to clarify the possible consequences of these changes on fetal tissues



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## **58. POST-PARTUM HEMORRHAGE PREVENTION: OXYTOCIN AND CARBETOCIN FACE TO FACE. A SINGLE CENTER RANDOMIZED DOUBLE BLINDED PERSPECTIVE TRIAL. PRELIMINARY DATA**

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### **INTRODUZIONE**

Postpartum haemorrhage (PPH) remains an important cause of both maternal morbidity and mortality and the risk is much higher for women undergoing cesarean delivery. Oxytocin represent one of the major preventive measures of PPH and is regarded as the gold standard uterotonic agent. However its half-life is short and it must be administered as a continuous intravenous infusion to attain sustained uterotonic activity throughout Cesarean section. Carbetocin is a synthetic analog of oxytocin that has a prolonged uterotonic activity with a similar side effect profile to that of oxytocin.

Primary aim of the study was to compare the efficacy of Carbetocin versus Oxytocin infusion in term of PPH prevention in high risk patients undergoing elective Cesarean Section (CS).

Secondary aim was to compare drugs in term of early to late maternal side effects and rate of rescue therapy (need of additional uterotonics)

### **MATERIALI E METODI**

We conducted a single center randomized double blinded perspective trial at Tertiary care University Hospital of Padua, between May 2012 and May 2014. According to sample size calculation before recruitment, 220 patients were estimated as necessary. In this preliminary reports we collected data from 160 eligible patients randomly allocated in Group\_A (84 patients, Carbetocin treatment) or in Group\_B (76 patients, Oxytocin treatment).

We considered eligible for the study pregnant women who delivered by elective CS (Modified Stark technique) and estimated at high risk for PPH due to the presence of at least one of the following conditions: placenta previa, multiple pregnancy, previous PPH, severe polyhydramnios (AFI>25), 3 or more previous CS.

We considered as exclusion criteria the following conditions: previous hyper-sensitivity to Oxytocin or Carbetocin, preeclampsia-eclampsia, severe systemic diseases (cardiovascular, renal, hepatic and neurological disfunctions), need for general anesthesia.

Group\_A women received just after baby was delivered Carbetocin 100 mcg in bolus iv while Group\_B Oxytocin 5 IU in 500 mL 0,9% NaCl solution as intravenous infusion. For all patients data regarding general features and pregnancy outcomes was collected.

We considered as outcome measure: total blood loss (mL), hemodynamic profile before and after drug administration (blood pressure, heart rate and peripheral capillary oxygen saturation), uterine tone (by using a 1-10 VAS scale), hemoglobin value and % of variation after comparison of values before and after procedures (adjusted for hematocrit), need for rescue uterotonic therapy, need for additional conservative or demolitive surgical procedures due to haemorrhage, maternal side effects (dyspnea, nausea, vomiting, headache, dizziness, flushing, chills, tremors, abdominal pain, itching, sweating, hypotension), need for maternal transfusion

### **RISULTATI**

Two groups were homogeneous for general features. The estimated mean blood loss was  $701.88 \pm 145.3$  mL for the carbetocin group and  $972.73 \pm 178.7$  mL for the oxytocin group ( $p < 0.05$ ). Despite no differences were found in terms of hemodynamic parameters, when compared for uterine tone two groups resulted significantly different (mean VAS score  $7.3 \pm 1.2$  versus  $5.4 \pm 2.2$ ;  $p < 0.05$ ).

No significant differences were found in terms of hemoglobin variation nor in term of need for transfusion (5 cases versus 8 cases, respectively).

Group\_B when compared with Group\_A showed a significant rate of uterotonic rescue therapy (39.2% versus 21.6%;  $p < 0.05$ ). No other differences were found after comparison between groups for remaining outcomes measure

### **CONCLUSIONI**

Our preliminary data clearly showed that Carbetocin may be considered a safe, effective and well tolerated drug for PPH prevention. The completion of the trial will permit us to better estimate the real advantages in using this drug.

Further studies focused on costs estimation are mandatory to estimate cost-efficacy of this strategy compared with Oxytocin administration

## **59. POST-PARTUM PELVIC REHABILITATION: AN INEXPENSIVE TOOL FOR EARLY DETECTION AND TREATMENT OF FUNCTIONAL AND ANATOMICAL DAMAGE. LONGITUDINAL COHORT STUDY**

### **LISTA AUTORI**

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### **INTRODUZIONE**

During fetal passage through the birth-canal, tissue damage may occur directly (excessive muscle and nerves stretching, connective tissue tearing, episiotomy, vagino-perineal tears) or indirectly (invasive operative procedures). Recent data reports an overall incidence of post-partum urinary incontinence ranging between 3% and 67%, with a rate of 21% after spontaneous and 36% after operative delivery. Peri-partum damage may involve the posterior perineal district and several studies report an involuntary loss of solid or liquid stool and flatus in 2-6% of primiparous women after non-complicated vaginal deliveries with a dramatic increase to 17-62% in the event of severe perineal laceration. Short-term sexual dysfunctions, such as dyspareunia and loss of desire, are commonly described after vaginal birth with an incidence of 22% and a reported increase to 86% in cases requiring postpartum perineal repair. Several conservative approaches (physical therapies, lifestyle modification, behavioural training, pharmaceutical therapy) have been proposed as first-line treatment while surgical intervention is reserved for non-responsive cases and/or for those affected by several anatomic defects. Pelvic floor muscle training (PFMT) is considered the most effective conservative treatment option in restoring both antepartum pelvic floor muscle strength (reducing the risk of pelvic organs prolapse) and physiological sphincter activity (reducing the risk of urinary and fecal incontinence) but data present in Literature is still fragmentary and inconclusive. The primary aim of the study is to compare the rate of early, intermediate and late pelvic floor dysfunction in women who participated in early post-partum pelvic floor rehabilitation as opposed to those who did not. Secondly, we aim to identify the intra-partum risk factors more strongly associated with postpartum pelvic floor disorders

### **MATERIALI E METODI**

We performed an observational longitudinal case-control study in which all women with uncomplicated, single, term pregnancies referred to the Delivery-Room of the Obstetric/Gynaecological Clinic of Padua-University between January-September 2012 were recruited. The Inclusion criteria were defined as the following: knowledge of Italian language, pre-conceptional body mass index (BMI) ranging between 18 and 25 kg/m<sup>2</sup>, weight increase during pregnancy less than 20 kg, fetal cephalic presentation, spontaneous or induced labour onset, analgesia request and administration during labour, spontaneous or operative vaginal delivery (with or without episiotomy). Exclusion criteria were defined as: parity greater than 2, large or small for gestational age fetuses, vaginal birth after caesarean section, personal history of pre-conceptional pelvic floor dysfunctions and/or pelvic surgeries, performance of PFMT during pregnancy, non-adherence to postpartum PFMT treatment and follow-up. Patients presenting with history of pre-conceptional diabetes, hypertension, dysthyroidism, autoimmune disease were excluded from the study. We selected 145 patients eligible for the study; for all patients data regarding general maternal features, type of labour (spontaneous or induced), request for analgesia, length of first and second stage, type of vaginal delivery (spontaneous or operative), episiotomy, degree of vaginal-perineal tears, fetal occiput position at birth, neonatal weight and cephalic circumference were also collected. At discharge, all patients were adequately counselled and invited to participate in a PFMT program beginning on the 30th day following delivery and lasting 90 days. Patients who agreed to and adhered to the PFMT program were included in Group-A (87patients) while patients refusing the treatment comprised Group-B (58patients).

Before initiating the PFMT program, all patients (both Group-A and Group-B) completed 3 specific validated self-administered questionnaires (Italian-version) on urinary, faecal and sexual functions: the UDI-6 (Urological-Distress-Index) short-form micturition symptoms questionnaire, the FISI (Faecal-Incontinence-Severity-Index) questionnaire for faecal incontinence detection and severity assessment and the McCoy (validated-Italian-version) questionnaire for sexual function evaluation. All three questionnaires were administered second and third time after delivery at 3 and 12 months

by telephone interview. The UDI-6 questionnaire score defined the severity of urinary distress; scores ranging from 6-to-10 was considered positive for mild urinary distress, from 11-to-15 suggestive for moderate urinary distress and a score higher than 15 for severe urinary distress. A FISI questionnaire score higher than 10 was considered positive for faecal incontinence. A score higher than 40 at McCoy questionnaire identified a sexual dysfunction. Statistical analysis was performed by SPSS software (Chicago, IL) for Windows version 19, applying parametric and non-parametric tests when appropriate. The Kolmogorov-Smirnov test was used to assess the normality of distribution. Continuous variables were expressed as absolute numbers, average  $\pm$  standard deviation, and analyzed by

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Student-t test or Anova test when appropriate; categorical variables were expressed as percentages and analyzed through the  $\chi^2$  test or the Fisher's exact test, when appropriate. Statistical significance was defined as p values < 0.05

## RISULTATI

The comparison between the two cohorts showed that groups were homogeneous for all the considered features except for maternal age at delivery ( $33.2 \pm 4.3$  in Group A versus  $35.6 \pm 4.2$  years in Group-B) [ $p < 0.01$ ]. At 30 days following delivery there were no reported cases of lower bowel dysfunction and faecal incontinence. Also, no patient had of yet resumed sexual activity. However urinary dysfunctional symptoms were reported within the study groups as follows: mild urinary dysfunctions affected 50.6% of Group-A patients and 51.7% of Group-B patients, moderate dysfunctions were detected in 23% and in 22.4% of the patients and severe urinary dysfunctions in 14.9% versus 15.5% of patients, respectively [ $p: n.s.$ ].

Data collected at 90 days after delivery showed that urinary symptoms persisted as mild in 29.9% versus 39.3% [ $p < 0.001$ ]; as moderate in 10.3% versus 21% [ $p < 0.001$ ], and severe in 4.6% versus 13.8% [ $p < 0.001$ ], in Group A and Group B patients respectively. Also regarding sexual activity 40.2% of the Group-A patients versus 70.7% of the Group-B patients complained absence of or dysfunctional intercourse [ $p < 0.001$ ]. Once again no patient referred faecal incontinence. One year after delivery, urinary symptoms persisted as mild in 14.9% versus 36.2% [ $p < 0.001$ ]; as moderate in 4.6% versus 10.3% [ $p < 0.05$ ], and severe in 4.1% versus 5.2% [ $p: n.s.$ ], in Group A and Group B patients respectively. Only 10.3% of the Group-A patients versus 24.1% of the Group-B patients complained of a dysfunction or absence of sexual activity at 12 months following delivery [ $p < 0.05$ ]. We performed statistical correlation analysis between known risk factors of postpartum urinary dysfunction and the severity of such dysfunction as determined by the UDI-6 scoring system at 30 days postpartum. We found that pre-conceptual BMI [ $p < 0.001$ ], weight gain during pregnancy [ $p < 0.001$ ], length of second stage of labour [ $p < 0.05$ ] and high neonatal birth weight [ $p < 0.001$ ] were significantly associated with moderate and severe urinary dysfunctions. No association found between parity, type of labour and delivery, length of the first stage of labour, analgesia request, vaginal-perineal tears and episiotomy rate, occiput position at birth, neonatal head circumference and moderate/severe urinary dysfunctions 1 month after delivery

## CONCLUSIONI

Currently, PFMT is considered the first choice in prevention and treatment of post-partum urinary incontinence. We estimated that four fifths of the urinary dysfunctions observed fall into the mild moderate category and may thus be resolved by implementation of early PFMT programs in 50% of the cases. Patients affected by a severe form of urinary dysfunction also benefited from a rehabilitation program with reduction of disease severity and accelerated healing time. On the contrary, patients who refused post-partum PFMT, on follow-up interview 3 months after delivery referred a significantly higher rate of intermediate/severe micturition symptoms without reduction in severity. Similarly, 1 year after delivery this cohort of patients reported an incidence of all degrees of urinary dysfunction comparable to that reported by the PFMT group at 3 months postpartum. Also sexual function were restored better in women who performed PFMT than who did not. In conclusion, early postpartum PFMT may be effective in the event of a functional impairment, provided the patient resumes normal activities. However, in approximately 5% of the cases, damage is caused by an anatomical lesion and therefore clinically unresponsive to conservative treatment. Early large-scale implementation of PMFT programs may be useful in detection of those cases which warrant anticipated surgical treatment. The high rate of patient satisfaction due to improved quality of life makes the post-partum PFMT a unique, repeatable, non-invasive, low-cost tool able to improve the quality of post-birth obstetrical care



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## **60. PREGNANCY OUTCOMES AFTER KIDNEY GRAFT IN ITALY: ARE THE CHANGES OVER TIME EFFECT OF DIFFERENT THERAPIES OR OF DIFFERENT POLICIES? A NATIONWIDE SURVEY (1978-2013)**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Kidney transplantation is often considered the best way to restore fertility on renal replacement therapy. Over time, immunosuppressive and support therapies improved, patients' age increased, and a more flexible approach allowed pregnancy also in advanced CKD stages. Aim of this study was to analyse materno-foetal outcomes in two cohorts of transplanted women who delivered a live-born baby in Italy in the last three decades (1978-2013, dichotomised in delivery before and after January 2000)

### **MATERIALI E METODI**

A survey involving all the Italian transplant Centers was performed, gathering data on all pregnancies recorded since the start of activity of each Center; the estimated nationwide coverage was 80%. Data on ESRD, dialysis, living/cadaveric transplantation, therapy, comorbidity, main materno-foetal outcomes were recorded and reviewed. Data were compared with a low-risk cohort of pregnancies from two large Italian Centers (Torino and Cagliari, TOCOS cohort)

### **RISULTATI**

The database consists of 222 pregnancies with live-born babies after transplantation, (83 in 1978-1999 and 139 in 2000-2013; 68 and 121 with baseline and birth data), and in 1418 low-risk controls. Age significantly increased over time (1978-1999: median  $30.7 \pm 3.7$  versus  $34.1 \pm 3.7$  in 2000-2013  $p < 0.001$ ); Azathioprine, Steroids and Cyclosporine A were the main drugs employed in the first period, Tacrolimus emerged in the second. The prevalence of early pre-term babies ( $< 34$  gestational weeks) increased from 13.4% in 1978-1999 to 27.1% in 2000-2013 ( $p = 0.049$ ); while late-pre-term babies (34-36 gestational weeks) decreased (38.8% versus 33.1%), thus leaving the prevalence of pre-term babies (52.2% and 60.2%;  $p = 0.372$ ), and mean birth weight: (2458 g versus 2399 g  $p = 0.530$ ) almost unchanged. Small for gestational age (SGA) babies decreased from the first to the second period (SGA  $< 5\%$ : 22.2% and 9.6%  $p = 0.036$ ). In spite of high prematurity rates, no neonatal death occurred since 2000.

The results of pregnancy in kidney transplant patients are significantly different from controls both considering all cases (preterm delivery: 57.3% vs 6.3%; early pre term: 22.2% vs 0.9%; SGA  $< 5\%$ : 14% vs 4.5%;  $p < 0.001$ ) and only stage 1 transplant patients (preterm delivery: 35% vs 6.3%; early pre term: 10% vs 0.9%; SGA  $< 5\%$ : 23.7% vs 4.5%;  $p < 0.001$ ); risks increase across CKD stages. Kidney function remained overall stable in most of the patients up to 6 months after delivery.

The multiple regression analysis performed in the transplant cohort highlights a higher risk of preterm delivery in later CKD stages, an increase in the combined outcome (SGA, preterm delivery, need for neonatal intensive care unit) in hypertensive patients and an increase in preterm delivery and a decrease in SGA across periods

### **CONCLUSIONI**

Pregnancy after transplantation has a higher risk of adverse outcomes, compared to the general population. Over time, the incidence of small for gestational age babies decreased, the incidence of "early preterm" live-born babies increased. While acknowledging the differences in therapy (cyclosporine vs tacrolimus) and in maternal age (significantly increased), the decrease in SGA and the increase in prematurity may be explained by an obstetric policy favouring earlier against the risk of foetal growth restriction

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## 61. PRENATAL DIAGNOSIS OF CONGENITAL AGENESIS OF INFERIOR VENA CAVA

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### INTRODUZIONE

Inferior vena cava interruption with azygos or hemiazygos vein continuation is considered to be rare congenital anomaly, its prevalence is 0.6-2% in patients with congenital disease and less than 0.3% among otherwise normal fetuses<sup>1</sup>. It's usually describe under the heading of congenital heart malformations, in associations with the syndromes of heterotaxy, or cardiosplenia, especially in its form of left isomerism or polysplenia. Agenesis of inferior vena cava malformation results from a connection failure between the right subcardinal vein and the right vitelline vein. Inferior vena cava (IVC) takes place through a complex mechanism of appearance and regression of three pairs of embryonic veins: cardinal, subcardinal and supracardinal. Consequently, the venous blood from the caudal part of the body reaches the heart via the azygos or hemiazygos vein that appear, dilated. Agenesis of IVC is often used to describe three different entities 1) Absence of the suprarenal IVC results from failure to form of the right subcardinal vein. The hepatic segment drains directly into right atrium, and blood from infrarenal IVC returns to the heart through the azygos and hemiazygos veins. There is often association with other cardiac or visceral anomalies (dextrocardia, atrial septal defect, atrioventricular canal, situs inversus, polysplenia, asplenia). 2) Absence of infrarenal IVC results from failure of the development of the right supracardinal vein. 3) Absence of the entire IVC that usually has not relation to the other congenital anomalies described previously. We report a case of isolated interrupted fetal inferior vena cava with azygos continuation diagnosed as an ultrasound finding in association with distended azygos vein, hypoplastic right kidney dislocated in the pelvis and hyperplasia of the left kidney

### MATERIALI E METODI

A 43-year-old woman, gravida 4, para 1, cesarean section 1, aborta 1, affected by chronic hypertension, treated with ACE-inhibitor (Lisinopril) until 8 weeks, was referred to our Centre for Perinatal and Reproductive Medicine, in Perugia, for sonography to rule out fetal anomalies. Her menstrual age was 22 weeks. Sonography was done with GE Voluson E6 ultrasound equipment and with the RAB 4-8D transabdominal transducer (4-8 MHz). Biometrics measurements corresponded to the menstrual age of 22 weeks. The patient had another scan at 24 weeks, and an amniocentesis was performed and was normal. There are two classic ultrasonographic markers that should raise a suspicion of an interruption of IVC with azygos continuation. The first marker: on a transvers view of the superior abdomen the absence of inferior vena cava. The second marker: "double vessel" image, can be seen in four-chamber view as the presence of two vessels of similar width in the region that should be filled exclusively by the aorta. "double vessel" is formed by the aorta and to its right the azygos vein. In IVC interruption with azygos continuation will have very different clinical manifestations in relation to its presentation as an isolated vascular anomaly with excellent prognosis, as in our case, or other forms with associated anomalies. A careful search for other structural anomalies is mandatory considering the poor outcomes of those cases. According to Sheley et al. postnatal survival was related to the severity of heart disease

### RISULTATI

In our case there was an interrupted inferior vena cava in association with distended azygos vein, hypoplastic right kidney, dislocated in the pelvis, and hyperplasia of the left kidney. A 'double vessel' image was seen in the plain of the four-chamber view of the fetal heart. Another important finding was in the transverse view of the superior abdomen, where the descending aorta was seen to the left of the midline constituted by the spine, and, next to it, on the right of aorta another vessel of similar caliber, thought to be the azygos vein. The fetus did not have other visible anomaly and on fetal echocardiography no findings in relation to heterotaxy or congenital heart malformation were observed, and the associations with other left isomerisms was ruled out. The hepatic veins and ductus venosus reached inferior vena cava near to right atrium preserved with the hypoplastic Eustachian valve. A 2860-g female infant with Apgar scores of 9 and 10 was delivered by Cesarean section, for failure to progress, at 39 weeks' gestation. The postnatal period was uneventful. Echocardiography was done when the neonate was 1 days old. The features observed on the prenatal scans were confirmed, 3 collateral vessels reached right atrium, do not overload, was shown. Neonatal examination including electrocardiography and abdominal ultrasound was normal. Finally angio-RMN when the neonate was 3 months old confirmed the diagnosis and circle of compensation. At present the child has some problems with renal function, regarding the vascular agenesis is clinically asymptomatic



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## CONCLUSIONI

The prenatal diagnosis of IVC interruption is a sonographic diagnosis by the failure to viewing IVC accompanied by the detection of other sonographic signs as "double vessel" as has been describe before. Seeing the IVC interruption forces us to rule out a more serious pathology like isomerism to conclude that the agenesis of IVC is an isolated process that we can confirm with an angio-MRI postnatally. Prenatal diagnosis of agenesis of IVC is important for several reasons on the one hand forced to pay more attention to the research of other cardiac abnormalities or syndromes. On the other hand, the isolated forms, clinically silent, has recently been confirmed as an important risk factor for deep vein thrombosis in young patients . Finally it is important to recognize this vascular anomaly before some surgical procedures during the life



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## **62. PRENATAL DIAGNOSIS OF GASTRIC AND SMALL BOWEL ATRESIA: A CASE SERIES AND REVIEW OF THE LITERATURE**

### **LISTA AUTORI**

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### **INTRODUZIONE**

To describe seven cases of gastrointestinal tract (GIT) obstructions and to report a skewed review of the literature

### **MATERIALI E METODI**

We performed a search of our permanent perinatal database about cases with prenatal ultrasound and MRI diagnosis of gastrointestinal tract obstructions between 2006 and 2013. All cases were followed until hospital discharge and prenatal diagnosis were confirmed by fetal MRI, postnatal imaging and/or intra-operative findings. Maternal age, parity, gestational age at diagnosis, ultrasound findings, gestational age at delivery, Apgar scores at 1 and 5 min, and postnatal outcome have been recorded

### **RISULTATI**

We identified seven cases of gastric and small bowel atresia. Karyotype was normal in six cases and abnormal in one co-twin [46,XY dup (20) (qq13.1q13.3)dn] of a dichorionic-diamniotic pregnancy. The mean  $\pm$  SD for maternal age, gestational age at diagnosis, gestational age at delivery, birth weight and Apgar scores at 1 and 5 min were  $30.8 \pm 4.8$  years,  $29.8 \pm 3.7$  weeks,  $2507.5 \pm 727.5$  g,  $5.6 \pm 2.1$ ,  $7.6 \pm 1.6$ , respectively. All fetuses undergone surgical procedures in the postnatal period and all of them were discharged live from the hospital

### **CONCLUSIONI**

Prompted antenatal detection of gastrointestinal tract obstruction using ultrasound proved to be diagnostic in all cases. Fetal MRI aid was a useful complementary diagnostic investigation. Correct prenatal diagnosis allows adequate counseling, delivery planning and management care by a multidisciplinary team

## 63. PRENATAL DIAGNOSIS OF PLACENTAL CYST

### LISTA AUTORI

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### INTRODUZIONE

A placental cyst refers to a simple cystic lesion that develops in relation to the placenta. Their estimated prevalence is at ~ 2 - 20 % of all pregnancies. Color Doppler interrogation shows no evidence of any vascular flow. They have a controversial etiology but, in general, the outcome of the pregnancy is normal. In this article we report the case of a woman with a large placental surface cyst and review its clinical importance

### MATERIALI E METODI

An intrauterine cystic area with regular margins and with corpuscular liquid content was found by ultrasound in the placenta of a 42-year-old gravida 3 para woman was referred for a routine follow-up examination at 21 weeks of gestation.

Her past obstetrical history had been unremarkable. She had conjugal Rhesus incompatibility.

Ultrasound evaluation revealed that the placenta was lying posteriorly and that there was a cystic lesion protruding from the fetal plate, immediately above a lacunar area. It measured 4.4 X 3.2 cm, was surrounded by a thin membrane and contained an area of echogenic material within it of 2.4 X 0.91 cm.

The lesion was not close to the cord insertion, who results marginal. The lesion was compressible by the fetal limb. The 3D imaging was correctly identified the joint and the continuity of the mass with the fetal placental surface.

A color Doppler study of the cyst and Umbilical cord was normal. The fetal growth and the amniotic fluid were regular.

Previous ultrasound exam at 8 weeks of gestation was reported as normal.

During our counseling session we mentioned to the patient that the clinical significance of placental surface cysts depends on the association of fetal growth restriction and that most placental surface simple cysts are associated with normal pregnancy outcomes. The patient agreed to a follow-up ultrasound evaluation.

Subsequent ultrasound examinations at 27th and 32nd weeks' gestation showed a normal fetal growth. Except for the growing cyst, and the apparent reduction of the hyperechogenic content, the prenatal course was uneventful up to 36 weeks. At that time, for the bulky presence of the fetus, has been difficult to measure the cyst, about 8 cm.

A healthy female baby weighing 2,450 g was born spontaneously at 36 weeks and 5 days of gestation. Apgar score were 9 and 10 at 1 and 5 minutes, respectively. Postnatal physical examination of the baby was normal. The placenta weighed 520 g, measured 15 X 18 cm, and had a 60-cm three-vessel cord with velamentous insertion.

On the fetal surface of the placenta a collapsed cystic structure containing a thrombotic mass of about 3 cm with walls of the amnion, was found, located independent from the cord insertion.

A histopathological examination revealed that the lesion was a 8 cm subchorionic cyst, below which there was a 2,6 cm laminated thrombus filled with fibrin

### RISULTATI

Subchorionic hematomas are frequent and usually innocuous and asymptomatic. It may appear as a poorly reflective lesion in the placenta displacing the chorionic and free membranes. This lesion is likely to be the result of a first-trimester marginal placental abruption that has led to blood pooling beneath the chorionic membrane, rather than collecting behind the placenta as happens during the third trimester. As the area degenerates, so the hematoma takes on a cystic appearance, eventually becoming echo-free. When reabsorbed, subchorionic bleeds may present as an hyperechoic deposits on the fetal surface of placenta. It has also been suggested that subchorionic intervillous thrombi may undergo cystic degeneration, leading to cysts on the surface of the placenta. Eddy currents in the intervillous space in this location have been postulated to lead to increased fibrin deposition. Finally some authors suspect that these cysts form in an area of subchorionic fibrin deposition related to X cells (Trophoblasts outside the villi with secretory activity). The chorion becomes thinned by the cyst and balloons outward along with the amnion. They are usually singular and tend to occur more frequency in case of diabetes mellitus or maternofetal Rhesus incompatibility. Sonographically are found as echo-free cavities under the fetal plate. They don't show any blood flow on Color Doppler. Usually don't interfere with fetal circulation. However, in the case reported by Kirkinen and Jouppila, the placental cyst caused fetal growth restriction because of constriction and interference with umbilical cord circulation. There are a number of possible differential diagnoses when considering the finding of a cystic lesion

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in the placenta such as pseudocysts of umbilical cord, maternal lakes, subamniotic hematomas and chorioangioma. Other causes of solid placental masses, such as teratoma and large placental infarcts, are exceedingly rare, although they should be considered in the differential diagnosis because of their well-known association with poor pregnancy outcome. No association between subchorionic hematoma and velamentous cord insertion has been reported in the literature

## **CONCLUSIONI**

The type of lesion we report here seems to be the same as what has been described as chorionic, subchorionic, subamniotic, or membranous cysts. Cystic lesions of placenta are most commonly seen after 25 weeks menstrual age. Their etiology remains controversial and there are contradictory opinions as to their clinical importance. Large or multiple cysts may be a causative factor in IUGR especially when attached in close proximity to the umbilical cord insertion site.

We have followed the evolution of this cyst in size, ultrasonographic, color doppler and 3D features, his relationship with the cord, the fetus and the placenta. We could have had the support of his nature by pathological evaluation. Our case demonstrates that, in the evolution of the pregnancy, this type of lesion did not find correlations with fetal pathologies and pregnancy complications related to his presence



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## 64. PRENATAL PRESACRAL MASS: A CHALLENGING DIAGNOSIS

### LISTA AUTORI

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### INTRODUZIONE

The sacrococcygeal teratoma (SCT) is the most common extragonadal germ cell tumor, representing 15% of neonatal oncological diseases. SCT affects more frequently females than males (F/M ratio = 2/4:1) with a reported incidence of 1 in 20,000–40,000 live births. Generally SCT occurs sporadically but a family history can be reported in 10% of cases.

SCTs may be recognized prenatally after the 18th week of gestation even if they are typically reported around 32nd week of gestation when teratoma appears as an exophytic mass originating from the sacral region. The differential diagnosis are myelomeningocele, neuroblastoma, hemangioma, lipoma and leiomyoma. The diagnostic work-up soon after birth usually includes abdominal-pelvic x-rays and CT scan in order to identify calcifications or sacral anomalies and to define the involvement of neighboring structures, respectively. MRI is performed in the suspicion of a spine involvement or for the differential diagnosis. Evaluation of serum markers such as  $\alpha$ FP and  $\beta$ HCG is essential for diagnosis and prognosis

### MATERIALI E METODI

We present a case of prenatal diagnosis of anterior sacrococcygeal cystic mass resulted as a SCT after surgical resection

### RISULTATI

A neonate (female) was delivered by caesarean section at 32+6 weeks of gestational age on suspicion of spina bifida. The mass was first detected in the fetus by ultrasound and confirmed by MRI scan afterwards, revealing a completely liquid appearance due to cystic teratoma without complications; the examination did not exclude the possibility of an anterior meningocele, which was reported in the maternal family history. Maternal serology, vaginal swab and screening for chromosomal diseases were normal. At birth good adaptation to extrauterine life, auxological data within range. She was asymptomatic and neurological problems were not evident. Ultrasonography of the lower back performed in the first day of life showed the presence of a cyst (30x25x32 mm) in the subcutaneous tissue, posterior and caudal to the medullary cone, which was compatible with spinal dysraphism. Blood exams showed an increased alpha fetoprotein level ( $> 60500$  ng/ml, normal value  $\leq 48,406 \pm 34,718$  ng/ml). Pelvis and lumbosacral MRI was performed showing an homogeneous presacral midline mass with signal characteristics of fluid lesion adjacent to rectum wall without spine cord abnormalities and no evidence of communication between the mass and the neural structures. Given that the mass might be a sacrococcygeal teratoma, surgery was performed at one month of life with complete excision of mass. Posterior sagittal approach was used with sphincter sparing. Macroscopic feature of mass consisted of multiple cyst with different content. The histological diagnosis was of "mature multilocular teratoma". Last follow up done at one month after surgery and patient was well and healthy

### CONCLUSIONI

To date the diagnosis of presacral mass can be done in antenatal period by ultrasound and fetal MRI. However the differential diagnosis of presacral mass with cystic feature is so much difficult and many possibilities can be considered. For this reason, the surgical management is the first option of treatment and the histological exam is the single most important procedure to definitive diagnosis

## 65. PREVENZIONE DELLA TRASMISSIONE VERTICALE DELL'INFEZIONE DA HBV

### LISTA AUTORI

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### INTRODUZIONE

La trasmissione materno-fetale rappresenta una modalità frequente di trasmissione dell'infezione da HBV e può avvenire sia per via verticale (intrauterina, al momento del parto e durante l'allattamento), sia per via orizzontale (contatto giornaliero). In assenza di interventi specifici, circa il 90% dei nati da madri HBsAg e HBeAg positive ed il 5-20% dei nati da madri HBsAg positive e HBeAg negative si infetta. Anche dopo lo sviluppo di vaccini efficaci, l'1-9% dei nati da madri con infezione da HBV acquisisce tale infezione ed il maggiore fattore di rischio sembra essere rappresentato dal livello di HBV-DNA.

La prevenzione dell'infezione verticale da HBV rappresenta un compito complesso. Lo screening universale dell'HBsAg nelle gravide è essenziale. Le gravide HBsAg positive devono essere valutate da uno specialista infettivologo in modo da definire lo stato della malattia epatica (livello di HBV-DNA e stato dell'HBeAg) e porre l'eventuale indicazione ad una terapia antivirale.

Alla nascita, la profilassi è in grado di ridurre notevolmente il rischio di infezione. I nati da madre HBsAg positive devono ricevere la prima dose di vaccino anti-HBV e le immunoglobuline anti-HBV (HBIG) entro 24 ore dalla nascita. Comunque, anche con l'utilizzo di questa strategia combinata, persiste un rischio residuo di trasmissione verticale, che si osserva soprattutto nei nati da madre con alta carica virale (> 108 cp/ml) e positività per HBeAg.

Secondo la letteratura, più del 90% dei neonati che ricevono la profilassi post-esposizione e che completano il ciclo vaccinale mostra livelli protettivi di anticorpi anti-HBs e la memoria immunologica e la protezione a lungo termine si mantengono nel tempo.

Nel presente studio è stato valutato il tasso di infezione e di protezione anticorpale in bambini nati da madre HBsAg positiva presso l'U.O. di Neonatologia dell'Ospedale L. Sacco nel triennio 2013-2015

### MATERIALI E METODI

In tutti i neonati da madre HBsAg positiva, previa raccolta del consenso informato da parte dei genitori, è stata eseguita profilassi post-esposizione mediante vaccinazione con vaccino monovalente (Engerix-B 10 microgr: 0.5 ml im.) entro 12 ore dalla nascita, associata a somministrazione in sede diversa di immunoglobuline (HBIG: 200 UI im per i nati con peso > 2000 gr e 100 UI im per i nati pretermine con peso < 2000 gr).

Tutti i neonati sono stati inviati alla ASL di riferimento al fine di garantire un adeguato completamento del ciclo vaccinale (II, III e IV dose di vaccino da somministrare al 2°, 3° e 11° mese di vita rispettivamente); i soggetti, inoltre, sono seguiti con visite ambulatoriali per valutare le condizioni generali e la crescita staturale-ponderale (3 e 15 mesi di vita), per verificare l'adeguata esecuzione del calendario vaccinale (3 e 15 mesi di vita) e per eseguire la ricerca di HbsAg e HbsAb (15 mesi di vita) per valutare, rispettivamente, l'eventuale passaggio dell'infezione e la risposta immunologica al termine del ciclo vaccinale

### RISULTATI

Nel triennio 2013-2015 sono nati 41 neonati da madre HBsAg positiva.

In nessuno dei soggetti è stata documentata una positività di HBsAg e in tutti i casi è stata verificata un'adeguata protezione anticorpale al termine del ciclo vaccinale

### CONCLUSIONI

La prevenzione della trasmissione verticale dell'infezione da HBV è una sfida importante, che coinvolge ginecologi, infettivologi e pediatri. La trasmissione perinatale dell'infezione può essere controllata mediante la combinazione di screening materno universale per HBsAg, eventuale trattamento antivirale, profilassi post-esposizione e test post-vaccinazione. Una sempre migliore applicazione di tali strategie potrebbe portare ad una riduzione della percentuale di fallimento della profilassi perinatale, attualmente ancora troppo elevata (5-10%)

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## **66. PROCEDURAL PAIN IN NEWBORNS: AN OVERVIEW ABOUT DIFFERENT ANALGESIC TOOLS**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Heel pricks and venipunctures are commonly performed in Neonatal Units to obtain blood samples for analyses. The Premature Infant Pain Profile (PIPP) is a widely used scale for evaluate acute pain in term and preterm babies. Our aim was to assess how effective are the analgesic strategies commonly used during painful routine procedures, and to identify the most effective analgesic strategy

### **MATERIALI E METODI**

We performed a PubMed research from 1999 to 2013. We retrieved all papers in English language that evaluated pain during neonatal heel prick or venipuncture. We included only the papers that expressed PIPP scores as means and standard deviations, or means and 95% confidence intervals

### **RISULTATI**

Fifteen papers met the inclusion criteria. Among them, only two studies used the same analgesic method. We did not find any significant difference between heel prick and venipuncture. A significative difference with placebo was evident when oral sugar was used at concentrations greater than 10%. Sensorial saturation and non-nutritive sucking along with solution of 10% of glucose seemed to be the most effective analgesic tools

### **CONCLUSIONI**

A large amount of analgesic methods was used. Newborns' pain is still far to be correctly treated; which is the best type of analgesia is still to be decided, but those that use multiple stimuli seem to be the more effective analgesic tools



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## 67. REDUCED RENAL VOLUMES AND ELEVATED LEVELS OF CYSTATIN-C IN THE URINE OF NEONATES WITH IUGR

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### INTRODUZIONE

Nephrogenesis is normally completed by the third trimester between 32 and 36 weeks of gestation; at the end of this period, each kidney has 900.000-1.000.000 nephrons, although the number can vary widely, in correlation with birth weight; once the nephrogenesis has stopped, there is no possibility of forming new nephrons later in life. An increasing number of investigations shows an association between intrauterine growth retardation (IUGR) and limited fetal kidney development, as first documented by autoptic studies.

In this regard, exposure to IUGR can negatively impact the nephrogenesis, supporting the hypothesis that IUGR represents a risk factor for impaired renal function resulting from a reduced nephron number and a decreased renal size, causing loss of filtration surface area, single nephron hyperfiltration, glomerular hypertension and long-term renal disease as clearly demonstrated by epidemiological studies. The assessment of kidney growth is currently performed using ultrasounds scans; however, to date, no biochemical marker has been evaluated in association to renal volume reduction and IUGR. Cystatin C (Cys-C) is a strongly basic secretory protein produced at a constant rate in all nucleated cells. Due to its low molecular weight (13,3 kDa), Cys-C is freely filtered in the kidney glomerulus with no retrieval back to the circulation; in proximal tubular cells, Cys-C is predominately reabsorbed and subsequently catabolized; thus, in the urine, the concentration of Cys-C is normally low and high levels reflect an abnormal reabsorption by tubular cells.

The aim of this study was to investigate the urinary excretion of Cys-C simultaneously with the assessment of renal volumes, in AGA and IUGR neonates, in order to evaluate its clinical value in IUGR newborns

### MATERIALI E METODI

Twenty 20 neonates with IUGR and 34 healthy controls defined as AGA (Adequate for Gestational Age) were prospectively recruited from the newborn nursery at S. Maria della Misericordia's Hospital. The diagnosis of IUGR was assigned to neonates with a birth weight below the 10th centile for gestational age and with early altered placental fetal hemodynamics (evaluated by Doppler US).

Whole renal and renal cortex volumes were evaluated by echo 3-D combined with Vocal II volume software, a general imaging 3D quantification software, (GE Ultrasounds, USA), at 30-40 day.

Morning urine samples were collected using a U-bag collection device, at the same day.

Urinary Cys-C levels were measured with The DetectX® Human Cystatin C kit (Arbor Assays, Catalog Number K012-H1; Ann Arbor, Michigan 48108 USA), an enzyme-immunoassay (EIA) designed to quantitatively measure human Cys-C present in biological samples and tissue culture media, according to the manufacturers' instructions

### RISULTATI

Renal cortex volume was closely related to whole renal volume and both of them correlated to gestational age and to birth weight ( $p < .0001$ ). Their measurements in IUGR newborns were significantly lower than those found in AGA newborns (mean  $\pm$  SD; whole renal volume:  $19.83 \pm 4.5$  vs  $32.68 \pm 4.16$ ; renal cortex volume:  $8.0 \pm 1.95$  vs  $14.1 \pm 2.9$ ); conversely, urinary Cys-C levels in IUGR were significantly higher than in AGA neonates (mean  $\pm$  SD:  $18.0 \pm 13.7$  vs  $3.46 \pm 4.61$ ) (Fig.1). The overall data of Cys-C showed a significant, inverse correlation with whole renal and renal cortex volumes, birth weight and gestational age

### CONCLUSIONI

IUGR impacts adversely the number of nephrons in the newborn's kidney; neonates below the 10th percentile of birth weight had 30% fewer glomeruli than the neonates with birth weights above the 10th percentile. However, if the growth restriction occurs at a late stage of gestation, when nephrogenesis is complete (or nearing completion), this relationship does not exist. Recently, it has been described that a reduced complement of nephrons at the beginning of life, in infants born IUGR, may increase the risk of kidney damage and lead to long-term risk of renal disease. When the number of nephrons is reduced, the compensatory hypertrophy pushes the glomeruli to function under increased intracapillary hydraulic pressure, which, over time, causes damage to the capillary walls. First, in this study we found that offspring with IUGR showed a statistically significant elevation of urinary Cys-C correlated to significant reduction of renal cortex volume, compared to controls ( $p = 0.001$ ). Since urinary cystatin-C quantification has been validated as a good reflection of tubular function, its increased urinary elimination in IUGR could be indicative of a reduced degradation and reabsorption. In conclusion, detection of high levels of urinary Cys-C in IUGR neonates could be considered an early precursor of renal injury and a biochemical marker to identify IUGR neonates that could be monitored for risk of renal ultrafiltration, in addition to estimation of the renal cortex volume with 3D ultrasounds

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## 68. ROLE OF THE LACTOFERRIN IN THE PREVENTION OF PRETERM DELIVERY

### LISTA AUTORI

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### INTRODUZIONE

Preterm delivery is a pathological condition with multifactorial etiology, in which converge maternal, fetal or placental components. It represents the most important cause of neonatal morbidity and mortality and it is also the cause of pathological sequelae in the long term. In the clinical management of pregnancies at risk of preterm birth, the use of corticosteroids, effective for the induction of the fetal lung maturity, and the use of tocolytic drugs, are usually associated with the use of vaginal progesterone. The antimicrobial activity is very important in the context of preterm birth. Lactoferrin is a component of the innate immune system of mammals with bacteriostatic, bactericidal, fungicidal and anti-inflammatory activity. Its possible use as an adjuvant in the prevention of preterm delivery is also supported by some studies conducted on animal and human models.

The aim is to assess the effectiveness of vaginal lactoferrin versus vaginal progesterone in a selected category of patients presenting risk of preterm delivery, in particular its effectiveness in terms of prolongation in days of the gestation and improvement of neonatal outcome

### MATERIALI E METODI

This is a multicenter randomized study that includes singleton pregnant women, admitted for risk of preterm birth and a reduced cervix below 25 mm, between 24 and 34 weeks of gestation. Inclusion criteria are: cervical length below 25 mm, in the presence or absence of funneling; uterine neck no shortened by 50% and no dilated more than one centimeter; number of contractions of not more than 4 in 30 minutes or 8 in one hour; singleton pregnancy; the absence of clinical and/or biochemical signs of suspected chorioamnionitis or premature rupture of membranes. When the patient meet the inclusion criteria, is randomized and is treated or with bovine vaginal lactoferrin 300 mg or 200 mg vaginal progesterone, up to 34 sg. During the study all women were monitored with sonography examination, biochemical and microbiological markers

### RISULTATI

Fifty patients were enrolled, 23 in lactoferrin group and 28 in progesterone one. These preliminary data show that there was not difference between the groups in terms of prolongation in days of the pregnancy (56.5 days,  $p=1$ ). Thirty-nine percent of women treated with vaginal progesterone experienced spontaneous preterm birth versus 15% of those treated with vaginal lactoferrin. Women treated with lactoferrin showed a decrease of inflammation markers during the recovery. Four newborns were hospitalized in NICU, 2 of lactoferrin group and 2 of progesterone group, with greater morbidity and more days of hospitalization in the last one

### CONCLUSIONI

There is no evidence that vaginal lactoferrin is more effective than vaginal progesterone in prevention of preterm birth. Furthermore we showed that vaginal lactoferrin represents, in a selected pregnant population, a possible alternative of vaginal progesterone, probably due to its anti-inflammatory activity that could prevent uterine contractions, cervical modifications and finally preterm delivery



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## **69. SERUM VITAMIN D LEVELS IN A SAMPLE OF CAUCASIAN PREGNANT WOMEN AT FIRST TRIMESTER LIVING IN MILAN**

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### **INTRODUZIONE**

Vitamin D deficiency in pregnancy has been associated with an increased risk of pre-eclampsia, gestational diabetes mellitus, preterm birth, small-for-gestational age infants, impaired fetal skeletal formation causing infant rickets and reduced bone mass. Immune dysfunction, placental implantation, excessive inflammation and hypertension in the mother have also been associated with vitamin D deficiency. Despite the important role of vitamin D in pregnancy, there is little data available about exposure to this vitamin in Caucasian pregnant women living in Italy.

The aim of this study was to measure serum 25-hydroxyvitamin D (25(OH) D) in a sample of women at first trimester of pregnancy living in Milan and to investigate the association with sun exposure and dietary pattern

### **MATERIALI E METODI**

Eighty-seven pregnant women ( $18.5 < \text{BMI} < 29.9 \text{ kg/m}^2$ ) were enrolled between 11 and 14 weeks gestational age at Sacco Hospital, based in Milan. At the enrollment, anthropometric measures were assessed, blood samples were collected for the assessment of serum 25(OH) D, and questionnaires about sun exposure and food frequency consumption were administered

### **RISULTATI**

The sample included 67 normal weight and 20 overweight pregnant women. Severe vitamin D deficiency (25(OH) D  $< 20 \text{ ng/ml}$ ) was found in 46% of the sample while only 18.4% of the sample showed normal serum levels of 25(OH) D ( $\geq 30 \text{ ng/ml}$ ). 17% of women with severe deficiency and 44% of women with normal levels were taking multivitamin supplements containing  $10 \mu\text{g}$  of vitamin D. A significant association was found with sun exposure ( $\beta=0.24$ ,  $p=0.03$ , adjusted for multivitamin supplement), while no significant relation was observed with food potentially a source of vitamin D such as dairy products, eggs and fish

### **CONCLUSIONI**

Our data confirm that vitamin D deficiency is frequent and suggest that lifestyle counseling and supplement prescription should be encouraged in pregnant women

## **70. SONOGRAPHIC ASSESSMENT OF PLACENTAL LOCATION: A MERE NOTIONAL DESCRIPTION OR AN IMPORTANT KEY TO IMPROVE BOTH PREGNANCY AND PERINATAL OBSTETRICAL CARE? A LARGE COHORT STUDY**

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### **INTRODUZIONE**

Ultrasound imaging has become an integral component of routine prenatal medical care; both the American College of Obstetricians and Gynecologists and the American Institute of Ultrasound in Medicine recommended that the standard obstetric sonogram in the second and/or third trimester should include the evaluation of placental position and morphology, the estimation of amniotic fluid volume, and the evaluation of both the morphology and function of the umbilical cord.

While abnormalities in amniotic fluid volume and umbilical cord Doppler velocimetry immediately alert the sonographer, sonographic assessment of placental location (PL), after exclusion of previa or marginal insertion, is often limited to a mere notional description without any link to possible implications on pregnancy and childbirth.

There is a relative paucity of data regarding PL and subsequent pregnancy and delivery outcomes. Furthermore, studies of its association with specific obstetric complications have reached contradictory conclusions and no consensus has yet been achieved regarding the relationship between PL and non-vertex fetal presentation (FP) at term.

The first aim of the study was to evaluate the existence of a correlation between sites of PL and FP at birth. Secondly we evaluated if specific sites of PL were associated with spontaneous cephalic version before delivery in the cohort of patients with non-cephalic FP observed sonographically at the beginning of the third trimester of pregnancy.

Finally, we investigated possible correlations between the site of PL and maternal features (age, parity, smoking habits, pre-conceptional BMI, type of previous delivery), characteristics of pregnancy (spontaneous or assisted conception, pregnancy weight gain, gestational age at delivery, third trimester complications), delivery and neonatal outcome (mode of delivery, third stage complications, neonatal features and well-being at birth, placental weight and morphology)

### **MATERIALI E METODI**

In the period between January-2012 and September-2013 we conducted an observational prospective cohort study on 1056 pregnant women referred to the Ob/Gyn Unit of Padua University for routine third trimester scan (gestational age 29-31 weeks).

We considered eligible for the study single fetus pregnancies having complete clinical records of all antenatal visits beginning from the first trimester and defined as uncomplicated upon recruitment, patient proficiency in Italian language and with an expressed intention to continue pregnancy care until delivery at our Clinic. We excluded pregnancies with a maternal history of pre-gestational diabetes and/or hypertension, patients on dietary calcium supplementation due to an estimated increased risk for preeclampsia, history of previous uterine surgery (including both the cervix and corpus uteri), with the exception of uncomplicated cesarean section (CS), patients who chose VBAC (vaginal birth after cesarean) or attempted external cephalic version, placenta previa, abnormalities in amniotic fluid volume (oligo and polyhydramnios) and estimated fetal weight greater than 75° or lower than 25° centile.

A standard ultrasound was performed on all eligible patients at the beginning of the third trimester of pregnancy (29-31 gestational weeks) and at term (38 gestational weeks). Patients who delivered preterm were evaluated sonographically upon delivery room admission.

The ultrasound examination was performed by one of the researchers (SG) previously trained in the use of intrapartum ultrasound. The trans-abdominal scan was performed in maternal supine position with a 3.5 MHz convex probe AB2-7-RS (Voluson e6 compact-GE Healthcare, GE Medical Systems Ltd, Hatfield, AL9 5EN).

Data regarding maternal features (age, parity, mode of delivery in previous pregnancies, pre gestational BMI, weight gain during pregnancy) was collected for all patients.

At recruitment, the following data was entered into a computerized database: spontaneous or assisted conception, gestational age, FP and eco-biometry, placental location (anterior, posterior, lateral, or fundal) and amniotic fluid index.

Following delivery, data regarding gestational age, third trimester pregnancy complications (gestational diabetes, hypertension/preeclampsia, threat of preterm birth, placental abruption, pPROM, preterm birth), fetal presentation, mode of delivery (vaginal spontaneous or operative, cesarean section elective or urgent), length and complications of the third stage of labour (for vaginal delivery alone) was collected for all patients included in our study.

We also considered neonatal sex, weight, umbilical pH values and necessity of intensive care.

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Finally, we completed the dataset by recording information concerning placental fresh weight and macroscopic features (regular, bilobed, succenturiate lobed, circumvallate/circummarginate, velamentous cord insertion).

Statistical analysis was performed by SPSS software (Chicago, IL) for Windows version 19, applying parametric and non-parametric tests when appropriate. The Kolmogorov–Smirnov test was used to assess the normality of distribution. Continuous variables were expressed as absolute numbers, average  $\pm$  standard deviation, and analyzed by Student-t test or Anova test when appropriate; categorical variables were expressed as percentages and analyzed through the  $\chi^2$  test or the Fisher's exact test, when appropriate. Statistical significance was defined as p values  $< 0.05$

## RISULTATI

The correlation of data regarding the site of PL and FP at birth showed significant statistical differences between anterior and non-anterior insertions: pregnancies with an anterior PL had a 1.4% of non-cephalic fetuses (all breech presentations) as opposed to 8.9% in posterior (7.9% breech, 1.0% transverse presentations), 6.2% in fundal (all breech presentations) and 7.2% in lateral insertions [ $p < 0.05$ ]. Similarly, regarding placental site and FP observed at the beginning of the third trimester, the percentages of non-cephalic fetal presentations showed a statistically significant difference: 11.1% of anterior (54 breech, 10 transverse presentations), 44.3% of posterior (134 breech, 11 transverse presentations), 29.6% of fundal (23 breech, 1 transverse presentations) and 31.9% of lateral insertions (18 breech, 4 transverse presentations) [ $p < 0.001$ ].

The concordance between FP at the beginning of the third trimester and the presentation at birth showed a percentage of 90.3% in anterior PL while of 63.3% in posterior and 76.5% in lateral insertions [ $p < 0.001$ ].

Considering only non-cephalic fetuses we found a statistically significant decreasing probability of spontaneous cephalic version at birth: 88% in anterior, 80% in posterior, 77% in lateral, and 70% in fundal insertion sites [ $p < 0.05$ ].

Considering maternal obstetrical history, we found a significant association between previous CS and posterior PL in the following pregnancy [ $p < 0.05$ ]. We observed a posterior PL in 37.1% of patients who delivered by CS versus 25% of those who delivered vaginally. Additionally patients with posterior PL showed a significantly higher rate of CS 27.5% when compared to those with PL in different uterine sites 18.6% [ $p < 0.01$ ].

Considering pregnancy outcome in relation to PL, we found significant differences only in the diagnosis of gestational hypertension which was identified in 5.5% of posterior insertions, 3.1% of anterior insertions, 1.2% of fundal insertions and no cases observed in pregnancies with a lateral insertion [ $p < 0.05$ ].

Finally, significant differences were also found in terms of fresh placental weight, with the highest weight detected anteriorly (mean value  $632.22 \pm 112.39$  grams) and the lowest posteriorly (mean value  $582.56 \pm 121.08$ ) [ $p < 0.05$ ].

## CONCLUSIONI

In the era in which reducing the primary cesarean delivery rate represents a worldwide priority, an investigation focused on PL and its impact on fetal presentation at term should be relevant.

Our data clearly demonstrated that PL may have a strong impact on non-cephalic FP at birth.

In particular placental location may behave as an intrauterine factor potentially capable of influencing the physical conditions (gravity, maternal posture, fetal neurological development) that favor the fetal body axis posture that is manifested by cephalic presentation. Probably because the anterior site of PL is associated with a greater placental volume as opposed to other insertion sites.

It may be possible to hypothesize that fetuses with an anterior PL at the beginning of the third trimester may "passively" assume, by body rolling rather than by sudden extension of the legs and/or by kicking due to low fetal weight and immaturity of the central nervous system, the most convenient position as influenced by gravity.

Our data clearly demonstrated that while only 11.1% of fetuses with anterior PL were found to be in breech presentation at the beginning of the third trimester of pregnancy, by delivery this fetuses had demonstrated the highest rate of spontaneous rotation into the cephalic position. This fact probably confirms the assumption that in the event of an anterior placental location, the most "spontaneous and natural" convenient behavior for the fetus is that of assuming cephalic presentation.

On the contrary, fetuses with posterior, fundal, or lateral PL, shift from breech to cephalic later in intrauterine life. This fact might be explained by two theoretical assumptions: the first being that, when the placenta is located in a non-anterior site, the fetus has the "need" to assume a "gravity position" later in gestation, the second is that in a non-anterior placental site, a cephalic positioning generally requires an "active" fetal involvement that depends on a higher degree of neuromuscular development typically reached in later stages of gestation.

In conclusion, considering the placenta as an "active and integral part of gestation" may help us comprehend the physiopathological mechanisms responsible for events previously considered as "casual or idiopathic"



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## 71. THE FETUS IS WHAT THE MOTHER EATS

### LISTA AUTORI

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### INTRODUZIONE

In the last years, there has been a thrilling development and profound changes in our understanding the effect of maternal nutrition on development and health of the fetus and child. Several studies have established the health benefits of the "Mediterranean Diet" (MD), and have related the adherence to this diet with a reduced susceptibility to develop obesity, metabolic syndrome, type 2 diabetes, cardiovascular and neurodegenerative diseases and cancers. As a consequence the monitoring of dietary intake has become an integral part of pregnancy. Dietary changes have a low cost and low risk compared to medical interventions, and even a moderate increase in vegetables and plant foods intakes may be of public health importance. Regarding placental development, the placenta plays a key role in nutrients' supply regulation of the fetus and in hormones production. Therefore, any factor or stimulus that alters the trophoblast's hormonal function causes alterations of placental function and therefore could induce an error in the fetal programming, which predispose to chronic disease in adulthood, especially cardiovascular ones. Pregnancy has been considered a cardiovascular "stress test" that opens a window on women's future cardiovascular diseases and which might be used as a measure of future cardiovascular risk. The purpose of our study is to demonstrate the link between Mediterranean Diet adherence in pregnancy and materno-fetal outcome

### MATERIALI E METODI

Sixty-one pregnant woman will be enrolled at the Reproductive Medicine Unit of the University of Naples Federico II, during routine ultrasound screening in the second trimester of pregnancy, from October 2014 to date. Inclusion criteria are age between 18 and 40 years, no metabolic diseases in the current or in previous pregnancy, absence of major fetal defect. All the participating woman signed an informed consent. At recruitment and following time-point (28-32 weeks) the patients received a nutritional validated questionnaire in addition to measurement and evaluation of biochemical and ultrasonographic standard parameters. We have collected personal and anthropometric data of pregnant women at enrollment; weight and height were appropriately taken using a several weight scales and stadiometer for medical use. We assessed the degree of pregnant women's Mediterranean diet adherence and investigated the correlation between lifestyle in pregnancy and the onset of complications such as gestational diabetes, preeclampsia, or the risk of preterm delivery and neonatal outcomes. Student's t-test was used to compare continuous variables (maternal age, gestational age at delivery, BMI) and the chi-squared test was used to compare all maternal and perinatal outcomes. The food questionnaire PREDIMED used to assess the Mediterranean diet adherence is divided into 14 points. It was given a quantitative score to Mediterranean diet adherence. We divided the pregnant women in two groups according to the median: A group with low adherence (score from 0 to 7) and B group with high adherence (score from 8 to 13)

### RISULTATI

We compared two groups of homogeneous pregnant women for data on pre-pregnancy weight, weight gain, blood pressure, maternal and fetal outcomes. We selected 23 patients in A group and 38 pregnant with high adherence (B group). In A group we found two gestational diabetes (8%), one case of pre-eclampsia (5%) and preterm labor in three patients (13%). In B group we found one case of gestational diabetes (3%), three patients with pre-eclampsia (8%) and preterm labor in two pregnant women (11%).

The A and B groups showed no significant differences in terms of pregnancy's outcomes and development of complications. Women with greater Mediterranean diet adherence had less weight gain during pregnancy than those with low adherence. Statistical analysis of the results showed no significant differences with respect to: birth weight, APGAR score. The birth weight of children studied was 3196.58 +/- 455.62. Pregnant women with low adherence have given birth to children with an average weight of 3155.85 +/- 468.54 and those with high adherence an average weight of 3218.38 +/- 449.44 ( $p = 0.422$ ). The APGAR score in A group was 8.19 +/- 0.52 to 9.02 +/- 0.37 1 minute and 5 minutes; in B group was 8.04 +/- 0.71 ( $p = 0.184$ ) at 1 minute and 8.93 +/- 0.36 ( $p = 0.146$ ) at 5 minutes. No statistically significant difference was found between the two groups

### CONCLUSIONI

The available data are still preliminary and very few. We believe it is necessary to continue the study and expand the sample size, to obtain results of greater significance. Although we have not yet provided highly significant data, our study has, however, allowed to highlight good compliance of the women surveyed and a high degree of liking for nutritional suggestions in pregnancy. Nutritional support for the mother, especially if provided by highly qualified professionals, could represent a useful and valuable aid in maintaining optimal clinical conditions during pregnancy.



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We hope to demonstrate that the adherence to dietary advice to consume a diet abundant in vegetables and fruit may be beneficial with regard to perinatal and maternal outcomes. A reduction in circulating inflammatory biomarkers observed in subjects adhering to the MedDiet could be one of the mechanisms, as chronic low-grade inflammation is considered a pathogenetic factor. Pregnant women should consume a well-balanced diet rich in a variety of macro- and micronutrients; variation in the quality or quantity of nutrients consumed by mothers during pregnancy can exert permanent and powerful effects upon developing tissues



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## 72. THE IMPACT OF BODY MASS INDEX ON MATERNAL AND NEONATAL OUTCOMES

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### INTRODUZIONE

Obesity has become an epidemic worldwide. Maternal obesity contributes to increase morbidity and mortality for mother and child. Obese women are less likely to go into labor spontaneously, they are more likely to have a prolonged pregnancy and increased risk of induction of labor. After birth, obese women are less likely to breastfeed successfully, have a longer hospitalization and higher risk of postnatal infection. Obesity is also associated with a higher risk of neonatal complications including stillbirth, congenital anomalies, admission to intensive care, and neonatal death. Few studies have analyzed birth outcomes using the classification of body mass index (BMI), according to the World Health Organization (WHO), obesity is divided into class I, II, and III. The objective of this study is to assess the impact of BMI using the WHO classification on maternal and neonatal outcomes

### MATERIALI E METODI

This is a retrospective study that analyzes the deliveries between 2010 and 2015 in a tertiary center. A total of 13,673 women were considered, divided into groups according to BMI pre-pregnancy. Exclusion criteria were: births less than 37 weeks gestation, pregnancies obtained with IVF, multiple pregnancies and the absence of maternal pre pregnancy BMI. The BMI ( $\text{kg} / \text{m}^2$ ) was calculated from height and weight measured during prenatal visits.

The WHO classification was used: underweight (BMI  $< 18.50 \text{ kg} / \text{m}^2$ ); normal weight (BMI 18.50 to  $24.99 \text{ kg} / \text{m}^2$ ; reference group); overweight (BMI 25.00- $29.99 \text{ kg} / \text{m}^2$ ); class I obese (BMI 30 to  $34.99 \text{ kg} / \text{m}^2$ ); Class II obese (BMI 35 to  $39.99 \text{ kg} / \text{m}^2$ ); and class III obese (BMI  $40 \text{ kg} / \text{m}^2$ ). Four groups were obtained: group of normal-weight patients (10,894), overweight women (2,025), obese class I (544), obese class II and III (210). Statistical analysis of data was performed using the Statistical Package for IBM Social Sciences (SPSS). Ordinal variables were analyzed using The Pearson Chi Square test and the Fisher Exact test for comparison between the two groups; continuous variables were analyzed using the Mann-Whitney U test runs on two independent samples. A p-value less 0.05 was considered statistically significant

### RISULTATI

The analysis was conducted by comparing the variables of the control group (patients of normal weight,  $n = 10,894$ ) with the three groups of cases divided by BMI. The comparison between the control group and the three groups of obese patients did not show statistically significant differences with regard to age, ethnicity, smoke, alcohol consumption, previous caesarean section, previous spontaneous labor. Comparing the group of normal weight with overweight and obese class I showed a statistically significant difference for previous miscarriages, cesarean section, afterbirth manual, fetal death in utero. It was interesting to note that babies born to normal-weight women were slightly longer (although the median was the same) but the birth weight was greater in infants born to overweight and obese class I mothers (abnormal distribution of fat from birth, most newborns were shorter and heavier in overweight women). Apgar at 1 and 5 minutes was worse in infants born to overweight and obese class I, the placental weight was greater for overweight while it was lower for obese class I compared to normal weight. Obese class II-III vs normal weight had an increased rate of caesarean section, manual afterbirth, and MIF. Although there was a higher percentage in the obese group, previous miscarriages were not significant in this group, probably because the sample was smaller. Interesting to note was that infants born to women of normal weight were as long as the infants born to obese class II (although here the median was different) but the birth weight was greater in infants born to mothers obese class II (abnormal distribution of fat since from birth). Apgar was worse in infants born to obese class II-III, the placental weight was greater for obese class II-III compared to normal weight

### CONCLUSIONI

This large retrospective study clearly shows that being overweight or obese increases the risk of adverse maternal and neonatal outcomes. In particular, for the categorization of sub classifications regarding obesity in this study, a relationship emerged between the increase in BMI (from overweight to obese class III) and an increased risk of adverse outcomes.

In terms of neonatal outcomes, the maternal BMI clearly influences the birth weight and women in class II-III obese are more likely to have a macrosomic baby. This study suggests that obese women are more likely to require specialized medical care during pregnancy and childbirth, and their newborns need more assistance after birth. It was also surprising to note that the rate of intrauterine fetal mortality increased to a statistically significant degree for all three groups of overweight and obese women compared to women of normal weight. Finally, women who are overweight or obese are less likely to have a normal birth without medical intervention, and are more likely to undergo cesarean section

## 73. THE IMPORTANCE OF THE CEREBROPLACENTAL RATIO IN FGR $\geq 34$ WEEKS

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### INTRODUZIONE

The cerebroplacental ratio (CPR) represents the interaction of increased diastolic flow to the brain (brain sparing) and decreased end diastolic flow in the umbilical artery (increased placental resistance).

It can be easily calculated by dividing the Doppler indices of middle cerebral artery (MCA) by the umbilical artery (UA).

Recent study correlated abnormal CPR with adverse perinatal events and associated post natal neurological outcome.

The purpose of this study was to describe the role of cerebroplacental ratio (CPR) in the prediction of adverse perinatal outcome in growth restricted fetuses (FGR), delivered  $\geq 34$  weeks and to determine whether this test should be considered for integration into clinical practice

### MATERIALI E METODI

Data regarding all consecutive singleton growth restricted fetuses diagnosed prenatally at the Department of Obstetrics and Gynaecology, MBBM Foundation, San Gerardo Hospital, Monza, Italy were collected in a dedicated database.

465 women delivered at  $\geq 34$  weeks were recruited.

Diagnosis of FGR was based on ultrasonographic measurement of abdominal circumference (AC) below the 10th percentile.

All patients were managed with ultrasonographic measurements of fetal biometry every two weeks, and in addition Doppler velocimetry studies of the fetal UA, MCA, and Uterine artery Doppler were performed. The frequency of testing was increased if results were abnormal or borderline. Obstetrical variables available within 2 weeks of delivery were considered for the analysis.

The middle cerebral artery and umbilical artery pulsatility indices were converted in CPR. Abnormal CPR, defined as a result less than 1, were related to a composite of adverse outcomes that included admission to the neonatal intensive care unit (NICU) for a period of 15 days or more, and/or hypoglycemia, hyperbilirubinemia, respiratory distress requiring respiratory support more than 24 hours, intraventricular hemorrhage, need for total parenteral nutrition, necrotizing enterocolitis, sepsis

### RISULTATI

Of 465 pregnancies meeting our inclusion criteria, a total of 81 cases (17%) had an adverse composite outcome.

There were 64 fetuses with an abnormal CPR (less than 1).

Of the 64 fetuses with an abnormal CPR, 45% showed adverse composite outcome vs 13% of fetuses with CPR  $\geq 1$  ( $p < 0.001$ ).

There were 70 (15%) cesarean sections for non-reassuring findings at cardiotocographic monitoring (i.e. bradycardia  $< 100$  bpm, late decelerations, or decreased variability). 31% of fetuses with CPR  $< 1$  was born by caesarean delivery because of fetal distress, compared with 13% of fetuses with normal CPR ( $p < 0.001$ ).

Neonates in the abnormal CPR group had significantly lower birth weight (1.960 g vs. 2.358 g,  $p$  95th percentile;  $p = 0.003$ ) were statistically related with adverse composite outcomes. Stepwise regression analysis showed that abnormal UA PI percentile (OR = 4.16, 95%CI 1.57-11.01) independently predicted occurrence of adverse neonatal outcomes.

In the group of fetuses born after 37th week, CPR  $< 1$  ( $p = 0.007$ ) and the abnormal Doppler of middle cerebral artery (MCA PI  $< 5$ th centile;  $p = 0.040$ ) were statistically related with composite adverse outcomes. Stepwise regression analysis showed that abnormal CPR (OR 4.04, 95%CI 1.57-10.40) independently predicted occurrence of adverse neonatal outcomes

### CONCLUSIONI

FGR fetuses approaching term (after 34 weeks) are at low risk for perinatal mortality: in our study population we did not experience any stillbirth or neonatal death in such population using close surveillance of fetal condition.

Our findings suggest that in growth restricted fetuses (AC  $< 10$ th centile), CPR is an element that identifies fetuses at risk for adverse composite outcome.

Between 34 and 36.6 weeks (late-preterm fetuses), abnormal UA PI provides the clinician with adequate information on risk of adverse neonatal outcome.

In fetuses at term, CPR  $< 1$  is the most important Doppler parameter which provides the clinician information on risk of adverse composite neonatal outcome.

The CPR evaluation, therefore, should be integrated in the clinical management as a predictive element of adverse outcome in fetuses at term

## 74. THYROID AUTOANTIBODIES AND PRETERM LABOR: OUR EXPERIENCE

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### INTRODUZIONE

Thyroid dysfunction is the second most frequent endocrine disease among reproductive-aged women. Most autoimmune diseases occur frequently and they have a potential implication for almost all aspects of reproduction, from fertility to pregnancy itself. Thyroid disease in pregnancy is increasing with rising average maternal ages in developed countries. The normal reference range of serum thyroid stimulating hormone (TSH) is modified during pregnancy. Specifically, production of thyroxine and triiodothyronine increases by approximately 50% to maintain the euthyroid state. Thyroid disease in pregnancy is associated with several adverse outcomes. Some of the most dangerous and costly complications of human pregnancy still remain controversial. Maternal thyroid disease, including subclinical and overt hypothyroidism and hyperthyroidism, is often associated with fetal loss in the first trimester, preeclampsia/eclampsia, intrauterine growth restriction, premature rupture of membranes, placental insufficiency, pre-term birth, caesarean delivery and low birth weight. The presence of thyroid autoantibodies is relatively common in women of reproductive age, with a prevalence of 6-20%. The aim of the study is to evaluate the correlation between preterm birth and presence/absence of thyroid autoantibodies in euthyroid women. We have linked to the presence or absence of thyroid autoantibodies to pregnancy and neonatal outcomes (preterm delivery and low birth weight)

### MATERIALI E METODI

Between June 2013 to June 2015, 110 pregnant women were enrolled in this observational prospective study conducted at the Reproductive Medicine Unit of the University of Naples Federico II. All subjects were screened following recommendations of the Endocrine Society, and gave birth to the hospital. Women with the following conditions were excluded: overt thyroid disorder, previous or present use of thyroxine or anti-thyroid drugs, other autoimmune disease, congenital heart disease and major fetal defect. Thyroid function was tested at the first antenatal examination and was based on trimester-specific reference values. Maternal and perinatal outcomes based on specific guidelines were recorded during this period. A delivery occurring between 28 and 37 completed weeks of gestation was considered premature. We assessed the fetal weight at birth: low birth weight (LBW) was defined as a live birth weight < 2500 g. Gestational age was previously based on last menstrual period, but ultrasound estimation has been increasingly used over time. The patients were divided into two groups: presence (group A) and absence (group B) of thyroid autoantibodies. All participants underwent monthly antenatal examinations until they delivered and were discharged from the hospital. Student's t-test was used to compare continuous variables (maternal age, gestational age at delivery, TSH and fT4 concentrations) and the chi-squared test was used to compare all maternal and perinatal outcomes

### RISULTATI

15/110 patients were positive for thyroid autoantibodies without elevated TSH levels (group A). B group consisted of 95 pregnant women without thyroid autoantibodies. In A group we selected: 6 patients (40%) with preterm birth < 34 weeks of gestation and with birth weight appropriate for gestational age; 9 women (60%) gave birth at term and among these women, 3 babies (33%) had low birth weight. In B group, 7 % of all pregnant women gave birth before the 34th week of gestation and their babies had an appropriate birth weight for the gestational age. 88 women (4%) gave birth at term, but only 84 babies had an appropriate weight for gestational age (96%). Preterm birth was more frequent in euthyroid mothers with thyroid autoantibodies than in euthyroid women without them (40% versus 7 %, P 0.0003). In the A group low birth weight infants were more than in the B group (33% versus 4%, P 0.015)

### CONCLUSIONI

Thyroid hormones play a key role in pregnancy for both mother and fetus.

Several studies have shown an association between abnormal thyroid status and different diseases which would support the recommendation of universal screening for thyroid disease in pregnancy. In agreement with the literature data, our study confirms that thyroid dysfunction are frequently associated with maternal-fetal complications. We find a positive correlation between the presence of thyroid autoantibodies with preterm delivery (p0.0003) and low birth weight (p0.015). Data continue to emerge on the association between thyroid disorders and adverse maternal-fetal outcomes, however an association does not imply the determination of a positive cause-effect relationship.

Thyroid autoantibodies increase the risk of preterm birth and birth weight not appropriate for gestational age. We conclude that thyroid autoimmunity in pregnancy may detrimentally affect pregnancy and birth outcomes. A systematic screening of antibodies and periodic monitoring of the concentration of thyroid hormones may be helpful for a correct management of all patients. Our data emphasize the importance of a thyroid screening in women at risk for thyroid disease during pregnancy and the need for early detection and treatment of thyroid diseases to reduce adverse maternal and fetal outcomes

## **75. TWO MINUTE TRAINING OF NEONATAL BAG AND MASK VENTILATION: IS IT EFFECTIVE IN A LOW RESOURCE SETTING?**

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### **INTRODUZIONE**

Effective bag and mask ventilation is the most important intervention in neonatal resuscitation. A previous study conducted in a high resource setting shows that the quality of face-mask ventilation in a manikin model improved significantly after a structured two-minute training. The effect of this intervention in a low-resource setting remains unknown.

The aim of the study was to assess whether a short training, effective in a high resource country, was able to improve the quality of face mask ventilation in a low resource setting

### **MATERIALI E METODI**

The study was conducted at the Hospital of Kouvè (Togo). Before and after a two-minute training session based on 5 points, local health caregivers were asked to ventilate a neonatal modified manikin (leak-free, with a 50 ml test lung). Using a computerized system (New Life Box Trainer), we measured the following parameters for 1 minute: respiratory rate (RR), peak inflation pressures (PIP) and leak

### **RISULTATI**

Twenty-six subjects (14 males, 12 females), including 2 doctors, 3 medical assistant, 6 midwives and 15 nurses, participated in the study. The median age of participants was 36 years (IQR 29-41). Almost all of them (21/26, 80.8%) had already attended a training in neonatal resuscitation in the last 2 years. The RR (range recommended between 40 and 60 acts/min) was 62 breaths/min (IQR 41-73) and 48 breaths/min (38-60) in the first and second round, respectively ( $p=0.07$ ). The percentage of breaths with PIP in the recommended range (between 20 and 30 cmH<sub>2</sub>O) significantly improved from 1.2% (0-5.1) to 16% (0-59) between the first and second test ( $p = 0.0003$ ). Pressures above 35 cm H<sub>2</sub>O were considered excessive. Between the two trials, the proportion of acts with PIP > 35 cmH<sub>2</sub>O increased from 0% (0-30.8) to 31.6% (0-73.5); ( $P = 0.08$ ). The percentage of significant leak (> 25%) decreased from 98% (91-100) to 49% (25-72), ( $p < 0.0001$ )

### **CONCLUSIONI**

A 2-minute training on face-mask ventilation was useful in a high resource setting, but has a limited impact health caregivers in a low resource country. Further studies are needed to identify appropriate tools and methods to optimize the training of this life-saving procedure in these contexts

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## 76. UN CASO DI TOXOPLASMOSI CONGENITA

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### INTRODUZIONE

La toxoplasmosi è una zoonosi causata dal protozoo *Toxoplasma gondii*. L'infezione verticale può avvenire in utero o durante il parto per via vaginale. La frequenza dell'infezione congenita è direttamente proporzionale all'età gestazionale, mentre la gravità dei danni fetali è tanto maggiore quanto più precoce è l'infezione materna

### MATERIALI E METODI

Nato a 37+2 settimane gestazionali da parto eutocico da gravidanza a rischio per infezione materna da *Toxoplasma gondii*, verosimilmente al 4° mese di gravidanza. La madre è stata seguita presso il paese di origine (Pakistan) fino a pochi giorni prima del parto; è stata pertanto iniziata terapia con rovamicina solo nei 4 giorni antecedenti il parto. Alla nascita indici vitali buoni, Apgar 9/10. Peso alla nascita 2250 g (< 3° centile), lunghezza 47 cm (25°-50° centile), circonferenza cranica 33 cm (10°-25° centile). Gli esami ematochimici eseguiti sono risultati nei limiti di norma mentre la sierologia per *Toxoplasma* ha evidenziato positività per IgG (> 400 U/ml) e per IgM (11.7 U/ml). A completamento diagnostico sono stati eseguiti: ecografia cerebrale, con riscontro di formazione iperecogena ovoidale bilaterale di circa 1.5 cm situata nella porzione anteriore dei ventricoli laterali compatibile con coagulo intraventricolare in esiti di pregressa emorragia della matrice; ecografia addominale risultata nella norma; fundus oculi che non ha evidenziato lesioni coriorretiniche; otoemissioni presenti bilateralmente; valutazione NPI con riscontro di lieve ipotonìa assiale. In quarta giornata di vita, non appena disponibile l'esito sierologico, è stata intrapresa terapia con pirimetamina (1 mg/kg/die in somministrazione quotidiana per 6 mesi, quindi somministrata 3 volte alla settimana per altri 6 mesi) e sulfadiazina (100 mg/kg/die) e supplementazione con acido folinico come da Linee guida. Il piccolo è stato successivamente seguito presso la nostra US di Infettivologia Pediatrica con controlli clinico-sierologici seriati. Le ecografie cerebrali di controllo hanno evidenziato un progressivo completo riassorbimento del coagulo intraventricolare, i potenziali evocati uditivi sono risultati nella norma così come le successive valutazioni NPI. Agli esami sierologici si è osservata la negativizzazione delle IgM per *Toxoplasma* e la negatività delle IgA. La terapia è stata proseguita fino all'anno di vita ed è stata ben tollerata. Il piccolo sta ancora eseguendo follow-up presso il nostro Centro

### CONCLUSIONI

In Italia lo screening sierologico per la Toxoplasmosi è raccomandato dalle linee guida sulla gravidanza fisiologica. Il trattamento farmacologico è necessario in qualsiasi fase della gravidanza la donna abbia contratto l'infezione per ridurre il rischio di trasmissione materno-fetale ed, in caso di infezione, ridurre la gravità delle sequele fetali. Devono essere inoltre trattati tutti i neonati infetti, indipendentemente dalla presenza di segni di infezione, in considerazione del fatto che la terapia può interrompere la malattia acuta evitando ulteriori danni anatomici



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## 77. UPDATE ON BEST AVAILABLE OPTIONS IN OBSTETRICS ANESTHESIA: PERINATAL OUTCOMES, SIDE EFFECTS AND MATERNAL SATISFACTION. FIFTEEN YEARS SYSTEMATIC LITERATURE REVIEW

### LISTA AUTORI

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### INTRODUZIONE

In modern obstetrics, different pharmacological and non-pharmacological options allow to obtain pain relief during labour, one of the most important goals in women satisfaction about medical care. In absence of a medical contraindication, maternal request is a sufficient indication for pain relief during labour: it is considered unacceptable to let an individual experience pain when it is possible to avoid with safe medical assistance. Universal guidelines consider both neuraxial techniques, epidural and spinal analgesia (SA), the gold standard in pain relief during labour. In developed countries, the most used approach is the epidural analgesia (EA), despite its administration rate and pharmacological schemes greatly differ depending on anaesthesiologist experiences, available sources and local guidelines. The modern trend in considering epidural analgesia as the first option in pain relief during labour seems to be due to its advantages such as possibility of utilizing the inserted catheter for further dose administration both during labour and in post-partum period, maternal self-administered pain relief, absence of significant neuromuscular block, and finally a lower drug dose in comparison to the spinal approach. The aim of this review is to compare all the analgesia administration schemes in terms of effectiveness in pain relief, length of labour, mode of delivery, side effects and neonatal outcomes

### MATERIALI E METODI

A systematic literature search was conducted in electronic databases MEDLINE, EMBASE, Scisearch and the Cochrane Library in the interval time between January 1999 and March 2013 that we considered as a reasonable period to systematically review the most recent options for labour analgesia. We considered only articles in English language. All original descriptions, case series, retrospective evaluations and review articles comparing or describing maternal outcomes (as patients general features, parity, length of labour, trends in cervical dilatation, mode of delivery), incidence of drug side effects (as hypotension, pruritus and nausea), VAS (visual analogue scale) values at three different interval time [T0 (at the time of drug administration), T1 (after the time of administration until to 30 min), T2 (30–120 min)] and, finally, maternal satisfaction were included. Concerning the newborns, pH and Apgar score (at first and fifth minute after delivery) were recorded. Key search terms included: "labour analgesia", "epidural anaesthesia during labour" (excluding anaesthesia for caesarean section), "epidural analgesia and labour outcome" and "intra-thecal analgesia". A manual search of reference lists of included studies and review articles was successively performed. References of the retrieved articles were analyzed to identify any work missed by the initial search. In the considered interval time, on the basis of our key search, more than 120 articles were available in the scientific literature database but only 43 satisfied our selection criteria. Among these, 20 studies were excluded since they aimed to compare different analgesic drug schemes for each technique, but they did not consider different techniques. The remaining 23 studies were eligible for our data analysis. A total of 10,331 patients were analyzed: 5,578 patients underwent Epidural Analgesia (EA), 259 patients underwent Spinal Analgesia (SA), 2,724 underwent Combined Spinal and Epidural analgesia (CSEA), 322 underwent Continuous Epidural Infusion (CEI), 168 underwent Intermittent Epidural bolus (IB), 684 underwent Patient-controlled infusion (PCEA) and 152 underwent Intra-venous Patient-controlled epidural analgesia (IVPCEA). We also considered 341 patients who underwent PCEA in association with CEI and 103 patients who underwent PCEA in association with automatic mandatory bolus (AMB). Patients were comparable for age, cervical dilatation, BMI and gestational age

### RISULTATI

Seven studies analyzed EA. The mean length of labour was 294 min. Vaginal delivery (VD) occurred in 69%, operative delivery (OP) in 15% and caesarean section (CS) in 15%. Apgar <7 was registered in 5.8% (1') and in 2% (5'). They reported hypotension in 2.8% cases, pruritus in 8.8%, nausea in 9.3%, VAS score of 9.8 at T0, 1.2 at T1 and 2.1 at T2. Five studies analyzed CSEA. The mean length of labour was 258 min. VD occurred in 68%, OP in 11% and CS in 21%. Apgar <7 was registered in 1.4% (1') and 0% (5'). They reported hypotension in 2.8%, pruritus in 31.7%, nausea in 10%, VAS score of 9 at T0, 1 at T1 and 1 at T2. Five studies analyzed CEI. The mean length of labour was 345 min. VD occurred in 73.4%, OD in 14.2% and CS in 12.4%. Apgar <7 was registered in 2.2% (1') and 0.8% (5'). They reported hypotension in 2% cases, pruritus in 9.5%, VAS score of 7 at T0, 0 at T1 and 1 at T2. Three studies analyzed IB. The mean length of labour was 273 min. VD occurred in 82%, OD in 10% and CS in 7.5%. Apgar <7 was registered in 6 and 3% (1') and in 2 and 5% (5'). Hypotension was reported in 2% cases, pruritus in 6% and a VAS score of 6 and 9 at T0, of 0 and 3 at T1, of 1 and 3 at T2. Twelve studies analyzed PCEA. The mean length of labour was 376 min. VD occurred in 68%, OD in 19% and CS in 16%. Apgar <7 was registered in 4% (1') and in 1.3% (5'). They described hypotension in 1%, pruritus in 33%, nausea in 3%



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and a VAS score at T0(7,8,7), at T1(0,4,2) and at T2(2,2,2). Three studies analyzed IVPCEA. The mean length of labour was 559 min. VD occurred in 73%, OD in 16% and CS in 11%. Apgar <7 was registered in 14.4%(1') and 1%(5'). Nausea was reported in 37.5 and 50% and a VAS score of 8 at T0, 5 at T1 and 6 at T2. Nine studies analyzed PCEA+CEI. The mean length of labour was 366 min. VD occurred in 70%, OD in 13% and CS in 17%. Apgar <7 was registered in 2%(1') and in 2%(5'). They reported hypotension in 0 and in 6.50%, pruritus in 46%, nausea in 3% and a VAS score of 8.6 at T0, 2 at T1 and 2 at T2. Three studies analyzed PCEA+AMB. The mean length of labour was 402 min. VD occurred in 64%, OD in 7% and CS in 28%. Apgar <7 was reported in 6%(5'). Hypotension was reported in 0 and 3.2%, pruritus in 57% and nausea in 6%

## **CONCLUSIONI**

No significant differences occurred among all the available administration schemes of neuraxial analgesia. In absence of obstetrical contraindication, neuraxial analgesia has to be considered as the gold standard in obtaining maternal pain relief during labour. The options available in the administration of analgesia should be known and evaluated together by both gynaecologists and anaesthesiologists to choose the best personalized scheme and obtain the best women satisfaction. Since it is difficult to identify comparable circumstances during labour, it is difficult to standardize drugs schemes and their combinations



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## **78. USE OF DYDROGESTERONE IN PREGNANT WOMEN WITH SUBCHORIONIC HEMATOMA IN THE PREVENTION OF PRETERM BIRTH**

### **LISTA AUTORI**

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### **INTRODUZIONE**

Subchorionic hematoma (SCH) is one of the most frequent complications of the 1st trimester of pregnancy and is associated with the risk of maternal and neonatal complications. Therefore, the problem of this pregnancy complication treatment and its effectiveness remains very important. In M.G.Tuuli et al., 2011. meta-analysis and meta-analysis of Kathy L.Kyser, 2013, the association of SCH with preterm birth was shown. In this regard, we conducted the study, the purpose of which was to evaluate the efficacy of dydrogesterone in treatment of SCH in the 1st trimester

### **MATERIALI E METODI**

The study was conducted in the Rostov-on-Don Perinatal Centre (Rostov-on-Don, Russia) in 2014-2015. Study group comprised 90 pregnant women in the period of 6-12 weeks with SCG, diagnosed in  $7,4 \pm 1,1$  weeks. Ultrasound study was made on the Philips HD 11. In dependence on the therapy, all pregnant women were divided into 2 groups. 1st group received complex therapy - tranexamic acid 500-1000 mg for 2 or 3 days, multivitamins, folic acid 3 g per day. 2d group had monotherapy with dydrogesterone: 40 mg at one time, followed by 10 mg every 8 hours for three times, i.e. 70 mg on the 1st day, followed by 20 mg x 2 times per day until 16 weeks of pregnancy, with gradual withdrawal in 22 weeks

### **RISULTATI**

The volume of RCH was  $0.68 - 3.2 \text{ cm}^3$  ( $1.3 \pm 0.43 \text{ cm}^3$ ). Middle internal diameter of the yolk sac in women of the 1st group was  $4.0 \pm 0.89 \text{ mm}$ , while in the 2d group -  $4.55 \pm 0.67 \text{ mm}$  ( $p < 0.05$ ). To compare the frequency of characteristics in studied groups we used the method of comparison of independent groups using the Mann-Whitney and the Fisher's criteria.

5 (11%) pregnancies in the 1st group and 3 (6.7%) pregnancies in the 2d group ( $p > 0.05$ ) ended in spontaneous abortion in the I trimester. 2 (4.5%) pregnancies of the 1st group (the cause of one was antiphospholipid syndrome, the other - abscessed endometritis according to histological examination) and 3 (6.7%) pregnancies of the 2d group ( $p > 0.05$ ) ended in late abortion in terms of 12-22 weeks. Pregnant women with prolonged pregnancy  $n = 77$  (85.5%), were subjected to further analysis of the clinical observations including complications of the second half of pregnancy (1st group  $n = 38$ , 2d group  $n = 39$ ). Premature birth in patients of the 1st group met in 6 (16%) cases and in the 2d group (treated with dydrogesterone) - in 1 case (2.5%) ( $p = 0.0436$ ). The frequency of premature births in the group of women receiving dydrogesterone was significantly lower compared with pregnant women who received therapy without dydrogesterone ( $p = 0.0436$ )

### **CONCLUSIONI**

The use of dydrogesterone in pregnant women with subchorionic hematoma is considered as prevention of preterm birth in this group of patients

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## 79. WHICH UTEROTONIC IS BETTER TO PREVENT THE POSTPARTUM HEMORRHAGE? LATEST NEWS IN TERMS OF CLINICAL EFFICACY, SIDE EFFECTS, AND CONTRAINDICATIONS: A SYSTEMATIC REVIEW

### LISTA AUTORI

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### INTRODUZIONE

Postpartum hemorrhage (PPH) is defined by the World Health Organization as a blood loss of at least 500 mL after vaginal delivery (VD) and 1000 mL after cesarean section (CS) and/or the necessity of blood transfusion within 24 hours of delivery. PPH complicates 6% of all deliveries and it is responsible for nearly one-quarter of all the worldwide maternal death. VDs are complicated with primary PPH in 14.4%, 5% and 36% of cases respectively in VDs with physiological management of the 3rd stage of labour, with the 3rd active stage of labour and in CS. Most of the PPH occur in women without identifiable risk factors and so we recommended preventive measures for all the birth-giving women. To Reduce the occurrence of PPH by 40% there are many evidences supporting the routine administration of oxytocin or ergot alkaloids after CS and in the 3rd stage of labour for VD. During the last 2 decades several alternative treatments have been explored as to reduce the occurrence of PPH. The aim of this systematic review was to analyze the availability of uterotonics for PPH prevention and to clarify indications and contraindications in choosing among different drugs

### MATERIALI E METODI

We realized a systematic review searching in the electronic databases MEDLINE, EMBASE Sciencedirect and the Cochrane Library between January 2007 and May 2012. The search terms used included "postpartum hemorrhage", "blood loss prevention", "uterotonics drugs" and "uterine atony". Studies providing ambiguous or insufficient data on obstetrical outcomes regarding clinical efficacy, side effects, and contraindications were excluded. The tested interventions were all the uterotonic drugs (oxytocin, carbetocin, PGs, alkaloids, and their association) administered after the delivery of the infant as a part of the active management of the third stage of labor and CS

### RISULTATI

Intramuscular (im) injection of oxytocin (5 or 10IU) is the 1st choice for prophylaxis of PPH in women without risk factors during the 3rd stage of VD; slow intravenous (iv) injection of oxytocin (5IU) is used to encourage uterus' contraction and to decrease blood loss in women delivering with CS. The iv oxytocin has a short half-life and it is helpful during CS because it maintains uterine contractility during surgical procedures when the PPH usually occurs. 10IU iv of oxytocin is not used because it causes maternal hypotension and arrhythmias. Iv/im ergot alkaloids reduce mean blood loss, PPH, postnatal Hb<10g/dL, the use of therapeutic uterotonics and the length of the 3rd stage of labour, but they increase blood pressure and pain. There are no dose-response curves describing ergot alkaloids use during CS. Methylergonovine is considered the 2nd line uterotonic agent in the prophylaxis and treatment of PPH, because of its side effects. Syntometrine is considered an alternative 2nd line agent in patients with no hypertension problem. A meta-analysis shows statistically reduction in PPH risk in women treated with syntometrine when compared to 5IU of oxytocin, but there is no statistically significance when 10 IU of oxytocin are used. 600 µg of oral misoprostol is less effective than 10 IU im/iv oxytocin and has more side effects. It is safer to use 400 µg of sublingual misoprostol than 600 µg and this dose is an alternative to oxytocin during the 3rd stage of labour for PPH prevention among low-risk women. For PPH treatment misoprostol is less effective than oxytics, but it is more readily available in a third world country and so it is considered a 1st line choice in that situation. Carboprost is the 1st line PG for PPH treatment when other agents are no longer effective, although this needs further studies. Carbetocin is used in women with hypertensive disorders and with cardiac problems, it has long half-life and a hemodynamic profile similar to oxytocin. Iv bolus over 1 minute of 100 µg of carbetocin should be used in elective CS for PPH prevention instead of oxytocin and to decrease therapeutic uterotonics

### CONCLUSIONI

Active management reduces maternal blood loss and the PPH risk (risk ratio 0.50 between women who receive uterotonic and patients who do not receive them). The use of prophylactic oxytocics should be offered routinely during the 3rd stage of labour as it reduces the PPH risk of 60%. The prophylactic use of uterotonics should be individualized



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## 80. WOMEN'S CHOICE OF POSITIONS DURING LABOUR: RETURN TO THE PAST OR A MODERN WAY TO GIVE BIRTH? A COHORT STUDY IN ITALY

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### INTRODUZIONE

In developed countries, during labour, pregnant women have to assume recumbent position to have easier monitoring of fetal wellbeing. Recumbent position is associated with more operative deliveries, severe pain, abnormal fetal heart trace and greater episiotomy rate. Occipito posterior position (OP) is frequently associated with intrapartum complications. Some authors investigated if maternal laboring position may have a role in facilitating spontaneous rotation to occipito anterior position (OA) without statistical evidence. The primary endpoint of our study was to compare recumbent and alternative positions in term of labour process, type of delivery, neonatal wellbeing. The secondary endpoint was to establish if differences exist in intrapartum fetal rotation due to maternal positions

### MATERIALI E METODI

An observational cohort study on primiparous pregnant women admitted to the delivery room of University of Padua (Department of Woman and Child Health) was conducted. We considered uncomplicated single pregnancies with fetuses in cephalic presentation. We excluded all cases of vaginal delivery in previous cesarean section, cephalic fetal presentation after manual rotation of the fetus from OP to OA, labour induction and augmentation. For all patients we recorded general data: age, BMI and gestational age at birth. We collected data on labour process: length of 1st and 2nd stage, fetal OP at the labour onset and at the delivery, analgesia request rate and intra-labour pain with numeric rating scale (NRS) score. We recorded data on mode of delivery: spontaneous, operative vaginal delivery or emergent caesarean section (CS). We also collected data on need of episiotomy and rate of perineal tears in cases of vaginal deliveries. Neonatal wellbeing at birth was studied with Apgar score at 5th and fetal pH. Patients (225 women) were included in 2 Groups: GroupA when they spent more than 50% of their labour in recumbent position (supine or lateral) and in GroupB when they preferred an alternative position, without medical or midwifery prescription. Alternative maternal positions were considered as follows: -upright position when the woman is standing by herself or against to a support; -squatting position when the patient crouches during contraction and then recuperates during relaxation; -sitting position when the pregnant is sitting; -position "on all fours" when the woman is kneeling and bent forward in order to support her weight with arms. Regarding the analgesia, all women received epidural analgesia without the use of opioid when required

### RISULTATI

A total of 225 patients were eligible; 69 in GroupA and 156 in GroupB. In GroupB the 46.1% of women assumed the upright position, 21.1% the sitting position, 16.2% the "on four position" and 16.6% the squatting position. GroupA and GroupB showed similar maternal characteristics (age, BMI, gestational age at the delivery). We found significant statistical differences as concern the length of 1st and 2nd labour stages expressed in minutes (mean value respectively in the 2 Groups  $336.1 \pm 161.1$  versus  $192.1 \pm 125.8$ ;  $84.4 \pm 57.8$  versus  $34.4 \pm 32.6$ ;  $[p < 0.001]$ ). GroupA and GroupB showed significant differences in term of analgesia request rate (GroupA 34.8% versus GroupB 9.6%)  $[p < 0.0001]$  and NRS score (GroupA  $7.1 \pm 1.6$  versus GroupB  $3.7 \pm 1.2$ )  $[p < 0.001]$ . Regarding the mode of delivery, in GroupA and GroupB we reported a total of 47.8% and 87.1% of vaginal route, 26.1% and 7.1% of operative vaginal delivery, 26.1% and 5.8% of CS respectively  $[p < 0.001]$ . Dystocia occurred in 13.05% and 0.7%, abnormal fetal heart rate occurred in 13.05% and 5.1% respectively in GroupA and GroupB  $[p < 0.05]$ . Episiotomy was performed in 100% of Group-A patients who delivered by vaginal route compared to the 32.7% of GroupB  $[p < 0.001]$ , while 1st-2nd degree vaginal tears occurred, respectively, in 5.9% versus 49% of the cases  $[p < 0.001]$ . No differences were found between the two groups in terms of neonatal outcomes. The OP rate at the labour onset resulted 40.6% in GroupA and 36.5% in GroupB  $[p = n.s.]$ . Considering OP cases (28 cases in GroupA and 57 cases in GroupB) a strong significant difference was found in terms of delivery outcome. Significant differences in terms of OP persistence at delivery were also found in those delivering vaginally: in GroupA OP persisted until birth in 39.6% of the cases, while in GroupB only in 28% of the cases  $[p < 0.001]$ . Considering only GroupB, no differences were found comparing alternative position for all the outcomes analyzed. CS was necessary in 46.4% patients of GroupA and 12.3 % in GroupB  $[p < 0.0001]$

### CONCLUSIONI

Changing positions during labour can positively influence childbirth experience and the labour's course. The non-recumbent labours have advantages thanks to gravity effect on uterine perfusion, contractions effectiveness and fetal alignment to the pelvic diameters and angles. Vertical positions are associated with lower pain and reduced labour length during the 1st stage, resulting in an increased women's comfort. Our study reported a significant reduction in length of 1st and 2nd labour stages in patients assuming alternative positions. This confirmed a

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positive effect of gravity in effective uterine contractions and fetal alignment to the birth canal. We assumed the positive effect of alternative positions concerning episiotomy, operative vaginal delivery and vaginal tears rate. This finding can be related to a better maternal perineum compliance to the fetal head descent, reducing anatomical and functional perineal damage and consequent dyssynergia. Our study recorded a significantly lower analgesia rate with a vertical position, compared to the recumbent one (due to lower perineum reflex muscle contraction of upright position). OP position represents a risk factor for poor maternal and neonatal outcomes: a persistent OP is linked to adverse obstetrical events, such as prolonged 1st and 2nd labour stages, increased epidural analgesia rate, higher risk of postpartum hemorrhage, increased CS, operative vaginal deliveries, and 3rd and 4th degree perineal tears rate. These intrapartum conditions are frequently related to lower neonatal outcomes. Maternal vertical position during labour resulted facilitating the fetal head rotation from OP to OA, reducing the rate of operative vaginal deliveries and CS. Unfortunately, we did not discriminate which vertical position has to be preferred. In absence of prepartum/intrapartum maternal-fetal complications, all women should be encouraged to move and to deliver in the most comfortable position, preferring a vertical position when OP is diagnosed



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## **81. THREE STEPS METHOD TO SCREEN CONGENITAL HEART DISEASE AT 11-13+6 WEEKS: VALIDATION OF A NEW HIGH DEFINITION IMAGING MODE TO DETECT FETAL CARDIAC STRUCTURES**

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### **OBIETTIVO**

We designed a prospective study to test the feasibility of the first level screening for cardiac defects at the time of Nuchal Translucency (NT) measurement using a new high definition blood flow imaging mode (e-flow). We also compare the quality of first level operators visualization both with B-Mode and e-flow mode

### **METODI**

636 consecutive fetuses between 11 and 13 + 6 weeks referred for NT at San Paolo Hospital were examined by first level operators. In each fetus the cardiac morphology was studied in two sections, the four chambers view (transvers or apical) and great vessels sections (three vessels) visualized with B-mode and e-flow mode.

The cardiac sections were independently and double blinded evaluated by first level operators and then by an expert echo-cardiographer.

The operators evaluated the quality of imaging (good, sufficient or insufficient) and the cardiac morphology (normal, abnormal or suspicious).

The tricuspid regurgitation was checked by color Doppler and e-flow.

In the suspicious of cardiac anomaly the patient were referred to second level echocardiography.

Neonatal follow up were collected by a telephone questioner.

Efficacy of e-flow was evaluated as percentage of success in obtaining reliable images of the heart and the great vessels, and percentage of concordance between first level and expert supervisors operators evaluation

### **RISULTATI**

We analyzed 636 consecutive fetuses. Four chambers view was obtained in 89,5% (569/636) with B-Mode and in 99,8% (635/636) with e-flow mode. The quality of four chambers view for first operators with B-Mode was Good in 45,3% (258/569), Sufficient in 35% (199/569) and Insufficient in 19,7% (112/569). The same section with e-flow was valuated as Good in 78,3% (497/635), Sufficient in 20,8% (132/635) and Insufficient in 0,9% (6/635). The concordance of evaluation was respectively 52,5% (299/569) for B-Mode and 75,2% (478/635) for e-flow mode. A normal heart morphology was found in 89,7% (408/455) with B-Mode and in 98,1% (630/630) with e-flow mode while an abnormal heart morphology was found in 0,8% (4/455) with B-Mode and in 0,5% (3/630) with e-flow mode. A suspected abnormal heart was found in 9,5% (43/455) with B-Mode and in 1,4% (9/630) with e-flow mode. The concordance of evaluation of cardiac morphology was respectively 60% (273/455) for B-Mode and 88,4% (557/630) for e-flow mode.

Three vessels view was obtained in 84% (534/636) with B-Mode and in 97,3% (619/636) with e-flow mode. The quality of three vessels view for first operators with B-Mode was Good in 20,1% (150/534), Sufficient in 31,3% (167/534) and Insufficient in 40,6% (217/534). The same section with e-flow was valuated as Good in 74,5% (461/619), Sufficient in 23,6% (146/619) and Insufficient in 4,1% (13/619). The concordance of evaluation was respectively 51,7% (276/534) for B-Mode and 69,9% (433/619) for e-flow mode.

A normal three vessels morphology was found in 60,1% (262/436) with B-Mode and in 96,5% (579/600) with e-flow mode while an abnormal three vessels morphology was found in 0,4% (2/436) with B-Mode and in 0,3% (2/600) with e-flow mode. A suspected abnormal three vessels was found in 39,5% (172/436) with B-Mode and in 3,2% (19/600) with e-flow mode. The concordance of evaluation of three vessels morphology was respectively 56,2% (245/436) for B-Mode and 86,7% (520/600) for e-flow mode

### **CONCLUSIONI**

The percentage of visualization of four chambers and great vessels increases with the use of e-flow mode (89,5% vs 99,8% and 84% vs 97,3%) and the high concordance of evaluation of normality between the first and the second operators using the e-flow mode (60% vs 88,4% and 56,2% vs 86,7%) stress the feasibility of the first level screening for major cardiac defects at the time of Nuchal translucency screening

## **82. IODINE SUPPLEMENTATION IN WOMEN DURING PRECONCEPTION PERIOD, PREGNANCY AND LACTATION: CURRENT CLINICAL PRACTICE BY ITALIAN GYNECOLOGISTS**

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### **CONTENUTO E OBIETTIVO**

Iodine is an essential component of the thyroid hormones and iodine deficiency is considered the most common cause of preventable intellectual impairment worldwide. Population iodine status in Italy is still mildly deficient and this is particularly important for pregnant and lactating women who require increased iodine intake for normal fetal development. In the United States, where overall population iodine status is adequate but pregnant women are mildly iodine deficient, the American Thyroid Association, the Endocrine Society, the Teratology Society, and the American Academy of Pediatrics recommend that women receive prenatal vitamins containing 150 mcg of iodine daily during preconception, pregnancy, and lactation. These recommendations are shared by the European Thyroid Association.

The aim of this study was to evaluate the awareness about iodine nutrition among Italian Gynecologists, and to document current clinical practice regarding recommendations for iodine supplementation for women during preconception, pregnancy, and lactation

### **METODI**

Members of the SIMP (Società Italiana di Medicina Perinatale) were invited to participate in a web-based survey

### **RISULTATI**

422 respondents completed the survey. 65% of respondents considered the current iodine status of Italian pregnant women to be deficient and more than 90% considered iodine supplementation useful for these women. Respondents who would always or often recommend iodine-containing prenatal multivitamins for women planning pregnancy, pregnant women and lactating women were 26%, 44%, and 38%, respectively; while respondents who would rarely or not recommend iodine-containing vitamins were 46%, 34%, and 36%, respectively. For those respondents who prescribe iodine enriched vitamins, 67% recommended the iodine enriched supplements during the first trimester of pregnancy and approximately 60% during the second and the third trimesters. The daily amount of iodine supplementation recommended in women planning pregnancy, pregnant women, and lactating women was 50 mcg daily or less in 62%, 50%, and 54%, respectively; while 150 mcg daily was recommended by 29%, 24%, and 23% of respondents, respectively; and 250 mcg daily or more by 9%, 26%, and 23%, respectively

### **CONCLUSIONI**

In contrast to the International recommendations and despite the important issue of iodine deficiency in Italy, approximately 55% of Gynecologists who answered the survey would not recommend or would recommend an inadequate dose of iodine supplementation for women planning pregnancy, pregnant women, and breastfeeding women. Our findings demonstrate that a lack of awareness for iodine supplementation among healthcare professionals is still present and suggest that a more vigorous approach to correct iodine deficiency be instituted

### **ACCORDIMENTI**

This work was possible thanks to the support of Fondazione Bracco. We would like to acknowledge Dr Sabatelli for the technical assistance in forwarding the survey

## 83. ADHERENCE TO MEDITERRANEAN DIET IN A SAMPLE OF OBESE CAUCASIAN PREGNANT WOMEN

### LISTA AUTORI

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### INTRODUZIONE

BACKGROUND and AIM Maternal obesity is associated with several negative pregnant outcomes, including, hypertensive conditions, preeclampsia, gestational diabetes, macrosomia, required induction of labor, cesarean section, preterm birth and increased risk of childhood obesity and diabetes.

Few are the studies that describe food habits in obese pregnant women, although this information may be very important to plan nutritional counseling.

The aim of this study was to evaluate in a sample of obese Caucasian pregnant women the adherence to Med-Diet, a healthy dietary pattern associated to lower cardiovascular risk in the general population

### METODI

Caucasian obese pregnant women ( $BMI \geq 30 \text{ kg/m}^2$ ) were enrolled at Sacco Hospital, based in Milan. At the enrollment, anthropometric measures and personal anamnestic data were collected and a validated food frequency questionnaire to assess mediterranean dietary pattern was administered

### RISULTATI

The sample included 16 obese pregnant women (mean age:  $34 \pm 4$  ys; mean gestational age:  $21 \pm 6$  wks; mean pre-pregnancy BMI:  $39.5 \pm 4 \text{ kg/m}^2$ ). 81% were Italian, while 19% were from Eastern Europe and living in Milan. 50% had a lower secondary school degree, 51% were smoking and 69% were unemployed.

62% of obese women showed a low adherence to Med-Diet (Score < 8). In particular, 81% consumed less than 2 servings of vegetables/day, and 93% less than two servings of fruit; 56 ate red meat or processed meat every day; 50% habitually used butter to dress and 44% ate baked products more than 3 times/wk. 70% declared to eat legumes less than 3 times/week, 93.8% fish less than 3 times/week and 81% nuts less than 2 times/week

### CONCLUSIONI

These data suggest that it is necessary to plan nutritional counselling in obese pregnant women to improve the quality of their diet and to prevent gestational complications

## 84. BLOOD FLOW VOLUME IN UTERINE ARTERIES AND UMBILICAL VEIN: A NEW TOOL IN PATHOPHYSIOLOGY UNDERSTANDING OF FETAL GROWTH RESTRICTION NEAR TERM

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### OGGETTO

"Small for gestational age" (SGA) fetus is a definition coined at the beginning of the '70s, and it is still used to indicate a fetus below the 10th percentile, with a normal Doppler velocimetric profile in uterine arteries and umbilical artery. The extensive use of this definition led to strengthen the idea that some fetuses could start their growth path at the 50th percentile and "physiologically" end it at or below the 10th centile. Placentation is routinely evaluated by means of qualitative assessment of Doppler velocimetric profile of the uterine arteries. Recently our research group proposed to move from a qualitative to a quantitative assessment on blood flow volume in the same arterial vessels. In early and severe intrauterine growth restricted fetuses (IUGR) umbilical vein (UV) blood flow was significantly reduced; uterine arteries (UTA) blood flow showed an inverse correlation with pulsatility index (PI) and a clear association between UTA flow reduction and impairment of birthweight.

The aim of the study was to calculate blood flow volume in UTA and UV in a population of SGA fetuses with gestational age at delivery >34 weeks. This group was compared with normal singleton pregnancies of comparable gestational age.

We hypothesized that quantification of arterial and venous blood flow volume could enable us to identify these "SGA" as, indeed, "mild" IUGR.

### METODI

Sixty-three singleton pregnancies complicated by a fetal abdominal circumference <10th percentile for gestational age were enrolled. All the cases had normal pulsatility index (PI) in umbilical artery and UTA until delivery. Each case underwent ultrasound examination: fetal biometry, amniotic fluid index, diameter and flow velocity measurements in both UTA and in UV. UV Diameter was measured by placing the calipers at the inner edge of the vessel on a perpendicular view of the vein; by rotating 90° the probe was then obtained the straight vein section for velocity measurement (beam angle <30°). UTA diameter was measured on a perpendicular vessel section identified by means of Power Doppler, velocity was measured on a Doppler velocimetric profile obtained on a longitudinal UTA section (beam angle <30°). UTA and UV Blood flow volume (ml/min) was then calculated and normalized for estimated fetal weight (ml/min/kg) by means of an ad hoc mathematical model previously proposed and validated by our research group

### RISULTATI

Nine cases had a birthweight >10th percentile and were excluded. UV blood flow volume expressed per kg fetal weight (ml/min/kg) was significantly reduced in study group (82.4 ml/min; i.r. 57.5 – 109.2), compared to controls (105.19 ml/min; i.r. 102.2 – 108.2) ( $p < 0,0001$ ). This reduction was due to a significantly lower flow velocity, while UV diameter remained within the normal range for fetal body mass (Fig. 1). UTA total volume flow (ml/min) was significantly reduced in cases (205,1 ml/min; i.r. 134,2 – 257,9) compared to controls (603.81 ml/min; i.r. 412.4 – 811.5) ( $p < 0,0001$ ) ( $p < 0,0001$ ), due to a smaller vessel, while flow velocity remained normal (Fig.2). When UTA blood flow volume was expressed for fetal weight, values of the study group (86.5 ml/min/kg; i.r. 57.5 – 109.2) overlapped normal range at the same gestational age (90.5 ml/min/kg; i.r. 60.1 – 109.9) ( $p=0,171$ ) (Fig. 3)

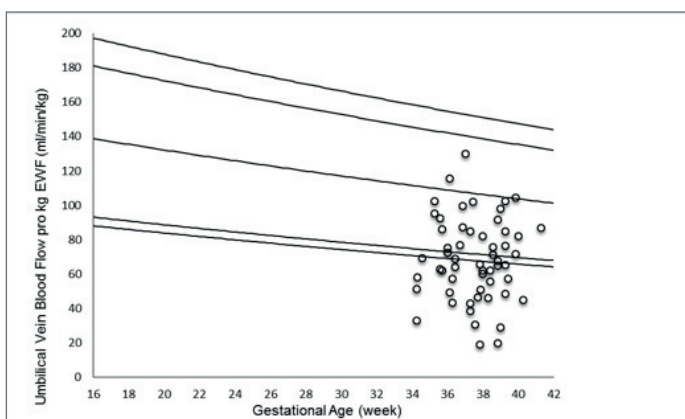


Figure 1. Umbilical Vein blood flow volume normalized for fetal weight (ml/min/Kg); 50<sup>th</sup> percentile:  $y = 168,49e^{-0,012x}$

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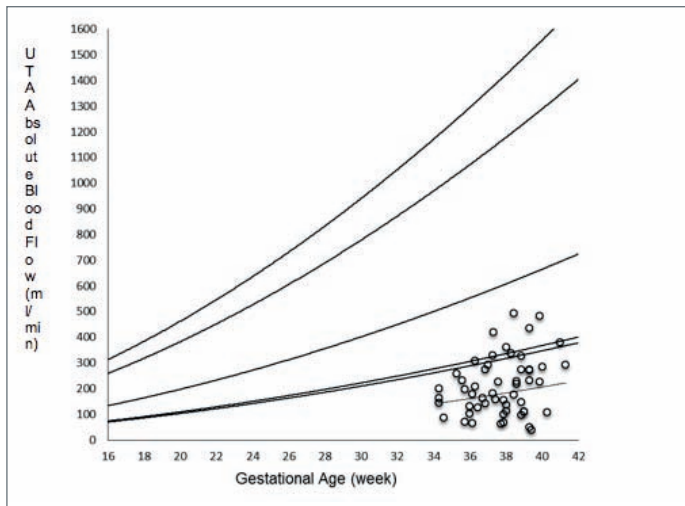


Figure 2. Uterine Arteries blood flow volume:  $Q = h \cdot \text{Velmedia} \cdot p \cdot (D/2)^2$ ; 50<sup>th</sup> percentile  $y = 1,036x1,7524$ ; study group  $y = 0,0353x^{2,3507}$

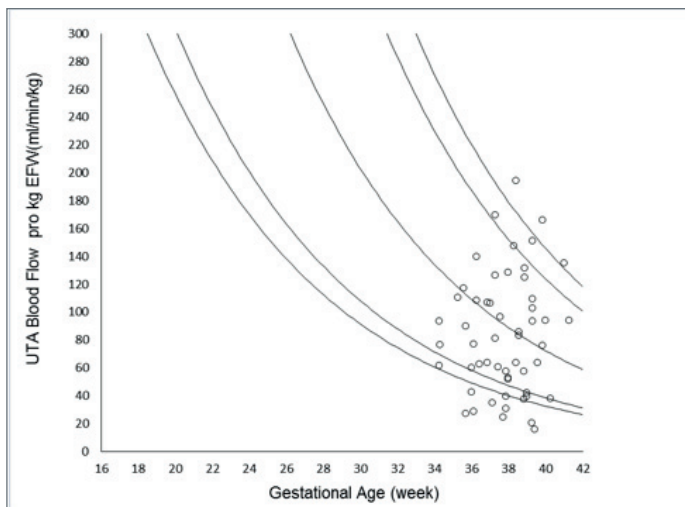


Figure 3. Uterine Arteries blood flow volume normalized for fetal weight (ml/min/Kg); 50<sup>th</sup> percentile:  $y = 4477,3e^{-0,103x}$

## CONCLUSIONI

UTA and UV blood flow volume reduction, either absolute and expressed for fetal body weight unit, had already been observed in early and severe IUGR fetuses. The same reduction was observed in these series of SGA fetuses near term. Since UTA blood flow volume normalized for fetal weight was within the normal range, fetal weight appears as a dependent variable of uterine blood flow. Therefore, hemodynamic results of these series completely lay in the growth restriction continuum, even if the population group represents the mildest expression of this fetal-placental unit disease. On one side, these results add information about pathophysiology of placentation in mild IUGR cases, on the other side they could bring to a new way to take care of this neonates after birth



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