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Società Italiana di Medicina Perinatale

29 Settembre
1 Ottobre 2022

GENOVA

23° CONGRESSO NAZIONALE AGORÀ SIMP

SIGO
SOCIETA' ITALIANA
DI GINECOLOGIA E OSTETRICIA

Conference Proceedings

of

23rd Agorà SIMP National Congress

Genoa, September 29th- October 1st, 2022

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Società Italiana di Medicina Perinatale

23° CONGRESSO NAZIONALE AGORÀ SIMP 2022 GENOVA 29 Settembre • 1 Ottobre 2022

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Vol. 35 - Supplement N. 1 - ISSN 2385 - 0868

Italian Journal
of
Gynæcology & Obstetrics

The Official Journal of the
Società Italiana di Ginecologia e Ostetricia
(SIGO)

Conference Proceedings
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23rd Agorà SIMP National Congress
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The abstracts contained in this Supplement were evaluated and accepted by the Organizing Committee, without formal external peer review by the Journal's Editor/Reviewers.

*Note that the asterisk after author's surname states the Corresponding author in each abstract

First trimester screening: the increasing value of the test beyond aneuploidies analysis

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DOI: 10.36129/jog.2022.S01

Objective. The aim of the study was to investigate the ability of first trimester maternal serum pregnancy associated with plasma protein A (PAPP-A), fetal fraction (FF), and uterine arteries pulsatility index (PI) in predicting obstetric complications.
Materials and Methods. This is a population-based retrospective cohort study conducted on all the women with singleton pregnancies booked for non-invasive prenatal testing at Fondazione Policlinico A. Gemelli between June 2015 and January 2021. 512 women were enrolled.
Results. Low PAPP-A (cut-off < 0.4 MoM) was associated with fetal losses (5.9% *vs* 1.5% p < 0.0001), preeclampsia (7.7% *vs* 1.8% p = 0.049) low-birth weight neonates (< 2500 g; 19.2% *vs* 7.9% p = 0.045), preterm delivery before 34 weeks (11.5% *vs* 3.4% p = 0.039) and before 28 weeks (3.8% *vs* 0.5% p = 0.055). Low FF (cut-off < 7%) was associated with high BMI (p < 0.0001), caesarean section (54.1% *vs* 27.3% p = 0.009) and preterm delivery before 37 weeks (32.4% *vs* 16.4% p = 0.032). High uterine arteries PI (cut-off ≥ 95° percentile) was associated with fetal losses (10% *vs* 0.6% p = 0.018), very low-birth weight neonates (< 1500 g; 11.1% *vs* 0.6% p = 0.003) and preterm delivery before 37 weeks (55.5% *vs* 18.71% p = 0.008).
Conclusions. The first trimester biochemical assessment appears to play an important role not only for chromosomal anomalies, but also in early and successfully predicting and counselling women at higher risk of developing obstetric and perinatal complications.

NIPT *vs* combinated test for predicting aneuploidies: a case report

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DOI: 10.36129/jog.2022.S02

Background. Prenatal screening for trisomy 21-18-13 and selected sex chromosome aneuploidies can be performed using next-generation sequencing of cell-free DNA (cfDNA) in the maternal circulation or a combined test with free ß-hCG, PAPP-A dosage and nuchal translucency misuration.

Case presentation. A 32-year-old healthy caucasian woman, first spontaneous pregnancy, performed a non invasive prenatal test (NIPT) at 10 weeks of pregnancy which resulted in low risk for Trisomy 13, 18 and 21 and major aneuploidies. Fetal fraction was 4%.

At 13 weeks, the same patient performed a combined test with high-risk result for trisomy 18 and 21 (1:58 and 1: 204 respectively), low risk for trisomy 13 (1:1049). Despite medical advice, she did not undergo genetic counseling.

At 15 weeks of pregnancy the patient was diagnosed with internal abortion. The response of the molecular investigation on the skin biopsy was: condition compatible with triploid chromosomal structure. Histological examination of the placenta showed no abnormalities.

Conclusions. Triploidy is a rare chromosomal abnormality unrelated to maternal age. The prevalence at 12 weeks is about 1 in 2000 but it is highly lethal and very rarely observed in live births. NIPT has a high predictive value, but it still remains a screening test for the rare false negatives. The reasons for false negatives are: confined placental mosaicism, borderline low fetal fraction, maternal copy number variants, technical issues. In case of discrepancy between the two screening tests, it is always advisable to carry out genetic counseling.

Prenatal diagnosis of tuberous sclerosis complex: a case report

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DOI: 10.36129/jog.2022.S03

Objective. Tuberous sclerosis is a rare genetic condition that causes hamartomas to develop in different parts of the body. It has an autosomal dominant inheritance pattern with variable penetrance, and it can adversely affect maternal and fetal outcome.
Cardiac rhabdomyomas are an early manifestation of tuberous sclerosis. They can grow in size and number during fetal development, but they usually regress within the first years of life. However, the presence of a rhabdomyoma in the right atrium could lead to cardiac arrhythmias in both the antenatal and postnatal periods.
Materials and Methods. A 21-year-old primigravida performed an ultrasound at 20 + 2 gestational weeks and the fetus was diagnosed with an apical rhabdomyoma of the interventricular septum and a right atrial rhabdomyoma between the superior vena cava orifice and the posterior wall.
Results. A genetic examination was performed on the amniotic fluid revealing a paternal mutation for TSC1. The genetic investigations and the fetal ultrasound findings suggested the fetus was suffering from tuberous sclerosis. Therapeutic termination of pregnancy was performed at 21 + 1 weeks.
The pathological examination confirmed the presence of the rhabdomyomas.
Conclusions. Tuberous sclerosis occurs due to the deletion, rearrangement, and inactivating mutation of tumor suppressor genes TSC1 or TSC2 leading to the formation of hamartomas in many and different organs.
The early manifestation of tuberous sclerosis can be detected in prenatal screening and most commonly involves the heart and brain. The cardiac localization requires a careful evaluation of organ function in the postnatal period.

Voluminous chorionic cyst of the umbilical cord insertion site: a case report

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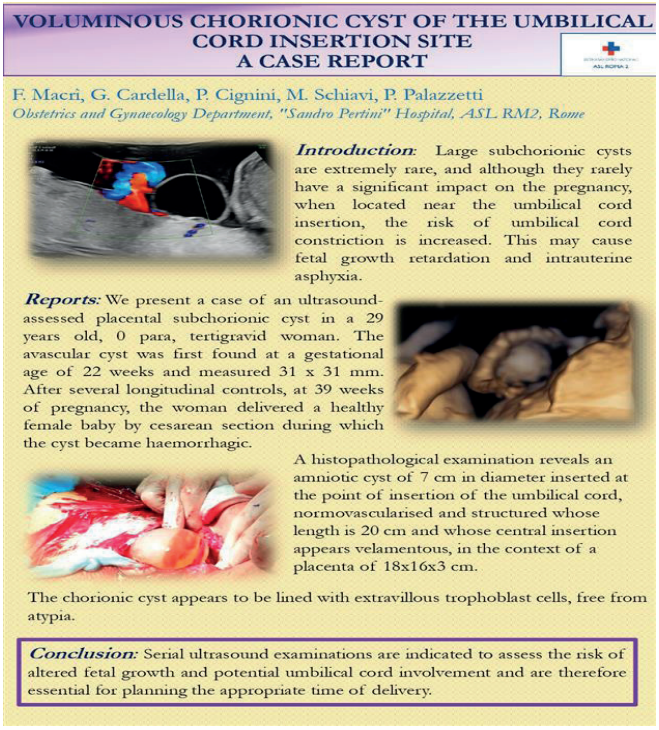
DOI: 10.36129/jog.2022.S04

Background. Large subchorionic cysts are extremely rare, and although they rarely have a significant impact on a pregnancy, when located near the umbilical cord insertion, the risk of umbilical cord constriction is increased. This may cause fetal growth retardation and intrauterine asphyxia.
Case presentation. We present a case of an ultrasound-assessed placental subchorionic cyst in a 29-year-old, 0 para, tertigravid woman. The avascular cyst was first found at a gestational age of 22 weeks and measured 31 × 31 mm. After several longitudinal controls, at 39 weeks of pregnancy, the woman delivered a healthy female baby by cesarean section during which the cyst became haemorrhagic. A histopathological examination revealed an amniotic cyst 7 cm in diameter located at the point of insertion of the umbilical cord, which was normovascularised and structured, 20cm in length and whose central insertion appeared velamentous, in the context of a placenta measuring 18 × 16 × 3 cm. The chorionic cyst appeared to be lined with extravillous trophoblast cells, free from atypia.
Conclusions. Serial ultrasound examinations are indicated to assess the risk of altered fetal growth and potential umbilical cord involvement and are therefore essential for planning the appropriate time of delivery.



Hidradenitis suppurativa, pyoderma gangrenosum and ulcerative colitis together during pregnancy: bad luck or is there any other explanation?

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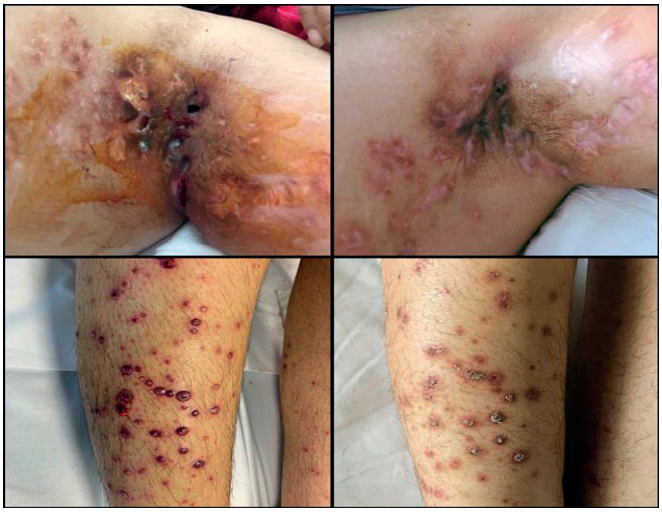
DOI: 10.36129/jog.2022.S05

Objective. We reported a case of the concurrent onset during pregnancy of suppurative hidradenitis (HS), pyoderma gangrenosum (PG) and ulcerative colitis (UC) in a previously healthy woman managed at our referral center.

Materials and Methods. This is a case report about a primiparous, 22-year-old Indian woman who was admitted to our emergency room at 24 weeks of gestation with fever and melena. At the visit, several pustular abscess lesions of the left axillary were found and the rettoscopy suggested UC. Following this, a rash with pustules appeared on her inferior limbs and worsened with the development of painful hemorrhagic ulcers. After a multidisciplinary team consultation, a diagnosis of an overinfected HS of the axilla and PG of the legs associated with UC was made. With antibiotic therapy, high-dose corticosteroid infusion and Mesalazine therapy the melena gradually stopped and, simultaneously, a nearly complete recovery of the cutaneous manifestations of HS and PG was obtained. At 34.5 weeks, she vaginally delivered a healthy neonate of 2200 g.

Results. HS, UC, and PG represent the components of an autoinflammatory immuno-mediated syndrome, called PCHS syndrome, only recently described. This is the first case of PCHS syndrome managed during pregnancy. The close monitoring and the enhancement of one of the associated conditions (UC) lead to the simultaneous improvement of the others, proving the link between these pathologies.

Conclusions. The physiology of pregnancy could create conditions that mimic inflammatory disorders amplifying the risk of developing autoinflammatory diseases in predisposed women. A multidisciplinary approach to the different diseases allowed a favorable course of the pregnancy itself.



Low level of PAPP-A MoM and obstetric outcomes in SGA and AGA babies: a retrospective cohort study

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DOI: 10.36129/jog.2022.S06

Objective. To compare obstetric and neonatal outcomes according to PAPP-A MoM at combined tests.

Materials and Methods. Retrospective cohort study of all combined tests performed in singleton pregnancies at the same institution between 2015 and 2021 with available pregnancy outcomes. The following was recorded for all women and babies: age and BMI, mode of conception, free-betahCG and PAPP-A values and MoM, CRL, NT and the risk for T21, T13 and T18, Gestational Age (GA) at delivery, birthweight, Apgar at 5 min, arterial pH (pHa) and base excess (BE), need for NICU, blood loss at birth. We defined adverse neonatal outcomes if any of the following occurred: Apgar < 7 at 5', pHa < 7.10, BE < -10 and NICU admission. We planned to compare obstetric outcomes between women with PAPP-A MoM above or below 0.42 MoM (5th cle).

Results. 1826 records were available; among these, 76 (4.2%) women had PAPP-A MoM < 5th cle, which did not differ according to mode of conception, maternal age or BMI (p > 0.05). Results of combined tests and obstetric outcomes according to PAPP-A MoM are shown in **Table 1**. We decided then to compare obstetric outcomes after excluding all SGA (n = 201, 11%). Having a PAPP-A MoM < 5th remained associated with lower free-betahCG MoM (p = 0.004), lower blood loss at delivery (p = 0.015) and lower birthweight (p = 0.033) but also increased the risk of adverse composite neonatal outcome (OR 2.1, 95%CI 1.1-4.1, p = 0.028).

Conclusions. AGA babies with PAPP-A MoM < 5th cle at combined tests have an increased risk of adverse composite neonatal outcome, warranting further investigations.

Table 1.

	PAPP-A MoM <= 5th centile (n=76)	PAPP-A MoM > 5th centile (N=1750)	p-value
Spontaneous Conception (n, %)	3 (3.9)	100 (5.7)	.51
Maternal age (median, IQR)	32.7 (30.1-35.5)	33.2 (30.2-36.3)	.44
Maternal BMI (median, IQR)	22.1 (20-25.5)	22.2 (20.1-25)	.80
Free-betahCG MoM (median, IQR)	0.65 (0.44-1.02)	0.94 (0.65-1.31)	<.001
High chance of T21 (n, %)	16 (21.1)	18 (1)	<.001
High chance of T18 (n, %)	5 (6.6)	4 (0.2)	<.001
High chance of T13 (n, %)	3 (3.9)	1 (0.1)	<.001
GA at delivery (median, IQR)	39.0 (38.2- 40.6)	39.4 (38.4-40.6)	.002
Blood Loss (median, IQR)	250 (200-500)	300 (200-400)	.011
Birthweight (median)	3120 (2653.8-3417.5)	3290 (2993.8-3580)	<.001
SGA (n, %)	18 (23.7)	183 (10.5)	<.001 OR 2.66 (CI95% 1.5-4.6)
Composite adverse neonatal outcome (n, (%))	13 (17.1)	184 (10.5)	0.07

sFlt-1/PlGF ratio, in pregnancies complicated by HDP and/or FGR, for prediction of maternal and perinatal complications

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DOI: 10.36129/jog.2022.S07

Objective. Hypertensive disorders (HDP) and fetal growth restriction (FGR) are characterized by placental oxidative stress and angiogenic imbalance. We hypothesized that the sFlt-1/PlGF ratio could be a valid diagnostic tool for predicting adverse maternal and perinatal outcomes.

Materials and Methods. We recruited pregnant women affected by isolated FGR or HDP. Ultrasound data and sera samples were collected at the diagnosis. Patients were classified according to the occurrence of maternal (abruptio placenta, HELLP syndrome, severe preeclampsia) and perinatal complications (perinatal death, cord pH < 7.1 or BE > -12, Apgar score < 7 at 5th minute, and major neonatal complications). The survey was divided into an interpretative statistical analysis of the test population and a subsequent predictive phase.

Results. We recruited 350 consecutive singleton pregnancies and respectively, 81 and 90 cases developed maternal and perinatal complications. Patients developing complications at delivery had a significantly higher sFlt-1/PlGF ratio (236.1252.5) at recruitment than those who did not (44.170.3) ($p < 0.001$). Multivariate analysis showed that for each 10-unit increase in the sFlt-1/PlGF ratio the chance of developing maternal and perinatal complications increased by 8% (OR 1.008, 95%CI 1.005-1.010, $p = 0.007$) and by 6% (OR 1.006, 95%CI 1.004-1.009, $p < 0.001$) respectively. We constructed a predictive model with Sn 75%, Sp 88%, AUC 81% for maternal ($p = 0.008$) and Sn 81%, Sp 89%, AUC 85% for perinatal complications ($p < 0.001$).

Conclusions. Our analysis showed that the sFlt-1/PlGF ratio, in a high-risk population, proved to be a useful tool for predicting the onset of maternal and perinatal complications, weeks prior to delivery.

Late third trimester diagnosis of a congenital haemangioma: a case report

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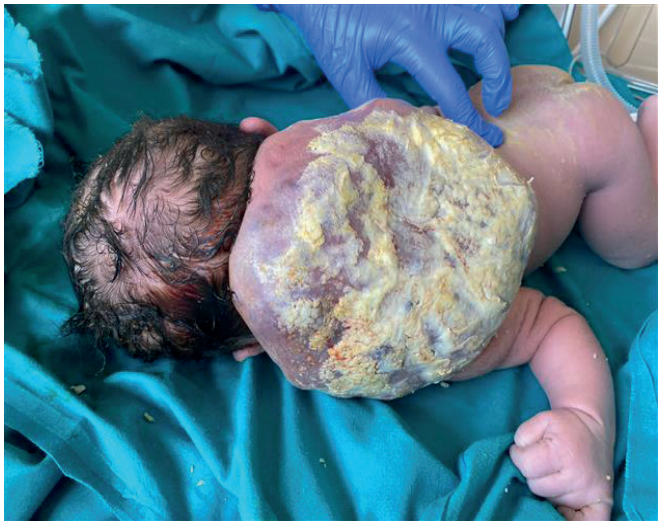
DOI: 10.36129/jog.2022.S08

Objective. We present the case of a child born with a voluminous rapidly involving congenital hemangioma on the back side of the neck.
Materials and Methods. The mother was 36 years old and had a non eventful personal history. The pregnancy was uneventful and her routine ultrasound scan showed no fetal abnormalities. She referred to hospital for contractions at 40 weeks. At the admission ultrasound, a voluminous soft tissue lesion measuring 14 × 15 cm was detected on the posterior side of the neck. The mass had a predominantly cystic appearance and was highly vascularized. Due to the risk of labour dystocia an uncomplicated caesarean section was performed. A healthy male weighting 4515 g and hemodynamically stable was delivered.
Results. The presence of a congenital hemangioma was confirmed but a blood sample showed severe anemia and thrombocytopenia that required several transfusions of blood, plasma, platelets and clotting factors. Due to the association of congenital haemangioma and thrombocytopenia a diagnosis of Kasabach-Merritt syndrome was made. Despite treatment with steroids and acetilsalicilic acid and subsequent sclero-embolization of the lesion, only partial reduction of the mass was obtained. Subsequently, the lesion was removed by surgery and a histological examination confirmed RICH's diagnostic hypothesis. After surgery, the child's conditions improved rapidly, he was finally discharged at 7 months in good conditions.



Conclusions. The Kasabach-Merrit syndrome is a rare condition whose prenatal diagnosis is rare. We describe the case of a rapidly evolving congenital hemangiomas in the late third trimester that highlights the importance of performing an admission ultrasound before labor.

First trimester prediction of uterine rupture in cesarean scar pregnancy

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DOI: 10.36129/jog.2022.S09

Objective. To elucidate the predictive accuracy of first trimester ultrasound for uterine rupture in women with CSP.

Materials and Methods. Retrospective analysis of women with a prenatal diagnosis of CSP at 6-8 weeks gestation. We tested the hypothesis that the severity of CSP can predict the risk of uterine rupture in the first and early second trimester of pregnancy.

Results. 119 women with a prenatal diagnosis of CSP were included in the analysis. Uterine rupture occurred in 7.6% of women, while 92.4% progress to the third trimester and all were found to be affected by PAS. All cases complicated by uterine rupture showed COS1 sign or "in the niche" insertion of the gestational sac compared to 13% and 14% of COS2 and "on the scar" insertion ($p < 0.001$ for both), respectively. At multivariate logistic regression analysis, only COS1 or "in the niche" insertion was independently associated with the risk of uterine rupture. When these figures were translated into a predictive model, COS1 insertion had a sensitivity of 100%, a specificity of 88.18%, while the corresponding figures for "in the niche implantation" were 100% and 87.27%, respectively.

Conclusions. This is the first study reporting the (predictive) accuracy of first trimester ultrasound in predicting uterine rupture in women with CSP. Ultrasound assessment of the relationship between the gestational sac and the area of the prior CD scar can predict the risk of uterine rupture in women with CSP.

First trimester fetal neurosonography: clinical feasibility and diagnostic performance

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DOI: 10.36129/jog.2022.S10

Objective. To report the clinical feasibility and diagnostic performance of first trimester fetal neurosonography in a low-risk population.

Materials and Methods. Prospective study including all fetuses with a low combined screening test scanned at 11-14 weeks of gestation. The aim of this study was to report the rate of visualization of the different fetal intra-cranial structures, as suggested by the ISUOG guidelines for the second trimester fetal neurosonography, at the time of the 11-14 weeks scan. The fetal central nervous system (CNS) structures assessed were interhemispheric fissure, frontal and posterior horns, thalami, third ventricle, peri-callosal artery and corpus callosum, cerebellum and cerebellar vermis.

Results. 167 fetuses were included. The interhemispheric fissure was assessed in all cases. Anterior and posterior horns of the cerebral ventricles were clearly differentiated in 98.5% and 98.7% of cases, while third ventricle in 45.2%. The pericallosal artery was visualized in 99.2% of cases while there was a direct visualization of the corpus callosum in only 15% of cases. Fetal cerebellum was clearly identified in 93.5% of cases and cerebellar vermis in 91%.

Conclusions. This is the first study exploring the diagnostic performance of first trimester fetal neurosonography at the time of the 11-14 weeks scan. First trimester assessment can identify most of the supra and infra tentorial intracranial structures.

Prevalence and risk factors of puerperal endometritis in a prospective cohort study in Modena, Northern Italy

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DOI: 10.36129/jog.2022.S11

Objective. The purpose was to investigate the prevalence of puerperal endometritis, diagnosed by cultural exams on endometrial tissue according to a diagnostic protocol. The secondary outcome was to evaluate the correlations of endometritis with obstetric outcomes.

Materials and Methods. This was a prospective cohort study including women who delivered at the Policlinic Hospital of Modena from January 2019 to July 2022. Tests were performed on mothers with puerperal pyrexia (> 38.4 °C in two measurements, at least 4h apart), endometrial, urine, and blood cultures. Moreover, thorax Rx, abdominal and gynecological US were routinely done. Obstetric outcomes and other cultural results were collected in clinical informatics charts.

Results. 155 women were included from 10,202 deliveries. Of these, 116 (75%) endometrial biopsies resulted positive, with a prevalence of puerperal endometritis of 1.14%. Women with puerperal endometritis significantly delivered with caesarean section rather than vaginally (39.6% *vs* 11.38%, P-value = 0.000). Regarding the diagnostic protocol, 36.5% of the 104 women who underwent urine culture resulted positive, while 20% of the 95 cases of blood cultures performed tested positive. Radiological examinations included: abdomen ultrasound (n = 76) and chest X-Ray (n = 76), which resulted completely negative in only 35.5% and 46.0% of the cases respectively. Finally, endometritis was clearly suspected after gynaecological US in only 18.9% of cases,

Conclusions. The prevalence of puerperal endometritis among women who delivered in our centre was 1.4%, similar to the rate in literature. In more than one-thirds of the cases, urine culture samples were also positive. Women who underwent caesarean section had a higher risk of endometritis compared with vaginal delivery.

Eclampsia: how to optimize maternal outcomes? Experience of a referral centre

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DOI: 10.36129/jog.2022.S12

Objective. Eclampsia is the occurrence of seizure during pregnancy or puerperium, and remains one of the major causes of maternal morbidity and mortality with an incidence of 1.6 to 10/10,000 deliveries in developed countries. According to the INOSS report, 45% of maternal eclampsia-related deaths could be prevented with appropriate care. Our aim was to describe the current management of eclampsia and to identify the most frequent clinical errors to improve maternal outcomes.

Materials and Methods. We performed a monocentric retrospective study on 7 cases which occurred between January 2016 and January 2021 at Careggi University Hospital, Florence. We analyzed medical history, course of pregnancy, characteristics of seizure, management, and maternal and fetal outcomes.

Results. Five cases occurred before delivery, 2 in postpartum. In 3 pre-partum cases, delivery was performed with an emergency cesarean section in general anesthesia.

Pharmacological treatment for hypertension and prevention of recurrence of seizures with Magnesium Sulfate resulted appropriate according to international guidelines.

The standard sequence of acute care during the seizure, stabilization of maternal conditions followed by delivery was not respected. In all pre-partum cases managed with emergency cesarean section, we found negative maternal outcomes: two cases of PRESS (Posterior-Reversible-Encephalopathy-Syndrome) and one case of maternal respiratory failure. Our data are consistent with the INOSS report.

Conclusions. Management of eclampsia is currently not appropriate, with consequent poor maternal outcomes.

Considering the rarity of this condition an adequate and recurrent staff training would be necessary. In fact better outcomes would be obtained by optimizing prenatal and intrapartum care.

First trimester screening of Hypertensive Disorders of Pregnancy: role of uterine arteries Doppler

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DOI: 10.36129/jog.2022.S13

Objective. Nowadays preeclampsia first trimester screening is not able to predict the different phenotypes of HDP, that are characterized by different times of onset, fetal growth and patterns of uterine arteries (UtA) Doppler velocimetry.
UtA Doppler velocimetry represents a proxy of placental function and provides indirect information regarding placentation process.
We investigated if, in patients at high risk for HDP according to the Fetal Medicine Foundation (FMF) algorithm, the presence of UtA-PI > 95th percentile represents a risk factor for adverse maternal and fetal outcomes.
Materials and Methods. Multicentric retrospective study on 244 patients with high risk FMF preeclampsia screening enrolled at "Piero Palagi" Hospital, Florence and at Careggi University Hospital, Florence.
Patients were divided into two groups: UtA-PI ≤ 95th percentile and UtA-PI > 95th percentile.
Maternal characteristics, maternal and fetal outcomes were compared.
Results. UtA-PI > 95th percentile is significantly associated with Fetal Growth Restriction, severe PE and HELLP syndrome and resulted as a possible risk factor for Apgar index ≤ 7 at 1st minute.
Moreover, smoke habit has been found to be a risk factor, while advanced maternal age, the use of assisted reproductive technology and chronic hypertension unexpectedly resulted protective factors.
Pre-pregnancy BMI resulted irrelevant.

Table 1. *Comparison of maternal characteristics, maternal and neonatal outcome between patients with UtA-PI ≤ 95th percentile and UtA-PI > 95th percentile.*

	Total (n=244)	AU pat (n=51) 20,55%	AU nor (n=193) 79,44%	p value	OR	CI
Age	34,07	32,59	35,54	**0,0003**		
Caucasian ethnicity	231 (94,67%)	49 (96,08%)	182 (94,30%)	0,6151	1,48	0,32-6,90
Smoking habit	11 (4,51%)	5 (9,80%)	6 (3,11%)	**0,0404**	3,39	0,99-11,59
BMI	24,71	24,49	24,92	0,1673		
Chronic hypertension	19 (7,79%)	2 (3,92%)	17 (8,81%)	0,2468	0,42	0,09-1,89
ART	46 (18,85%)	4 (7,84%)	42 (21,76%)	**0,0238**	0,31	0,10-0,90
CS	108 (44,26%)	22 (43,14%)	86 (44,56%)	0,8557	0,94	0,51-1,76
Induction of labour	81 (33,20%)	20 (37,74%)	61 (31,61%)	0,3047	1,40	0,74-2,64
AI ≤7	18 (7,38%)	7 (13,73%)	11 (5,70%)	0,0512	2,63	0,97-7,18
pH	7,26	7,26	7,26			
IUGR	57 (23,36%)	19 (37,25%)	38 (19,69%)	**0,0084**	2,42	1,24-4,73
Gestational hypertension	45 (18,44%)	8 (15,69%)	37 (19,17%)	0,5682	0,78	0,34-1,81
PE/HELLP	9 (3,69%)	5 (9,80%)	4 (2,07%)	**0,0092**	5,14	1,33-19,89

BMI: Body Mass Index; ART: Assisted Reproductive Technology; CS: Caesarean Section; AI: Apgar Index; IUGR: Intra Uterine Growth Restriction; PE: Preeclampsia; HELLP: Hemolysis, Elevated Liver enzymes and Low Platelets

Conclusions. Our study demonstrates that, in patients at high risk for HDP, UtA-PI > 95th percentile is associated with worse maternal and fetal outcomes. These data should guide clinicians in the management of pregnancy, suggesting a more intensive clinical and ultrasonographic follow-up in order to identify the onset of complications early on and to optimize therapeutic strategies.

Effect of Pravastatin on placental expression of EGFL7 in preeclampsia and intrauterine growth restriction: a new potential therapeutic approach

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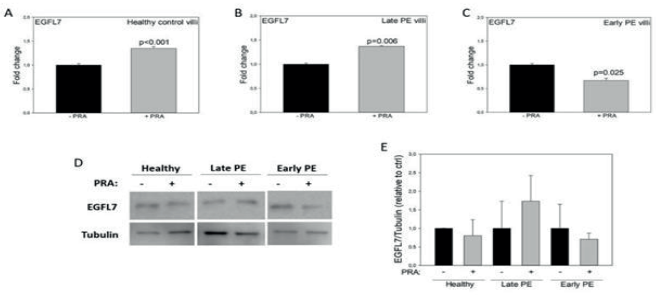
DOI: 10.36129/jog.2022.S14

Objective. Epidermal Growth Factor Like Domain 7 (EGFL7) is an angiogenic factor that we have recently identified in human placenta trophoblast. In pregnancies complicated by preeclampsia (PE) a significant EGFL7 downregulation in placental tissues is on the other hand accompanied by a significant increase in maternal plasma. Circulating EGFL7 can differentiate early- and late-onset PE (e-PE and l-PE) and isolated intrauterine growth restriction (IUGR) from e-PE. Pravastatin (PRA) is a lipid-lowering drug whose potential in the prevention and treatment of PE has been highlighted. The aim of our study is to evaluate the ability of PRA to modulate EGFL7 expression in human chorionic villous explant cultures from uncomplicated and PE- and IUGR affected pregnancies.

Materials and Methods. 19 women were enrolled for this study: 10 healthy controls, 4 e-PE, 3 l-PE and 2 IUGR. Chorionic villous explants were cultured for 24 hours with or without 10 μM PRA. The gene and protein expression of EGFL7 and other angiogenic factors were quantified by qRT-PCR and Western Blot analysis.

Results. PRA significantly increased EGFL7 gene expression in cultures obtained from healthy, l-PE and IUGR pregnancies ($p < 0.001$, $p = 0.006$, and $p = 0.014$, respectively), while its levels decreased in e-PE villi after PRA treatment ($p = 0.025$). This trend was confirmed at protein level.

Conclusions. Pravastatin is able to modulate the expression of EGFL7 in human placenta; the differences observed between l-PE and e-PE underlines once again the well-known different nature of the two forms of PE and isolated IUGR.



Central arterial pressure in pregnancies complicated by chronic hypertension: could it be an important diagnostic and prognostic value in clinical practice?

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DOI: 10.36129/jog.2022.S15

Objective. Normally clinical evaluation and management of patients with chronic hypertension in pregnancy focuses on the evaluation of laboratory parameters and peripheral blood pressure. The aim of the study was to investigate the haemodynamic parameters and central blood pressure values in patients with chronic hypertension during the II and III trimester.
Materials and Methods. We enrolled 39 patients, including 14 patients with chronic hypertension on methyldopa therapy. All the women underwent peripheral and central blood pressure measurement using USCOM BP PLUS and hemodynamic assessment using USCOM.
Results. Patients with chronic hypertension showed higher values of cMAP both in the second and third trimester (94.07 ± 7.84 *vs* 88.03 ± 7.95; 94.43 ± 10.17 *vs* 83.76 ± 10.03), higher pMAP (94.07 ± 10.08 *vs* 85.51 ± 9.92) and PKR (31.05 ± 11.92 *vs* 23.36 ± 9.93) in the third trimester, higher TVR (1131.23 ± 204.23 *vs* 986.22 ± 181.83; 1174.10 ± 224.23 *vs* 996.28 ± 229.83) in both the second and third trimester; a lower INO in the third trimester compared to the second (1.65 ± 0.21 *vs* 1.90 ± 0.17), as shown in **Table 1**.
Conclusions. It was already known that pregnancies complicated by chronic hypertension show a hypodynamic circulation, but peripheral blood pressure normally measured at the level of the brachial artery does not adequately reflect the conditions of the cardiovascular system; in fact, the most relevant differences were observed above all in central blood pressure values, both in the second and third trimesters, proving to be much more sensitive than peripheral pressure and therefore more suitable for the correct management of these patients.

Table 1.

cMAP	*Controls*	*CH*	*p*
II trimester	88,03 ± 7,95	94,07 ± 7,84	**0,0280**
III trimester	83,76 ± 10,03	94,43 ± 10,17	**0,0030**
p	0,1018	0,9173	
pMAP			
II trimester	90,42 ± 7,35	94,67 ± 7,27	0,0904
III trimester	85,51 ± 9,92	94,07 ± 10,08	**0,0143**
p	**0,0525**	0,1779	
CO			
II trimester	7,60 ± 1,09	7,03 ± 1,24	0,1443
III trimester	7,26 ± 1,65	6,76 ± 1,04	0,2353
p	0,3942	0,5379	
HR			
II trimester	85,90 ± 14,52	86,78 ± 13,49	0,8534
III trimester	85,28 ± 13,36	89,54 ± 10,96	0,3165
p	0,8758	0,5575	
TFc			
II trimester	384,02 ± 27,21	380,75 ± 48,88	0,7889
III trimester	380,29 ± 32,44	390,39 ± 32,41	0,3569
p	0,6616	0,5439	
SVV			
II trimester	19,75 ± 6,20	20,75 ± 12,34	0,7371
III trimester	19,89 ± 0,29	22,20 ± 8,57	0,1818
p	0,9107	0,7209	
SVR			
II trimester	986,22 ± 181,83	1131,23 ± 204,23	**0,0281**
III trimester	996,28 ± 229,83	1174,10 ± 224,23	**0,0239**
p	0,8644	0,6014	
PKR			
II trimester	21,89 ± 6,30	23,63 ± 3,69	0,3516
III trimester	23,36 ± 9,93	31,05 ± 11,92	**0,0374**
p	0,5349	**0,0350**	
INO			
II trimester	1,80 ± 0,27	1,90 ± 0,17	0,2192
III trimester	1,69 ± 0,41	1,65 ± 0,21	0,7361
p	0,2681	**0,0019**	

Maternal peripheral vascular resistance at mid gestation in chronic hypertension as a predictor of fetal growth restriction

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DOI: 10.36129/jog.2022.S16

Objective. Maternal Peripheral Vascular Resistance (PVR) appears to be an interesting tool to identify normotensive and chronic hypertensive patients who may develop early and late complications of pregnancy. We analyzed the relationship between maternal hemodynamics and fetal growth at mid gestation and delivery in chronic hypertension.

Materials and Methods. 152 chronic hypertensive patients were submitted to maternal echocardiography noting PVR at 22-24 weeks gestation and were followed until delivery noting therapy, birthweight centile and the diagnosis of FGR.

Results. A significant correlation was found between PVR at 24 weeks gestation and birthweight centile at delivery, while CO showed a weaker correlation coefficient.

PVR at 24 weeks gestation was predictive for birthweight below the 10th centile and for FGR according to Gordijn *et al*.

Patients treated with CCBs (Calcium channel blockers) with or without other drugs had lower PVR *vs* those treated without CCBs ($p = 0.019$). Treatment with beta blockers during pregnancy was a risk factor for a birth weight < 10° pc ($p = 0.020$) but not a risk factor for FGR according to Gordijn *et al*. ($p = 0.48$).

Conclusions. The main finding of this study was the strong correlation between PVR weeks before delivery and birthweight centile in patients with chronic hypertension. Higher PVR are an excellent predictor of FGR according to Gordijn *et al*. weeks before delivery. Therapy with Beta-blockers or CCBs might have different effects on maternal and fetal hemodynamics, and fetal growth too; these observations might open new areas of intervention to treat patients with altered hemodynamics.

Gut microbiota analysis in preeclampsia with fetal growth restriction

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DOI: 10.36129/jog.2022.S17

Objective. Some forms of preeclampsia (PE) present a strong link with metabolic diseases; also, gut dysbiosis has been identified for causing metabolic diseases, but the role of gut microbiome in the pathogenesis of hypertensive disorder of pregnancy (HDP) and fetal growth restriction (FGR) remains unknown.
Materials and Methods. We performed a prospective case-control study. 16S and metabolomic analyses were performed by IRCCS Humanitas comparing faecal microbiome and metabolome of HDP or isolated FGR (iFGR) and normotensive pregnant women.
Results. We recruited six preeclamptic patients with fetal growth restriction (HDP-FGR), 12 HDP, 19 iFGR and 12 controls. Through the alfa and beta diversity analysis, we observed that the HDP-FGR group separated from the others ($p = 0.003$). At the analysis of the phylum, only the iFGR group showed a reduction in terms of *Firmicutes* bacteria both compared to HDP-AGA and to the healthy pregnant population ($p < 0.001$). Regarding the genus, in the HDP-FGR group, in particular *Ruminococcaceae* and *Sellimonas* were enriched, while *Clostridia*, and *Dorea* were markedly depleted. In the HDP-AGA group, *Escherichia* and *Streptococcus* were higher, while *Clostridium* were depleted. The iFGR showed a reduction in *Coprobacter* and enriched in *Ruminococcaceae*.
Finally, the metabolomic analysis confirmed the 16S clusterization and suggested metabolomic alterations linked to the carbohydrate metabolism in the HDP-FGR ($p = 0.002$).
Conclusions. This study suggests that the gut microbiome of patients with HDP-FGR is significantly different from a healthy pregnancy and contributes to disease pathogenesis, while this is not the case in the HDP-AGA or iFGR, that is in agreement with the multiple causes of HDP-AGA and iFGR.

Aspirin for prevention of preeclampsia and adverse perinatal outcome in twin pregnancies: a systematic review and meta-analysis

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DOI: 10.36129/jog.2022.S18

Objective. To investigate the potential role of Aspirin in reducing the risk of preeclampsia (PE), as well as adverse maternal and perinatal outcomes in twin pregnancies.

Materials and Methods. Medline, Embase, Google Scholar, Cochrane and Clinicaltrial.gov databases were searched. The primary outcome was the incidence of PE. Secondary outcomes included gestational hypertension, fetal growth restriction (FGR), preterm birth (PTB), gestational age (GA) at birth, and adverse events secondary to aspirin administration. Subgroup analyses according to chorionicity, aspirin dose, and gestational age at administration were also performed. Head-to-head meta-analyses reporting results as summary odds ratios (OR) and mean differences were used.

The conclusion of the meta-analysis on the primary outcome was assessed using GRADE.

Results. Nine studies (2273 twin pregnancies) were included. When considering all studies, the risk of PE was lower in twin pregnancies treated compared to those not treated with aspirin (OR 0.72, 95%CI 0.53-0.99, p = 0.05), while there was no significant difference in the risk of gestational hypertension (p = 0.8), FGR (p = 0.6) or adverse maternal and perinatal events (p = 0.9) compared to those not treated. When considering only studies with aspirin dose > 100 mg/day, the risk of PE (OR 0.49, 95%CI 0.25-0.96, p = 0.04) was significantly lower in pregnancies taking compared to those not taking aspirin.

Conclusions. Administration of aspirin in women with twin pregnancies reduces the risk of PE. The findings from this study highlight the need for randomized controlled trials elucidating the actual role of aspirin in affecting maternal and perinatal outcome in twin pregnancies.

Fetal growth velocity and small for gestational age prediction

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DOI: 10.36129/jog.2022.S19

Objective. We aimed to evaluate the diagnostic accuracy of the fetal growth velocity to predict small for gestational age (SGA) fetuses. We further assessed the role of ultrasound examination reiterations and the differences between estimated fetal weight (EFW) and fetal abdominal circumference (AC).
Materials and Methods. We conducted a retrospective observational study considering all single pregnancies with at least two growth scans performed between 20 and 38 weeks gestation. Women with only one scan and twin pregnancies were excluded, and fetal growth velocity was assessed as a unit/week or z-score/week variation. The outcomes were SGA < 3rd and 10th centile.
Results. In total, 1412 women and 3397 ultrasound scans were considered. Our study showed that fetal growth velocity was predictive of SGA. The growth velocity evaluated as a unit/time was more predictive of the z-score/time evaluation and was notably valuable for diagnosing SGA < 3rd percentile. With the increase in the ultrasound scan reiterations, fetal weight growth velocity was more accurate in predicting SGA. There were no differences between the predictive value of the estimated fetal weight or the fetal abdominal circumference growth in predicting small for gestational age.
Conclusions. Fetal growth velocity is significantly predictive for SGA, especially for those born with a fetal weight < 3rd centile. Assessing growth velocity as units/time and with a broader number of reiterations increases prediction accuracy.

Non-invasive maternal hemodynamic assessment to classify high-risk pregnancies complicated by fetal growth restriction

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DOI: 10.36129/jog.2022.S20

Objective. To verify whether the use of the temporal criterion of 32 weeks' gestation is effective in identifying maternal hemodynamic differences between early- and late-onset fetal growth restriction (FGR), and to test the statistical performance of a classificatory algorithm for FGR.

Materials and Methods. A prospective multicenter study including singleton pregnancies with a diagnosis of FGR based on the international Delphi survey consensus was conducted. Hemodynamic assessment was performed by USCOM-1A. Comparisons between early- and late-onset FGR, FGR associated with hypertensive disorders of pregnancy (HDP-FGR), and isolated FGR (i-FGR) were performed. Finally, a classificatory analysis based on the Random Forest model was performed to identify variables with the ability to differentiate FGR phenotypes.

Results. During the study period, 146 pregnant women fulfilled the inclusion criteria. In 49 (48.1%) women, FGR was associated with HDP. Fifty-nine (57.8%) cases were classified as early-onset. Comparison of the maternal hemodynamics between early- and late-onset FGR did not show any difference. Similarly, non-significant findings were observed in sensitivity analyses performed for HDP-FGR and for i-FGR. In turn, comparison between pregnant women with FGR and hypertension and women with i-FGR, independently of the gestational age at FGR diagnosis, revealed substantial differences, with the former showing higher vascular peripheral resistances and lower cardiac output. The classificatory analysis identified both phenotypic and hemodynamic variables as relevant in distinguishing HDP-FGR from i-FGR ($p = 0.009$).

Conclusions. Our data show that HDP, rather than gestational age at FGR diagnosis, allows us to appreciate specific maternal hemodynamic patterns and to accurately distinguish two different FGR phenotypes.

Fetal Doppler parameters as predictors of fetal cardiac function in late-onset fetal growth restriction (FGR): a prospective study

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DOI: 10.36129/jog.2022.S21

Objective. The aim of the study was to evaluate the relationship between fetal Doppler parameters and functional echocardiography in a population of late-onset growth restriction fetuses (LFGR).

Materials and Methods. A single center prospective study including a consecutive series of non-anomalous singleton pregnancies with suspected LFGR. During routine follow-up, the assessment of fetal Doppler (umbilical artery (UA) and middle cerebral artery) was performed. Moreover, two-dimensional clips of the four-chamber view of the fetal heart were prospectively collected. The cohort population was divided into two groups: LFGR with normal UA Doppler (Group I) and LFGR with UA > 95°P (Group II). One dedicated operator effected a speckle tracking functional echocardiography with TomTec Gmbh software. Correlation between Doppler parameters and the fetal cardiac indexes was described with cross-sectional analysis.

Results. 17 cases fulfilling the eligibility criteria were included, and 61 cross-sectional measurements were analysed. A significantly higher Ejection Fraction (EF) (60 *vs* 55.1, p = 0.03) and Left Ventricle (LV) circumferential strain (-31 *vs* -25.7, p = 0.04) was found in group I compared with group II. A sub-analysis on a selected population of fetuses with a weight between the 3rd and the 10th percentile at birth was also performed. A significantly reduced LV global longitudinal strain (-18.6 *vs* -21.9, p = 0.01), LV global radial strain (-31.1 *vs* -47.5, p = 0.003), LV global circumferential strain (-24.4 *vs* -31.6, p = 0.03) and EF (52.5 *vs* 60.2, p = 0.004) was reported in Group I compared with Group II.

Conclusions. In a population of LFGR fetuses, a relationship was demonstrated between the UA Doppler and the left ventricular function.

The predictive role of aortic isthmus notch index in growth-restricted fetuses

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DOI: 10.36129/jog.2022.S22

Objective. Fetal growth restriction (FGR) represents a leading cause of perinatal mortality and morbidity. Fetal aortic isthmus has been used to evaluate the grade of fetal compromise. To assess the correlation between the fetal Doppler depth of the notch index (AoI-NI) in aortic isthmus, the severity of FGR and the perinatal outcome.

Materials and Methods. This retrospective study was conducted on 148 singleton fetuses, divided into five groups: 85 were AGA – appropriate for gestational age; 28 SGA – small for gestational age (estimated fetal weight – EFW < 10° percentile); 18 FGR A (EFW < 3° percentile); 12 FGR B (EFW < 10° percentile and uterine artery pulsatility index – UtA-PI > 95° percentile); 5 FGR C (EFW < 10° percentile and umbilical artery PI > 95° percentile). The composite negative outcome (preeclampsia, fetal distress, NICU hospitalization, fetal resuscitation and Apgar score < 7 at the 5th minute) was recorded.

Results. AoI-NI was significantly increased in the FGR C group with a median value of 0.26 (0.25-0.81), more than double that of the other groups, including FGR A and FGR B fetuses with median values respectively of 0.04 and 0.09. At the univariate and multivariate logistic regression, AoI-NI was significantly associated with the composite negative outcome with an Odds Ratio respectively of 33.14 (95%CI 1.93-567.94, $p < 0.05$) and 30.69 (95%CI 1.72-547.84, $p < 0.05$).

Conclusions. An increased AoI-NI could be associated with the most severe form of FGR. The increased aortic isthmus notch index was also significantly associated with the presence of the negative composite outcome.

Maternal hemodynamic findings as a tool to predict the risk of Left Ventricular Hypertrophy (LVH) in pregnant women with chronic hypertension (CH)

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DOI: 10.36129/jog.2022.S23

Objective. To evaluate the accuracy of hemodynamic parameters in predicting the risk of LVH in women with CH.

Materials and Methods. A prospective study including a cohort of singleton pregnancies with a diagnosis of CH according to ISSHP guidelines. A non-invasive hemodynamic evaluation by USCOM-1A and a trans-thoracic echocardiography were performed before 16 weeks of gestation. We also calculated the ratio between the Mean Arterial Pressure and the maternal Heart Rate (MAP/HR Ratio). LVH was diagnosed when Left Ventricular Mass Index was over 95 g/m^2. An adverse pregnancy outcome (APO) was defined in presence of one of the following complications: delivery < 32 weeks, superimposed preeclampsia, Intrauterine Growth Restriction, stillbirth.

Results. 49 women were included. Cardiac Output and Systemic Vascular Resistance showed the highest accuracy in predicting the risk of LVH (AUC 94.4 95%CI 0.86-0.99 cut-off 5.8 and AUC 94.0% 95%CI 0.86-0.99 cut-off 1387, respectively). The MAP/HR ratio also showed a good accuracy (AUC 80.6 95%CI 0.68-0.93, cut-off 1.20) while maternal age showed a fair accuracy (AUC 71.8%, 95%CI 0.57-86.0, cut-off 37.0). The incidence of an APO was significantly higher in those women with LVH (50% *vs* 18.5%, p = 0.019, OR 4.4, 95%CI 1.2-15.8).

Conclusions. Hemodynamic parameters by USCOM-1A can stratify the risk of pregnant woman with CH in presenting LVH and to identity those who are likely to have an increased risk of an APO.

Antenatal characteristics and perinatal outcomes of late-onset fetal growth restriction (FGR) diagnosed in diabetic pregnancies: a retrospective study

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DOI: 10.36129/jog.2022.S24

Objective. To assess the relationship between adverse perinatal outcome and the presence of pre-gestational or gestational diabetes (DM or GDM), in a cohort of late-onset FGR fetuses.
Materials and Methods. A retrospective case control study was conducted in two tertiary maternity hospitals. A cohort of diabetic women with late FGR fetuses was included as the case group and compared with a control group of non-diabetic women with late FGR fetuses. The following criteria were used for the definition of late FGR: abdominal circumference (AC) or estimated fetal weight (EFW) < 10 percentile > 32 weeks or a reduction of more than 50 percentiles of CA compared to second trimester ultrasound scan.
A composite adverse perinatal outcome (CAO) was defined in the presence of one of the following outcomes: newborn with pH < 7.1, Apgar at 5 min < 7, respiratory support at birth, neonatal hypoglycaemia, neonatal jaundice, admission to the NICU.
Results. Overall, over a period of 8 years, 516 pregnancies complicated by late-onset FGR were included, 62 (12.0%) of them occurring in diabetic women. Among them, 5 (1%) had pregestational diabetes, 42 (8.1%) GDM on diet and 15 (2.9%) GDM on insulin therapy. In the case group women had higher BMI at booking (25.3 ± 5.6 *vs* 22.4 ± 4.0, $p < 0.001$) and a higher incidence of multiparity (35/63, 55.6% *vs* 148/448, 33.0%, $p < 0.001$). No statistically significant difference in terms of CAO was found between the two groups, while a significantly higher incidence of CAO was demonstrated comparing diabetic women on insulin therapy with those on diet (17/20, 85%, *vs* 25/42, 59.5%, $p = 0.04$).
Conclusions. The need for insulin therapy in diabetic women with late-onset FGR fetuses seems to be associated with a higher incidence of adverse perinatal outcome.

Perinatal risk factors for neonatal hyperbilirubinemia in healthy term neonates: a retrospective case-control study

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DOI: 10.36129/jog.2022.S25

Objective. The aim of the study was to evaluate underlying causes and to define perinatal risk factors of neonatal jaundice in healthy term neonates, improving knowledge which would be valuable to help identify strategies for risk reduction.
Materials and Methods. The study was a retrospective, observational analysis conducted from January 1, 2022, to August 15, 2022. Data from infants with a gestational age ≥ 35 weeks and birth weight ≥ 2500 grams were prospectively collected. Two groups were identified: the first with infants' total serum bilirubin (TSB) level ≥ 12 mg/dL (205 μmol/L) and the second group with TBS levels in the normal range. Infants' data were cross-referenced with maternal information such as maternal disorders, delivery induction strategy and type of delivery.
Results. A total of 200 mother-infant pairs were included in the study. Normal vaginal delivery (46.4% *vs* 32.1%, p = 0.02) and Oxytocin induction (36.2% *vs* 28.1%, p = 0.03) were a risk factor for neonatal jaundice. Epidural analgesia was not statistically significant as a risk factor for neonatal jaundice (27.3% *vs* 29.1%, p = 0.32).
Conclusions. The delivery type affects neonatal jaundice development. Vaginal delivery and Oxytocin induction were the only perinatal risk factors for neonatal jaundice.

Cerebral redistribution in late-onset fetal growth restriction: not always the same story *(Winner of the SIMP EUBRAIN Award, in memory of J. Claudine Larroche for the study on PVL in 1962)*

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DOI: 10.36129/jog.2022.S26

Objective. To evaluate perinatal outcomes of late-onset FGR fetuses showing cerebral redistribution in relation to modifications of Doppler components of cerebroplacental ratio (CPR).

Materials and Methods. Multicentre retrospective study including non-anomalous singleton pregnancies complicated by late-onset FGR featuring CPR < 5° P. Perinatal outcomes were compared across four subgroups:

1. fetuses showing UAPI < 95° P and MCAPI > 5° P;
2. UAPI > 95° P and MCAPI > 5° P;
3. UAPI < 95° P and MCAPI < 5° P;
4. UAPI > 95° P and MCAPI < 5° P.

Results. 308 cases were included: 33.4% belonged to group 1, 28.8% group 2, 20.5% group 3, 17.2% group 4. Group 2 was associated with lower gestational age at delivery (37+0+2+1 *vs* 38+0+1+6, 37+5+1+6 and 37+5+1+6 weeks for groups 1, 3 and 4 respectively, p = 0.01) and birthweight (2178+509 *vs* 2451+470, 2362+496 and 2416+450 g for groups 1, 3 and 4 respectively, p < 0.01), higher incidence of cesarean delivery (49.4% *vs* 26.5%, 37.1% and 34.0% for groups 1, 3 and 4 respectively, p = 0.04), delivery < 37 weeks (47.2% *vs* 20.4%, 25.4% and 30.2%, for groups 1, 3 and 4 respectively, p < 0.01), need for respiratory support at birth (22.5% *vs* 7.8%, 7.9% and 9.4% for groups 1, 3 and 4 respectively, p < 0.01), NICU admission (42.7% *vs* 20.4%, 20.6% and 34.0% for groups 1, 3 and 4 respectively, p < 0.01), composite adverse outcome (38.2% *vs* 16.5%, 15.9% and 24.5% for groups 1, 3 and 4 respectively, p < 0.01) and longer neonatal hospital admission (8 *vs* 4, 5 and 6) for groups 1, 3 and 4, respectively, p < 0.01).

Conclusions. The worst perinatal outcomes in late-onset FGR with cerebral redistribution occur when characterized by increased UAPI but normal MCAPI.

Fetal growth restriction clinical practice guidelines: systematic review

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DOI: 10.36129/jog.2022.S27

Objective. To systematically identify and critically assess the quality of clinical practice guidelines.

Materials and Methods. Medline, Embase, Google Scholar, Scopus and ISI Web of Science databases were searched to identify all relevant CPGs on the management of pregnancies complicated by FGR. The risk of bias and quality assessment of the CPGs included were performed using AGREE II tool.

Results. The definition of FGR: 22.2 of CPS adopted the Delphi consensus, 55.6% an estimated EFW/AC < 10th centile, 11.1 an EFW/AC < 5th centile, one CPG defined FGR as an arrest or a shift in the rate of growth measured longitudinally. 55.5% recommended the customized growth charts. In case of AEDF/REDF in the umbilical artery: 11.1% recommended assessment every 24-48 h, 44.4% every 48-72 h, 1 CPG recommended assessment 1-2 times per week. In case of FGR with mild abnormalities in the UA, middle cerebral artery or cerebroplacental ratio or presence of FGR without Doppler abnormalities: one CPG recommended delivery at 34-37 weeks, one at 37, one at 36-37 weeks, while 6 CPGs did not report any recommendation. In case of FGR with AEDF in the UA: 44.4% recommended delivery by 32 weeks, 44.4% by 34 weeks, while one CPG generically recommended delivery before 37 weeks of gestation. In case of REDF: 44.4% suggested considering delivery by 30 weeks, 33.3% by 32 and one CPG by 34 weeks of gestation.

Conclusions. There is significant heterogeneity in the management of pregnancies complicated by FGR in published CPGs.

Fetal cardiac function in pregnancies complicated by fetal growth restriction undergoing induction of labour

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DOI: 10.36129/jog.2022.S28

Objective. To investigate fetal cardiac function in fetuses with late fetal growth restriction (FGR) prior to the induction of labour with mechanical.

Materials and Methods. Prospective multicenter study including singleton pregnancies complicated by late FGR and SG. Left and right sphericity index (SI), myocardial performance index, mitral (MAPSE) and tricuspid annular valve displacement were compared between the two groups. Analysis was stratified according to the occurrence of adverse perinatal outcome defined as the sum of cesarean section for fetal distress, abnormal acid base status and admission to neonatal intensive care unit.

Results. Four hundred and five pregnancies were included. Adverse perinatal outcome was detected in 21% of pregnancies. There was no significant difference in the maternal and pregnancy characteristics between the two groups. Fetuses with late FGR experiencing adverse perinatal outcome in labor had a lower median left (1.48, IQR 1.35-1.67 *vs* 1.527, IQR 1.26-1.17 *vs* , $p < 0.001$) and right (1.19, 95%CI 1.16-1.27 *vs* 1.36, IQR 1.12-1.43, $p = 0.003$). Fetuses with FGR experiencing adverse perinatal outcome also showed an impaired MPI compared to those having uncomplicated vaginal delivery, mainly due to the higher isovolumic relaxation time (67.1 ± 5.2 *vs* 51.4 ± 1.8, $p < 0.001$). Finally, fetuses with FGR had longer TAPSE (6.9 ± 0.2 *vs* 5.2 ± 0.2, $p < 0.001$) and MAPSE (5.8 ± 0.7 *vs* 4.6 ± 0.1, $p < 0.001$) compared to SGA fetuses.

Conclusions. Assessment of fetal cardiac function can predict the occurrence of adverse perinatal outcome in pregnancies undergoing IOL for late FGR.

Prenatal predictor of composite adverse outcome in pregnancies undergoing induction of labour for fetal growth restriction

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DOI: 10.36129/jog.2022.S29

Objective. To investigate prenatal predictors of adverse perinatal outcome in pregnancies undergoing induction of labor for late fetal growth restriction (FGR) with mechanical methods (cervical ballon).

Materials and Methods. Multicenter study including pregnancies with late FGR diagnosed using the new Delphi criteria undergoing IOL with mechanical materials. The prenatal predictors explored were maternal age, parity, body mass index, fetal weight, pulsatility index in the middle cerebral and uterine arteries, umbilical vein blood flow and amniotic fluid index. Multivariate logistic regression analysis and ROC analysis were used to build a multiparametric prediction mode. Adverse perinatal outcome was defined as the sum of cesarean sections for abnormal CTG trace, abnormal acid base status or admission to neonatal intensive care unit.

Results. Four hundred and five pregnancies were included. Adverse perinatal outcome was detected in 21% of pregnancies. At logistic regression analysis a low MCA PI (OR 1.23, 95%CI 1.1-1.4, $p < 0.001$), nulliparity (OR 5.4, 95%CI 3.3-7.4) and high PI in the uterine artery (OR 1.32, 95%CI 1.2-1.6, $p = 0.004$) were independently associated with an adverse perinatal outcome.

Conclusions. Fetuses with FGR are at a higher risk of adverse perinatal outcome after IOL. MCA and uterine artery PI were independently associated with an adverse perinatal outcome prior to the IOL.

Fetal cardiac function in twin pregnancies complicated by selective fetal growth restriction

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DOI: 10.36129/jog.2022.S30

Objective. To investigate fetal cardiac function in monochorionic (MC) twin pregnancies with selective fetal growth restriction (sFGR) according to the umbilical artery Doppler pattern.

Materials and Methods. Prospective study including pregnancies complicated by FGR. Left and right sphericity index (SI), myocardial performance index, mitral (MAPSE) and tricuspid annular valve displacement were compared in MC twins with sFGR (Type I: persistently positive EDF, Type II: persistent AEDF or REDF, type III instable Doppler pattern).

Results. 21 fetuses with type I, 27 with type II, 14 with type III and 62 appropriately grown twins were included. Compared to the non-FGR twin , left SI was lower in type I, type II, and type III sFGR twins ($p < 0.001$ for all). Fetuses with Type I, II and III sFGR had a longer TAPSE and MAPSE compared to the normally grown twin.

The MPI was higher in type I, II and III compared to controls. When comparing the different types of sFGR according to the UA Doppler pattern, the overall cardiac function was lower in type II compared to type I, while fetuses with type III sFGR showed an overall better performance compared to type II sFGR.

Conclusions. MC twins with sFGR had a sub-optimal cardiac function compared to the appropriately grown twins. Cardiac function was reduced in type II compared to type I while it was better in type III compared to type II.

Fetal cardiac function in pregnancies complicated by fetal growth restriction and small for gestational age

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DOI: 10.36129/jog.2022.S31

Objective. To investigate fetal cardiac function in fetuses with late fetal growth restriction (FGR) and small for gestational age (SGA).
Materials and Methods. Prospective study including singleton pregnancies complicated by late FGR and SGA according to the recently published Delphi consensus. Left and right sphericity index (SI), myocardial performance index, mitral (MAPSE) and tricuspid annular valve displacement were compared between the two groups. T-test and Mann-Whitney U test were used to analyze the data.
Results. Sixty-seven fetuses with FGR and 111 SGA were included in the analysis. There was no significant difference in the maternal and pregnancy characteristics between the two groups. Fetuses with late FGR had a lower median left (1.42, IQR 1.25-1.61 *vs* 1.57, IQR 1.46-1.68 *vs*, $p < 0.001$) and right (1.23, 95%CI 1.17-1.37 *vs* 1.46, IQR 1.33-1.59, $p < 0.001$). Fetuses with FGR also showed an impaired MPI compared to SGA, mainly due to the higher isovolumic relaxation time (65.3 ± 4.2 *vs* 42.4 ± 2.3, $p < 0.001$), while there was no difference in the ejection time and isovolumic contraction time between the two groups. Finally, fetuses with FGR had longer TAPSE (6.2 ± 0.3 *vs* 5.7 ± 0.6, $p < 0.001$) and MAPSE (5.6 ± 0.4 *vs* 4.2 ± 0.3, $p < 0.001$) compared to SGA fetuses.
Conclusions. Fetuses with FGR have a sub-optimal cardiac function compared to those with SGA.

The role of USCOM in predicting preterm delivery in women with threatened preterm delivery: a look into maternal cardiovascular maladaptation

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DOI: 10.36129/jog.2022.S32

Objective. The aim of this study was to investigate maternal hemodynamic profiles in women with a diagnosis of threatened preterm delivery (TPD) distinguishing between those who delivered early and those who remained undelivered until term.
Materials and Methods. Sixty-one patients with a diagnosis of TPD were enrolled in this prospective observational cohort study and assessed with Ultrasound Cardiac Output Monitor (USCOM®). The subjects were divided into groups according to week of delivery. Group 1 included women who experienced preterm birth (n = 35/61) while Group 2 was comprised of women who delivered at term (n = 26/61). Women with a diagnosis of fetal growth restriction or hypertensive disorders were excluded. Evaluated maternal features were cervical length, urinary culture and vaginal swab results. Perinatal and neonatal outcomes were also evaluated. The study was approved by our local Ethics Committee and all participants gave their informed consent at enrolment.
Results. No differences were found based on maternal age, body mass index, gravidity and parity, positive urinary culture or vaginal swabs, cervical length and neonatal birthweight percentile. Lower gestational age at delivery (31.9 ± 3.5 *vs* 38.9 ± 1.4, $p < 0.0001$), neonatal birth weight (1839.8 ± 643.5 *vs* 3129.2 ± 487.4, $p < 0.0001$) and 1st and 5th minute Apgar scores (respectively 7.6 ± 1.7 *vs* 8.7 ± 0.9 and 8.7 ± 1.1 *vs* 9.6 ± 1.0, $p < 0.0001$) were observed in Group 1 *vs* Group 2. Maternal hemodynamic data are shown in **Table 1**.
Conclusions. Among the women admitted for TPD the only discriminating factor between term and preterm delivery was an increased TVR in the preterm group. Increased TVR may possibly explain the higher lifetime cardiovascular risk described in preterm-delivering women.

Table 1.

Haemodinamic profile	Group 1 Preterm deliveries (n° 35/61)	Group 2 Term deliveries (n° 26/61)	p-value
Heart Rate (bpm)	86.51± 14.18	83.00 ± 12.96	0.32
Cardiac Output (L/min)	5.96 ± 1.51	6.20 ± 1.19	0.48
Stroke Volume (mL)	70.11 ± 19.45	76.04 ± 15.70	0.19
Total Vascular Resistance (TVR) (dynes x s/cm^5)	1220.80 ± 382.73	1094.00 ± 248.92	0.04

The familial pattern of spontaneous preterm birth: a case control study

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DOI: 10.36129/jog.2022.S33

Objective. To investigate the role of family history of preterm birth (PTB) as an individual risk factor for spontaneous preterm delivery.

Materials and Methods. This was a retrospective case-control study. 354 patients (Cases n = 177, Controls n = 177) were enrolled between 2018-2020. Cases were defined as women with history of spontaneous PTB and controls as women with history of full-term delivery. A telephone questionnaire was administered to investigate the family history of PTB of both the patient and her partner. Cases and controls were matched for the anamnestic risk factors for PTB.

Results. 17 of 173 women (9.8%) in the PTB group reported being born before term, compared to 5 of 169 women (2.9%) in the control group, with odds ratio (OR) of 3.57 (95%CI 1.29-9.92). Women who had preterm delivery also reported more frequently having a sibling who was born preterm (12.35% *versus* 4.24%) with OR of 3.18 (95%CI 1.31-7.7). Patients whose partner was born prematurely did not have increased risk of delivering their child prematurely. Similarly, no other association were found between partner's family history of PTB and risk of preterm delivery in the present pregnancy.

Conclusions. Pregnant patients who were born prematurely or have siblings born in a similar manner have an increased risk of PTB in their own pregnancies. Assessment of female family history of PTB at pre-conception or at the first antenatal appointment should be used to identify woman at risk of having a PTB in the present pregnancy and for appropriate counselling and follow-up.

Results

	Case Group	Control Group	Odds Ratio (CI 95%)	P value
Patient family history				
Personal history of premature birth	17/173 (9.82%)	5/169 (2.96%)	**3.57 (1.29-9.92)**	**0.0145**
Sibling born prematurely	21/170 (12.35%)	7/165 (4.24%)	**3.18 (1.31-7.7)**	**0.0103**
Other first/second degree relatives born prematurely	24/146 (16.44%)	15/134 (11.19%)	1.56 (0.78-3.12)	0.207
Partner family history				
Personal history of premature birth	11/169 (6.51%)	14/160 (8.75%)	0.72 (0.32-1.65)	0.44
Sibling born prematurely	6/141 (4.26%)	6/122 (4.91%)	0.86 (0.27-2.73)	0.797
Other first/second degree relatives born prematurely	9/141 (6.38%)	8/122 (6.56%)	0.97 (0.36-2.6)	0.954

Bold values are statistically significant (p- value < 0.05)

A prospective cohort study evaluating exclusive breastfeeding in late preterm infants

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DOI: 10.36129/jog.2022.S34

Objective. In late preterm neonates, born between 34 0/7 and 36 6/7 weeks gestation, breastfeeding can be arduous.
Materials and Methods. This is a prospective cohort study in which we evaluated exclusive breastfeeding at discharge, at 3 and 6 months of life among late preterm infants, aiming to identify the facilitators and challenges present. In our cohort, only late preterm neonates eligible for the rooming-in were included. We collected data about breastfeeding at discharge, at 3 and 6 months of life.
Results. 214 late preterm infants were included in the study. At discharge 70 infants (32.7%) were fed with
human milk and 144 (67.2%) were not. Women who were primiparous, who had hypertension, and who underwent cesarean sections had non-exclusive breastfeeding more frequently. Non-exclusive breastfeeding was associated with a low birth weight (< 2500 g), ≥ 2 blood glucose controls, weight loss > 10%, and longer hospital stay. Exclusive human milk feeding was associated with an early first latch-on and skin-to-skin contact ($p < 0.001$) . Late preterm neonates born at 35 weeks showed a significant increase in exclusive human milk feeding at 3 months compared to the rate at discharge ($p = 0.004$).
Conclusions. In this cohort, exclusive human milk feeding was more common with an early first latch-on and immediate skin-to-skin contact. Despite being formula-fed during hospitalization, at the follow-up there was an increase in infants born at ≥ 35 weeks gestation who were exclusively breastfed.

Neonatal outcomes in an expectantly managed prospective cohort of late preterm prelabor rupture of membranes

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DOI: 10.36129/jog.2022.S35

Objective. The aim was to assess the effects of expectant management in women with preterm prelabour rupture of membranes between 34 and 36+6 weeks (LpPROM) in terms of neonatal outcomes (NO). The secondary scope was to assess the risk of neonatal sepsis.

Materials and Methods. This is a multicentric, prospective cohort study that includes singleton infants born to mothers with LpPROM, managed using the same protocol, between January 2021 to August 2022.

The primary NO was a composite of neonatal death, non-invasive or invasive respiratory support, hypoglycaemia, new-born sepsis, confirmed seizures, stroke, intraventricular haemorrhage, basal nuclei anomalies, cardiopulmonary resuscitation, umbilical-cord-blood arterial pH < 7.0 or BE < -12.5, and prolonged hospitalization (5 days). Univariate analysis described the differences according to GA at delivery. Multivariate logistic regression was used to investigate the effects of GA at PROM, and PROM to delivery interval on the NO.

Results. 106/170 (62.4%) women with LpPROM did not deliver within 24 hours (expectant management). The median latency duration was 1 day, except for 36-37 weeks (3 days), having no effect on neonatal morbidity. Prevalence of neonatal sepsis was low 2/170 (1.2%) and did not differ between gestational weeks (**Table 1**). Multivariate analysis also showed, for a weekly increase in gestational age, a reduction of 57% on adverse NO, by adjusting for the newborn weight, PROM to delivery interval and corticosteroid (p = 0.004).

Conclusions. Expectant management of LpPROM should be encouraged because each passing week, significantly reduces the risk of adverse NO; moreover, the risk of neonatal sepsis does not increase in different gestational periods.

Table 1.

	34 w (N=14)	35 w (N=31)	36 w (N=114)	37 w (N=9)	P value
Delivery outcomes					
Indication to delivery					0.41
Spontaneous labor	10 (71.4)	18 (58.0)	65 (59.6)	2 (22.2)	
pPROM (no suspected triple I)	3 (25.0)	9 (29.0)	39 (34.2)	6 (66.7)	
Indicated	1 (8.3)	5 (16.0)	10 (8.7)	1 (11.1)	
Labor					0.01
No labor	**4 (28.6)**	**5 (16.1)**	**26 (22.8)**	**0**	
Spontaneous	**8 (57.1)**	**20 (64.5)**	**60 (52.6)**	**2 (22.2)**	
Induced	**2 (14.3)**	**6 (19.3)**	**28 (24.6)**	**7 (77.8)**	
Mode of Delivery					**0.05**
Spontaneous vaginal	10 (71.4)	21 (67.7)	81 (71.0)	6 (66.7)	
Operative vaginal	**0**	**2 (6.4)**	**7 (6.4)**	**3 (33.3)**	
Cesarean Section	**4 (28.6)**	**8 (25.8)**	**26 (22.8)**	**0**	
pPROM to delivery interval (days)	**1 (0-1)**	**1 (0-1)**	**1 (0-2)**	**3 (2 – 3)**	**0.000**
Maternal hyperpyrexia in labor (≥38°C)	0	0	3 (2.6)	0	0.69
Antibiotic treatment	14 (100.0)	30 (96.7)	110 (96.5)	**6 (66.7)**	**0.001**
Antenatal corticosteroids					**0.01**
No administration	**12 (85.7)**	**27 (87.1)**	**105 (94.6)**	**9 (100.0)**	
Before 34 weeks	**0**	**4 (12.9)**	**4 (3.6)**	**0**	
After 34 weeks	**2 (14.3)**	**0**	**2 (1.8)**	**0**	
Tocolysis	**1 (7.1)**	0	0	0	**0.01**
Neonatal outcomes					
Birthweight (g)	**2228.8 ± 345.6**	**2605.4 ± 311.2**	**2710.4 ± 327.7**	**2871.1 ± 316.5**	**0.000**
Apgar score ≤ 7 at 5'	**2 (14.3)**	**0**	**1 (0.8)**	**0**	**0.003**
Arterial pH ≤ 7.1	0	0	3 (2.7)	0	0.71
Respiratory support	**2 (14.3)**	**1 (3.2)**	**0**	**0**	**0.000**
Neonatal sepsis	1 (7.1)	1 (3.2)	0	0	0.08
Adverse neonatal outcome*	**8 (61.5)**	**11 (36.7)**	**22 (20.4)**	**1 (12.5)**	**0.000**

Latency from premature preterm rupture of membranes to delivery and correlation with gestational age

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DOI: 10.36129/jog.2022.S36

Objective. To evaluate the average latency from preterm premature rupture of membranes (pPROM) to delivery, and its correlation with the gestational age (GA) at pPROM.

Materials and methods. A retrospective study was performed on pregnancies complicated by pPROM from January 2018 to December 2021 at Careggi Hospital (Florence). GA at pPROM and at delivery were recorded and latency to delivery was calculated, after excluding patients carrying a pessary or cerclage, and cases of major fetal malformation. Patients were then divided into five groups according to gestational age at pPROM (< 24, 24 to 28, 28 to 32, 32 to 34, and 34 to 37 weeks). Descriptive and correlation analyses were performed.

Results. The incidence of pPROM during the study period was 2% (275/12,702 births). After applying the exclusion criteria, we selected a cohort of 237 pregnancies. Overall, the median GA at pPROM was 35.7 weeks (IQR 32.6, 36.4) and the median latency to delivery was 1 day, as pPROM occurred after 34 weeks in most patients (71%). **Table 1** reports data on latency and GA at delivery, after dividing groups of different gestational age at pPROM. Below 32 weeks of gestation, there was a significant inverse correlation between the GA at pPROM and the latency to delivery (Spearman's rho -0.45, p = 0.001).

Conclusions. Latency varies depending on the GA at pPROM: below 32 weeks of gestation, the earlier the pPROM occurrs, the longer is the latency to delivery. These data may be useful for patients' counselling.

Table 1.

Gestational age at pPROM	n	GA at delivery	Latency to delivery (days)	Delivery within 48h from pPROM	Delivery within 7 days	Placental abruption
All	237	35.9 (33.6, 36.4)	1 (0, 3)	174 (73%)	197 (83%)	2 (0.8%)
<24	11	26.8 (±1.8)	30.8 (±11.2)	0	0	0
24^{+0}-27^{+6}	29	28.4(±1.8)	15.5 (±13.1)	4 (13.8%)	11 (37.9%)	0
28^{+0}-31^{+6}	13	31.8 (±1.8)	13.8 (±10.5)	2 (15.4%)	5 (38.5%)	0
32^{+0}-33^{+6}	16	33.4 (±0.6)	2 (0.3, 5.0)	9 (56.3%)	13 (81.3%)	2 (12%)
34^{+0}-36^{+6}	168	36.3 (35.7, 36.5)	1.0 (0, 1)	159 (94.6%)	168 (100%)	0

Universal cervical length screening after 24 weeks is not useful *(Winner of the SIMP Award, in memory of Professor J. Francesco Branconi)*

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DOI: 10.36129/jog.2022.S37

Objective. To evaluate the accuracy of a single cervical length (CL) measurement performed after 24 weeks of gestation in predicting spontaneous preterm birth (sPTB) in asymptomatic singleton pregnancies at low anamnestic risk for sPTB.

Materials and Methods. Retrospective, single-centre cohort study. Data regarding maternal demographics, medical and obstetrical history, and pregnancy outcome of 2905 patients were collected. 1667 patients had CL measured at 24+0 to 27+6 weeks of gestation and 2363 patients at 28+0 to 32+0 weeks. 1125 patients were present in both gestational age windows. The predictivity of CL for sPTB was evaluated through logistic regression analysis. results were adjusted for confounding factors.

Results. sPTB occurred in 64 patients (2.19%). A shorter CL and a lower BMI were significantly associated with sPTB. In the 24^{+0}-27^{+6} weeks group, sPTB occurred in 33 patients (1.98%). CL had a moderate predictive value for sPTB (ROC curve analysis: AUC 0.71, CI 0.61-0.81). In the 28^{+0}-32^{+0} weeks group, sPTB occurred in 54 patients (2.29%). CL had a low predictive value for sPTB (ROC curve analysis: AUC 0.6, CI 0.53-0.66).

Conclusions. The predictive value of CL for sPTB in asymptomatic, low-risk patients after 24 weeks of gestation is low. CL assessment in this population should not be performed.

The predictive value of CL for sPTB in asymptomatic, low-risk patients between 24 and 28 weeks of gestation is moderate. Further research should focus on interventions to prevent sPTB in this population. The predictive value of CL for sPTB in asymptomatic, low-risk patients after 28 weeks of gestation is low. CL assessment in this population should not be performed.

24^{+0}-27^{+6} weeks of gestational age

	Preterm birth = 33	Term birth = 1634	OR (C.I. 95%)	p-value
Age	32.8(28 - 36)	33.6 (30 - 37)	0.98 (0.92 - 1.03)	0.41
BMI	22.64 (18.90 - 25.30)	23.72 (20.20 - 25.69)	0.96 (0.88 - 1.04)	0.70
Ethnicity				
White	29 (1.97%)	1442 (98.03%)	reference	
Black	1 (3.45%)	28 (96.55%)	2.58 (0.47 - 14.22)	0.28
South Asian	2 (3.03%)	64 (96.97%)	1.90 (0.50 - 7.12)	0.34
East Asian	0 (0%)	31 (100%)	0.78 (0.04 - 13.58)	0.86
Mixed	5 (1.43%)	69 (98.57%)	1.06 (0.20 - 5.60)	0.95
Cervical length	**29 (22 - 38)**	**37 (34 - 41)**	**0.91 (0.89 - 0.93)***	**<0.01**
Progesterone	**8 (5.44%)**	**25 (1.64%)**	**3.57 (1.61 - 7.93)**	**<0.01**

28^{+0}-32^{+0} weeks of gestational age

	Preterm birth = 84	Term Birth = 2407	OR C.I. 95%	p-value
Age	32.6 (28 - 38)	33.6 (30 - 37)	1.01 (0.99 - 1.02)	0.46
BMI	**21.84 (19.49 - 23.38)**	**23.43 (20.20 - 25.34)**	**0.91 (0.84 - 0.99)**	**0.02**
Ethnicity				
White	44 (2.16%)	1993 (97.84%)	reference	
Black	2 (4.26%)	45 (95.74%)	2.46 (0.66 - 9.22)	0.18
South-Asian	5 (3.48%)	111 (96.52%)	1.81 (0.67 - 4.88)	0.24
East Asian	2 (3.28%)	59 (96.72%)	1.88 (0.51 - 6.97)	0.34
Mixed	2 (1.94%)	101 (98.06%)	1.1 (0.3 - 4.03)	0.88
Cervical length	**30.5 (24 - 37)**	**36 (32 - 40)**	**0.92 (0.89 - 0.94)***	**<0.01**
Progesterone	**11 (5.53%)**	**43 (1.99%)**	**2.98 (1.53 - 5.8)**	**<0.01**

Second trimester cervical length screening: a prevalence study

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DOI: 10.36129/jog.2022.S38

Objective. A short cervix is a risk factor for preterm birth. The aim of this study is to evaluate the prevalence of short CL at the second trimester anatomy scan and its impact on preterm Birth (PTB) rates in the district of Modena and Parma, Northern Italy.
Materials and Methods. This is a multicenter, prospective cohort study (September 2020 to November 2021) screening women > 18 years for CL. Eligible women were those attending antenatal ultrasound morphology scans at National health system clinics in Modena and Parma districts. After informed consent, a transvaginal ultrasonogram was performed between 18+0 and 22+6 weeks of gestation. The *ad-hoc* database included known risk factors for PTB and delivery data. PTB < 37 weeks rate during the screening was compared with a previous control period, in the same districts (January to December 2019).
Results. Out of 5112 eligible women, 3083 participated in the screening. The remaining were randomly not screened mainly due to sonographer unavailability. The median CL was 40 mm (10^{th} centile = 34 mm). Overall, 28 (0.9%) women had CL ≤ 25 mm. Among them, 8 had PTB (28%) compared with 136 PTB (4.4%) in women with a normal cervix (p > 0.0001). PTB rates during screening period did not differ comparing to control period (145/2807, 5.2% *vs* 476/8387, 5.7%, p = 0.3) by the way, population doesn't look so different (**Table 1**).
Conclusions. Although poorly represented in our population, CL ≤ 25 confirmed to be a risk factor for PTB. CL universal screening seems not justified by the above findings.

Table 1. *PPT rate in screened population and in the control group.*

Preterm Birth	CL screening group (n, %)	Control group (n, %)	P value
< 37 weeks	(145/2.807), 5,16	(476/8.387), 5,70	0,31
34-36+6 weeks	(114/2.807), 4,06	(327/8.387), 3.90	0,70
< 32 weeks	(16/2.807), 0,57	(77/8.387), 0,92	0,08

Vaginal progesterone compared to intramuscular 17-alpha-hydroxyprogesterone caproate for prevention of recurrent spontaneous preterm birth in singleton gestations: a systematic review and meta-analysis

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DOI: 10.36129/jog.2022.S39

Objective. To evaluate the efficacy of vaginal progesterone compared with 17P in prevention of SPTB in singleton gestations with prior SPTB.

Materials and Methods. Searches were performed in electronic databases. No restrictions for language or geographic location were applied. We included all RCTs of asymptomatic singleton gestations with prior SPTB who were randomized for prophylactic treatment with either vaginal progesterone (intervention group) or intramuscular 17P (comparison group). The primary outcome was PTB < 34 weeks. The summary measures were reported as relative risk (RR) with 95%CI.

Results. Seven RCTs, including 1894 women were included in the meta-analysis. Women who received vaginal progesterone had a significantly lower rate of PTB < 37 weeks (36.2% *vs* 46.4%, RR 0.78, 95%CI 0.69 to 0.87), PTB < 34 weeks (14.6% *vs* 19.9%, RR 0.73, 95%CI 0.57 to 0.95), and PTB < 32 weeks, compared to women who received intramuscular 17P. There were no significant differences in the rate of PTB < 28 weeks. The rate of women who reported adverse drug reactions was significantly lower in the vaginal progesterone group compared to the 17P group. Regarding neonatal outcomes, vaginal progesterone was associated with a lower rate of NICU admission compared to 17P. Perinatal mortality occurred in 11/492 (2.2%) in the intervention group *vs* 21/474 (4.4%) in the control group (RR 0.51, 95%CI 0.25 to 1.01).

Conclusions. Daily vaginal progesterone started at about 16 weeks is a better alternative to weekly 17P for prevention of SPTB in women with singleton gestations and prior SPTB, and should be preferred in this population.

Sleep-disordered breathing and obstructive sleep apnea in pregnancy: the burden of patient BMI and risk of poor outcome

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DOI: 10.36129/jog.2022.S40

Objective. Sleep-disordered breathing (SDB) occurs more frequently in pregnant women than in the general female population. The first aim of the study was to evaluate the impact of BMI on the risk of SDBs/OSAS in pregnancy. The second outcome was to assess the feasibility of screening tools for SDBs in obese and overweight pregnant women *vs* controls. As a third aim, we investigated the incidence of perinatal adverse outcomes in an obese pregnant population at high risk for SDB and the evolution of risk across gestation.

Materials and Methods. Prospective observational study on 160 consecutive pregnant women attending prenatal care in our clinic. All the women were screened for SDBs in the three trimesters of pregnancy. Logistic regression analysis was used to identify the risk factors for SDB positivity. If the patient was positive to at least one test out of 3, in at least one trimester screening, she was classified as "case", otherwise as "control". The composite maternal and neonatal outcomes were compared between cases and controls with univariate analysis.

Results. 31 out of 44 patients screened positive in at least one survey (70.5%), while 4/31 resulted positive in all the questionnaires (12.9%). The incidence of positive screening test for SDB was significantly lower among the control group ($p < 0.01$). Obese patients with negative screening for SDB showed a significant difference in terms of FGR (11.4% *vs* 1.3%, $p < 0.01$), PTB (9.1% *vs* 3.6%, $p < 0.01$), preeclampsia (13.6% *vs* 2%, $p < 0.05$), PIH (15.8% *vs* 3.6%, $p < 0.01$) and GDM (45.5% *vs* 8%, $p < 0.05$) *versus* controls. Logistic regression demonstrated that the rate of FGR, PTB, PE, PIH, GDM and induction of labor (IOL) were all significantly higher in obese women with a positive screening test than in controls ($p < 0.05$). Induction of labor occurred more frequently in patients screened positive *vs* controls (11.4% *vs* 1.8%, $p < 0.05$).

Conclusions. The SDB questionnaires used in our study represent a simple, low-cost tool which is able to screen obese/overweight women at risk of sleep disorders of breathing in pregnancy. Our cohort was not further tested for SDBs, but the screening was useful to identify women worth testing, given the association of these conditions with pregnancy complications.

PERCENTAGES	PS	NS	p
FGR	16.1	1.3	<0.05
PRETERM LABOR	13	3.6	<0.05
PREECLAMPSIA	19.3	1.8	<0.05
GESTATIONAL HYPERTENSION	22.6	3.8	<0.01
GESTATIONAL DIABETES	64.5	8	<0.01
INDUCTION OF LABOR	16.1	1.8	<0.05

Dietary habits in twin pregnancies: what is the adherence to the Mediterranean diet?

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DOI: 10.36129/jog.2022.S41

Objective. The nutritional status of pregnant women has a significant impact on the future health both of the offspring and the mother. The Mediterranean Diet fits all the recommendations for pregnant women and specifically for multiple pregnancies. The Mediterranean Diet potentially decreases the incidence of pregnancy complications like preeclampsia and gestational diabetes that are more frequent in multiple pregnancies. The aim of our study was to investigate eating habits in multiple pregnancies, in order to evaluate the adherence to the Mediterranean Diet.

Materials and Methods. Dietary information was collected from 50 multiple pregnant women who referred to the Careggi Multiple Pregnancy Outpatient Service from November 2021 to June 2022. The women were all aged 18-43 years in all three trimesters of pregnancy. Eating habits information and anthropometric data were collected. The Mediterranean Diet adherence was investigated through the Medi-Lite score.

Results. Our collected data showed that most women had a normal pre-pregnancy weight (72%), while 18% were overweight and 2% obese. The mean pre-pregnancy BMI was 22.1. The entire group consumed the three main meals during the day, however 30% of women skipped their mid-morning snack and 16% their mid-afternoon snack. A moderate adherence to Mediterranean Diet was observed (9.8 ± 1.8), however only a minority of the sample showed optimal uptake of fruit (20%), vegetables (12%), fish (6%), legumes (12%), milk and dairy products (22%).

Conclusions. Women with multiple pregnancies showed suboptimal adherence to the Mediterranean Diet. Knowing the degree of adherence to the Mediterranean Diet is important in order to customize the diet for each individual patient.

Maternal obesity and breastfeeding: retrospective longitudinal observational study

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DOI: 10.36129/jog.2022.S42

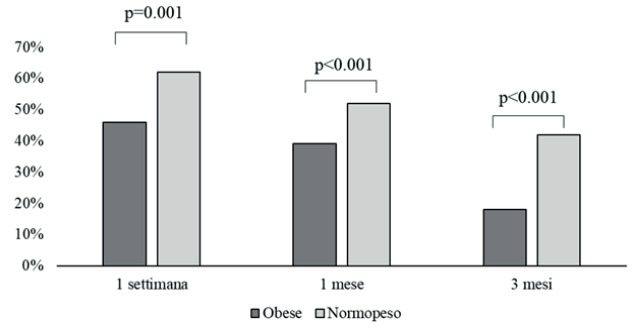
Objective. Evaluation of the relationship between maternal obesity and the onset and duration of breastfeeding.

Materials and Methods. This is a retrospective longitudinal observational study, including puerperas, who delivered a single fetus at term at the Obstetric Unit of Modena from 1 April 2020 to 30 April 2021, who completed the questionnaire "Madri" offered by MAMI (Italian maternal breastfeeding movement).

Results. 366/452 (81%) patients accepted to answer the questionnaire by telephone. Among these, 42.6% (n = 156) were obese at the time of delivery and 26% of them said they hadn't had the milky whip. Moreover, compared to normal weight women, the less obese had a physiological milky whip (between 48-72 hours after childbirth), (155, 74% *vs* 72, 46% p = 0.000) and were exclusively breastfeeding during hospitalization (155, 74% *vs* 81, 52% p = 0.001). The exclusive lactation rates at one week, one month and three months from childbirth are in **Figure 1**. After three months, the main reasons for withdrawal from breastfeeding were: the mothers' perception of having little milk for 30% of normal weight and 38% of obese women, maternal choice, 25% and 29% respectively, and breast rejection by the child, 22% and 18% respectively.

Conclusions. Maternal obesity seems to be associated with a more common failure to start breastfeeding, a shorter duration, less adequate milk production and a delayed onset of lactogenesis, compared to normal weight women. This suggests that healthcare professionals should consider obese women at risk of unsuccessful breastfeeding, and therefore follow-up strategies should be implemented in this population.

Table 1. *The rates of breastfeeding at one week, one month and three months from childbirth.*



Use of fetal MRI in fetuses referred with central nervous system abnormalities: a single-institution experience

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DOI: 10.36129/jog.2022.S43

Objective. To compare sonographic *vs* fetal MRI (fMRI) diagnosis in suspected central nervous system (CNS) abnormalities and to evaluate if the diagnosis using fMRI altered the management of the pregnancy.

Materials and Methods. A retrospective monocentric cohort study including all pregnant women undergoing a fMRI after ultrasound (US) for a suspected CNS malformation between 2010 and 2021 at Policlinico of Modena, University Hospital. For all cases we recorded: gestational age (GA) at US GA at fMRI, US and fMRI diagnosis, pregnancy outcome, postnatal or autoptic diagnosis. Malformations were categorized into 7 groups for analysis. The last US diagnosis before fMRI was used for comparison. We evaluated in which percentage the fMRI diagnosis differed from US and how it altered the management of the pregnancy.

Results. During the study period 97 pregnant women underwent fMRI (median GA at MRI: 30 (26.2-32.8) weeks) and a median time interval of 7 (2-12) days between US and fMRI. The fMRI diagnosis was different from the sonographic diagnosis in 29.9% (n = 29/97) of cases. The management was changed by the fMRI in 20/29 (69%) of cases, being ameliorated in 8/29 and worsened in 12/29. Considering the whole population, fMRI altered the management in 20.6% (20/97), worsening it in 12.4%.

In the worsened cases, in 4/12 fMRI showed additional cortical malformations, in 2/12 it showed germinal matrix cysts, in 1/12 it provided a diagnosis of teratoma, in the remaining cases it added additional information to characterize the anomaly. In cases with ameliorated prognosis (n = 8), in 2 cases the MRI did not confirm a suspicion of synechiae, in 6 cases the MRI was normal with a US diagnosis of narrow-hidden CSP (4 cases) or biometry of the corpus callosum < 5th centile (n = 2).

The pregnancy outcome was available for 80/97 (82.5%) fetuses; the remaining 17 were lost at follow up. Eleven (11/80, 13.8%) women opted for termination of the pregnancy: among these, three autoptic reports were not available; in the remaining 8 the concordance with prenatal diagnosis was 100%.

Sixty-nine fetuses were liveborn (86.3%); a post-natal ultrasound or MRI was available in 41/69 (59.4%) with a different/additional postnatal diagnosis in only 6/41 cases (14.6%) which are presented in **Table 1**.

Conclusions. fMRI represents an important tool in cases with suspected CNS anomaly; it adds information in 20% of cases with a better identification of cortical anomalies.

Table 1. *Comparison of prenatal and postnatal imaging (only additional findings are reported).*

Prenatal diagnosis	Additional Postnatal findings	Time of postnatal imaging
Monolateral ventriculomegaly and septum in the left frontal horn	Malrotation of the left hippocampal region; hemosiderinic focus in the left cerebellum area	79 days
Bilateral Ventriculomegaly, interhemispheric cyst	White matter hyperintensity of the parietal area and optical radiations	534 days
Mega cisterna magna	White matter hyperintensity of the lobar area bilaterally; thrombosis of midollar veins	45 days
Mega cisterna magna	Arachnoid cyst in the temporal-polar area	223 days
Sub-arachnoid cyst	Dilatation of the cervical ependymal canal (hydro syringomyelia?)	64 days
Arachnoid interehemispheric cyst	Partial hypo-agenesis of the corpus callosum (reduced growth of the splenium)	81 days

Hemodynamic evaluation in patients with type 1 diabetes mellitus in pregnancy

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DOI: 10.36129/jog.2022.S44

Objective. Type 1 diabetes mellitus (T1DM) increases the risk of fetal and maternal complications during pregnancy. Maternal hemodynamic maladaptation appears to underlie the pathogenesis of preeclampsia and fetal growth restriction; however, data on hemodynamics characteristics during pregnancy in diabetic women are limited.

The aim of our study was to compare maternal hemodynamic adaptations in pregnancies complicated by T1DM *versus* normal pregnancies.

Materials and Methods. A prospective case control study was conducted, comparing 47 singleton pregnancies complicated by T1DM and no other pregnancy comorbidities and 128 controls referred to our Unit from 2018 to 2021. Hemodynamic assessment was performed in both groups by Ultra Sonic Cardiac Output Monitor (USCOM) in four gestational age intervals: 14-20, 20-28, 28-34, > 34 weeks. We evaluated six hemodynamic parameters: cardiac output (CO), stroke volume (SV), cardiac index (CI), total vascular resistance (TVR), inotropy index (INO) and potential to kinetic energy ratio (PKR).

Results. The T1DM group had significantly lower values of CO, SV, CI and INO already at the first evaluation and until term; TVR and PKR were not significantly different in the early second trimester but were higher from 20-28 weeks until term.

Conclusions. T1DM women have a hemodynamic maladaptation to pregnancy. This condition could unmask a state of subclinical impairment of maternal cardiac function at conception. However, although T1DM patients have an unfavorable hemodynamic status from the beginning, neonatal outcomes are good thanks to a good glycometabolic compensation during all the pregnancy.

Maternal and fetal outcomes in women with gestational diabetes mellitus (GDM): does pre-pregnancy BMI make a difference?

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DOI: 10.36129/jog.2022.S45

Objective. The aim of this study was to analyze if pre-pregnancy BMI in women with GDM may influence maternal and fetal outcomes.

Materials and Methods. We evaluated the fetal and maternal outcomes of 1082 women with GDM who delivered in our hospital from January 2014 to December 2021. The patients were divided into two groups according to pre-gestational BMI (< or ≥ 30). Differences between the two groups were analyzed. Statistical analysis was performed using fisher exact test and t-test. P-value < 0.05 was considered statistically significant.

Results. 249 women (23%) were obese (BMI ≥ 30) and significantly more likely to experience induction of labor (83% *vs* 54%), insulin therapy (38% *vs* 19%) and to deliver a LGA infant (15% *vs* 10%).

Rates of vaginal delivery (89% *vs* 85%) and urgent labor caesarean section (CS) (13% *vs* 11%) were not different in the two groups, while the rate of elective CS was higher in the obese (26% *vs* 13%).

First trimester fasting glucose over 100 mg/dl was more common in the obese (20% *vs* 9%). The average levels of fasting glucose were also higher in this group (93 *vs* 88 mg/dl).

No differences in maternal age, neonatal weight, premature birth and analgesia rates were detected.

Neonatal hypoglycemia, jaundice, hypocalcemia, polycythemia, and respiratory distress were more common in obese women (25% *vs* 16%).

Conclusions. Obese women with GDM have an increased risk of severe disease, insulin therapy, labor induction and fetal adverse outcomes. It is mandatary in these patients to have intensive prenatal care.

	Obese woman	%	Normal weight woman	%	P value
	(N= 833)		(N = 249)		
Vaginal delivery	585/684	85.5	152/183	83	ns
Instrumental vaginal delivery	21/684	3	7/183	13.1	ns
Non-elective CS	78/684	11.5	24/183	1.6	ns
Elective CS	149	17.8	66	26.5	0.003
Induction of labor	372/684	54.4	125/183	68.3	0.007
Premature delivery	44	5.2	19	7.6	ns
Analgesia	262/684	38.3	74/183	40.4	ns
SGA	655	78.6	192	77.1	ns
LGA	82	9.8	39	15.7	
Nulliparity	385	46.2	78	31.3	< 0.0001
Diet therapy	677	81.2	155	62.2	< 0.0001
Insulin therapy	156	18.8	94	37.8	< 0.0001
Fasting glucose > 100 mg/dl	77	9.2	51	20.5	< 0.0001
Neonatal complication	129	15.5	63	25.3	0.0006
Maternal age	34.1		33.7		ns
Average fasting glucose	88.1 mg/dl		92.5 mg/dl		< 0.001
GA at delivery	38.5 ws		38.3 ws		ns
Neonatal weight	3191		3254		ns

Clinical features and perinatal outcomes of SGA neonates from pregnancies complicated by diabetes: a multicentre retrospective study

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DOI: 10.36129/jog.2022.S46

Objective. The objective of the study was to describe the perinatal outcomes of small-for-gestational age (SGA) neonates from pregnancies complicated by gestational diabetes (GDM) and diabetes mellitus (DM).

Materials and Methods. This was a retrospective multicentre study conducted in three tertiary maternity hospitals. Non-anomalous neonates from singleton pregnancies with a birthweight (BW) below the 10 percentile and from diabetic women were included as cases, while the control group consisted of SGA neonates from non-diabetic women.

A composite adverse perinatal outcome (CAO) was defined in presence of one of the following outcomes: newborn with pH < 7.1, Apgar at 5 min < 7, respiratory support at birth, neonatal hypoglycaemia, neonatal jaundice and admission to the NICU. The incidence of CAO was compared between the two groups.

Results. Overall, 767 SGA neonates were included in the study, 89 (11.6%) of them from women affected by GDM/DM (case group). In this latter group, a higher maternal BMI at booking (25.8 ± 5.6 *vs* 22.4 ± 3.8, p < 0.001) and incidence of multiparity (21/34 or 61.8% *vs* 92/277 or 33.2%, p = 0.001) was reported compared to the control group of nondiabetic women.

No statistically significant difference in terms of CAO was found between the two groups.

Conclusions. In this large cohort of neonates with a birthweight < 10th percentile, GDM or DM does not seem to be associated with an increased incidence of adverse perinatal outcome.

Assessment of maternal hemodynamics in patients with severe obesity: with or without a weight control during pregnancy

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DOI: 10.36129/jog.2022.S47

Objective. Maternal weight control during pregnancy plays an important role in the prevention of obstetric and maternal complications. The aims of this study were to evaluate maternal hemodynamics in severely obese pregnancies (BMI > 35) and to evaluate the influence of weight control during pregnancy.

Materials and Methods. 73 severely obese pregnant women were involved in this study, 29 maintained a stable weight or lost weight during pregnancy (group B), 44 patients gained weight (group C); these two groups were compared with 20 normal weight patients (group A). The hemodynamic assessment was performed in the third trimester of pregnancy.

Results. Patients of group C show lower values of SVR (815.4 ± 81.9) than group A and B (948.7 ± 131.8 and 994.8 ± 105.7 respectively) ($p < 0.001$). The CO was higher in group C (8.8 ± 1.4) than group A and B (7.5 ± 1.1 and 7.5 ± 1 respectively) ($p < 0.001$). The CI was significantly higher in group A (4.3 ± 0.6) than group B and C (3.6 ± 0.9 and 3.8 ± 0.4 respectively) ($p = 0.036$). Group C showed lower PKR (17.3 ± 4.6) than group A and B (22 ± 7.1 and 21.6 ± 6.2 respectively) ($p = 0.033$). The INO was significantly lower in group C and B (1.7 ± 0.3 and 1.6 ± 0.3 respectively) than group A (1.9 ± 0.4) ($p = 0.045$).

Conclusions. Our study shows that good weight control or weight loss during pregnancy improves maternal hemodynamics in severely obese patients, bringing them closer to those of patients with a normal weight.

	GROUP A NORMAL WEIGHT (n: 20)	GROUP B OPTIMAL WEIGHT CONTROL (n: 29)	GROUP C POOR WEIGHT CONTROL (n: 44)	P VALUE
SVR d.s.cm^{-5}	948,7 ± 131,8	994,8 ± 105,7	815,4 ± 81,9	<0,001 †‡
CO L/min	7,5 ± 1,1	7,5 ± 1	8,8 ± 1,4	<0,001 †‡
CI L/min/m^2	4,3 ± 0,6	3,6 ± 0,9	3,8 ± 0,4	0,036 †§
HR bpm	89,7 ± 15,8	94,2 ± 15,4	93,5 ± 11,3	ns
SV cm3	88,1 ± 16,3	80,9 ± 14,7	94,2 ± 13,7	0,02 ‡
PKR	22 ± 7,1	21,6 ± 6,2	17,3 ± 4,6	0,033 †‡
TFc ms	377,5 ± 39,8	356 ± 68,3	392,5 ± 39,9	ns
INO W/m^2	1,9 ± 0,4	1,6 ± 0,3	1,7 ± 0,3	0,045 †§
SBP mmHg	116 ± 8,9	126 ± 10,7	120 ± 10,7	0,025 §
DBP mmHg	74,2 ± 7,8	76,6 ± 9,5	73,2 ± 6,9	ns

SVR: Systemic Vascular Resistance; **CO:** Cardiac Output; **CI:** Cardiac Index; **HR:** Heart Rate; **SV:** Stroke Volume; **PKR:** Potential to Kinetic Energy Ratio; **TFc:** Time Flow corrected; **INO:** Inotropy Index; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure

† group C vs group A; **‡** group C vs group B; **§** group A vs group B

Maternal hemodynamics in patients with severe obesity and gestational diabetes

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DOI: 10.36129/jog.2022.S48

Objective. Severe obesity during pregnancy induces a low-grade chronic inflammatory state, systolic and diastolic dysfunction and impaired arterial and venous function.
The aim of this study was to evaluate maternal hemodynamics in severely obese pregnancies (BMI > 35) compared with severely obese with Gestational Diabetes (GD).
Materials and Methods. 90 severely obese pregnant women were involved in this study, 73 without GD (group B) and 17 with GD (group C); these were compared with 20 normal weight patients without GD (group A). The hemodynamic assessment was performed in the third trimester.
Results. The SVR was higher in group C (1173.4 ± 164.5) than group B and A (842.2 ± 73.6 and 948.7 ± 131.8 respectively) ($p < 0.001$). The CO was higher in group B (8.7 ± 0.7) than group C and A (6.6 ± 1 and 7.5 ± 1.1 respectively) ($p < 0.001$). The SV was significantly decreased in group C (74.6 ± 17.3) than group A and B (88.1 ± 16.3 and 89 ± 11.6 respectively) ($p = 0.013$). Group C showed lower values of INO (1.5 ± 0.3) than group A (1.9 ± 0.4) ($p = 0.007$) and B (1.7 ± 0.3) (p = ns). The PKR was higher in group C (26.6 ± 9.8) than group B (18.7 ± 5.1) ($p = 0.01$) and A (22 ± 7.1) (p = ns).

Conclusions. Obese patients with GD show an hypodynamic circulation, high vascular resistance, low CO and INO. The pathological hemodynamic adaptation worsens in GD patients, through endothelial dysfunction, vascular rigidity and alterations in the heart muscle as shown by systolic and diastolic dysfunction.

	GROUP A NORMAL WEIGHT (n: 20)	GROUP B OBESE (n: 73)	GROUP C OBESE + GD (n: 17)	P VALUE
SVR d.s.cm^{-5}	948,7 ± 131,8	842,2 ± 73,6	1173,4 ± 164,5	< 0,001 †‡§
CO L/min	7,5 ± 1,1	8,7 ± 0,7	6,6 ± 1	< 0,001 †‡§
CI L/min/m^2	4,3 ± 0,6	3,9 ± 0,3	3 ± 0,3	< 0,001 †‡§
HR bpm	89,7 ± 15,8	96,9 ± 14,5	92,1 ± 13	ns
SV cm3	88,1 ± 16,3	89 ± 11,6	74,6 ± 17,3	0,013 †‡
PKR	22 ± 7,1	18,7 ± 5,1	26,6 ± 9,8	0,01 ‡
TFc ms	377,5 ± 39,8	375,4 ± 80,7	374 ± 31,5	ns
INO W/m^2	1,9 ± 0,4	1,7 ± 0,3	1,5 ± 0,3	0,007 †
SBP mmHg	116 ± 8,9	122,6 ± 8,8	127 ± 16	0,049 †
DBP mmHg	74,2 ± 7,8	71,4 ± 9,3	80,8 ± 8,8	0,007 †‡

SVR: Systemic Vascular Resistance; **CO:** Cardiac Output; **CI:** Cardiac Index; **HR:** Heart Rate; **SV:** Stroke Volume; **PKR:** Potential to Kinetic Energy Ratio; **TFc:** Time Flow corrected; **INO:** Inotropy Index; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure; **GD:** Gestational Diabetes

† group C vs group A; ‡ group C vs group B; § group A vs group B

Role of maternal hemodynamics and fetal ultrasound parameters to predict adverse pregnancy outcomes in women with gestational diabetes mellitus

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DOI: 10.36129/jog.2022.S49

Objective. To evaluate the effect of poor maternal glycemic control on maternal hemodynamics and fetal ultrasound parameters and their association with adverse pregnancy outcomes, to offer a personalized management in gestational diabetes mellitus (GDM).

Materials and Methods. This was a prospective case-control study of 57 women with GDM and 23 normal pregnancies as a control group. Women with GDM were divided into good-GDM and poor-GDM groups according to their glycemic control at examination. All the groups were submitted, between 31-33 weeks of gestation, for a maternal hemodynamics measurement, using a non-invasive device (USCOM-1A®) and a fetal ultrasound evaluation to assess fetal biometry, velocimetry Doppler and interventricular septum (SIV) thickness. Data of perinatal outcomes were obtained.

Results. The poor-GDM group showed higher values of CA, Estimated Fetal Weight (EFW) and fetal SIV thickness, compared to the good-GDM group and control group. They also reported higher Umbilical Vein blood flow and umbilical vein medium diameter, compared to the others. Maternal hemodynamics in women with GDM, despite their glycemic control, showed higher RVS and lower CO, CI and INO. A higher rate of induction of labor and cesarean sections occurred in women with uncontrolled GDM. They also showed a higher neonatal birthweight and higher risk of neonatal intensive care unit admission.

Conclusions. Fetal SIV thickness, umbilical vein blood flow and diameter and fetal biometry showed a correlation with a poor glycemic control in women with GDM. Maternal hemodynamics assessment was also compromised in these women. These parameters may offer a better pregnancy management by detecting potential adverse outcomes in GDM.

Table 1. *Fetal biometry, Fetal velocimetry Doppler and maternal hemodynamics assessment. Comparison between two groups: † group C vs group A; ‡ group C vs group B; § group A vs group B.*

	Phisiological pregnancy (Group A)	*Well-GDM (Group B)*	*Poor-GDM (Group C)*	*P-value*
Fetal biometry				
EFW (gr)	1983,4 ± 380,4	1958,8 ± 448,1	2316,3 ± 621,3	***0,029*** †, ‡
SIV (mm)	4,7 ± 0,8	4,5 ± 0,5	5,3 ± 0,8	***< 0,01*** †, ‡ ns §
Fetal Velocimetry Doppler				
PI AO	0,86 ± 0,2	0,84 ± 0,1	0,87 ± 0,1	ns
PI ACM	1,89 ± 0,1	1,84 ± 0,4	1,79 ± 0,2	ns
CPR	2,2 ± 0,5	2,0 ± 0,3	2,1 ± 0,2	ns
QVO (ml/min)	154,2 ± 16,3	177,6 ± 32,5	216,1 ± 40,5	***0,004*** †, ‡
DIAM VO (mm)	6,8 ± 0,7	6,8 ± 0,5	7,4 ± 0,7	***0,04*** †, ‡
Maternal Hemodynamics Assessment				
RVS	814,2 ± 127,6	962,5 ± 270,4	983,5 ± 161,4	***0,03*** †, §
CO	8,4 ± 1,3	7,5 ± 1,5	7,2 ± 1,3	***0,039*** †, §
CI	4,4 ± 0,8	4,05 ± 0,8	3,6 ± 0,7	***0,008*** †, ‡
HR	94,1 ± 15,7	89,4 ± 12,1	92,52 ± 11,7	ns
SV	91,4 ± 15,7	83,9 ± 17,6	79,6 ± 19,2	ns
PKR	21,0 ± 8,1	25,7 ± 14,4	26,4 ± 9,6	ns
TFc	374 ± 37,9	392,2 ± 40,2	381,6 ± 41,7	ns
INO	1,9 ± 0,4	1,7 ± 0,5	1,5 ± 0,3	***0,017*** †

An atypical case of edema of the umbilical cord and histological chorioamnionitis in a fetus with normal growth and abnormal umbilical artery Doppler: a case report

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DOI: 10.36129/jog.2022.S50

Objective. Chorioamnionitis is a severe condition of pregnancy that increases fetal and neonatal morbidity. It can be distinguished in Clinical and Subclinical/Histologic forms defined by inflammation of the chorion and placenta associated with intrauterine bacterial infection and umbilical infiltration.

Materials and Methods. A 27-year-old primigravida with uncomplicated pregnancy and no comorbidities underwent a routine ultrasound scan at 31 weeks' gestation. The biometric fetal parameters and the amniotic fluid were within the normal range.

The Doppler velocimetry of Umbilical Artery was persistently altered with a pulsatility index of 1.5-1.6, while the Middle Cerebral Artery PI was normal: 2.00.

Several pathological conditions were clinically excluded.

Results. After 12 hours the UA PI was 1.7 (> 95th percentile) with normal PI of MCA 2.17 and a subsequently reduced CPR (cerebro-placental ratio) 1.27 (2nd centile). The ductus venosus and the umbilical vein Doppler were normal.

The patient was hospitalized and corticosteroids were administered for fetal lung maturation, then a cesarean section was performed for the worsening of UA Doppler. A neonate of 1770 g was born with an Apgar score of 8 at 1st minute and 9 at 5th minute. The umbilical cord showed an increased consistency during clamping and cutting.

The hystological examination highlighted edema of the umbilical cord and amniochorial membranes with foci of chorionamniositis and congested umbilical vessels.

Conclusions. The edema of the umbilical cord linked to a hypothetical funisitis might explain the increase of the resistance in the umbilical artery.

Further studies are required to evaluate the effects of histological chorioamnionitis and funisitis on long-term neonatal outcomes.

Lifestyle intervention can guarantee an adequate gestational weight gain and improve perinatal outcomes in a cohort of obese women

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DOI: 10.36129/jog.2022.S51

Objective. Although there is no agreement, the Institute of Medicine (IOM) recommends 5-9 kg of gestational weight gain (GWG) for all obesity classes. This study evaluates if a lifestyle intervention (LI) can guarantee an adequate GWG affecting perinatal outcomes.

Table 1. *Maternal and pregnancy characteristics and perinatal outcomes.*

	Control (N=1309)	Lifestyle intervention (N=565)	P value
Maternal age ≥ 40	401 (30.6)	151 (26.7)	0.09
Nulliparity	**434 (33.1)**	**213 (37.7)**	**0.05**
Ethnicity			**0.000**
Caucasian	**709 (54.1)**	**402 (71.1)**	
African	**251 (19.1)**	**83 (14.7)**	
Maghrebian	**290 (22.1)**	**60 (10.6)**	
Others	**59 (4.5)**	**20 (3.5)**	
Low Education level (≤8 years)	673 (51.4)	279 (49.4)	0.37
Obesity classes			**0.001**
Class I	**971 (74.2)**	**373 (66.0)**	
Class II	**257 (19.6)**	**144 (25.5)**	
Class III	**81 (6.2)**	**48 (8.5)**	
Mean BMI	**33.4 ± 3.3**	**34.2 ± 4.3**	**0.000**
ART	30 (2.3)	9 (1.8)	0.34
Pregnancy assistance			**0.02**
Public (family centers)	**960 (73.4)**	**449 (79.5)**	
Private (Gynecologist)	**349 (26.6)**	**116 (20.5)**	
Gestational Diabetes Mellitus	**401 (30.6)**	**202 (35.7)**	**0.03**
Gestational hypertension	**89 (6.8)**	**58 (10.3)**	**0.000**
Excessive GWG (≥ 9kg)	**361 (27.6)**	**133 (23.5)**	**0.04**
Adequate GWG (5-9kg)	**512 (39.1)**	**272 (48.1)**	**0.0001**
Insufficient GWG (<5kg)	**436 (33.3)**	**160 (28.3)**	**0.01**
Labor induction	481 (36.7)	208 (36.8)	0.47
Cesarean Section	377 (28.8)	162 (28.7)	0.49
Operative delivery	67 (5.1)	21 (3.7)	0.09
Preterm Delivery (<37 weeks)	96 (7.3)	47 (8.3)	0.41
Birthweight	3333.5 ± 579.4	3323.2 ± 602.3	0.72
LGA	265 (20.2)	105 (18.6)	0.18
SGA	**98 (7.5)**	**29 (5.1)**	**0.03**

Materials and Methods. Prospective cohort study including singleton obese women (BMI ≥ 30) delivered at a tertiary hospital between 2016 and 2020. A group was randomly referred to an *ad-hoc* clinic for LI. The LI started at the 9-12th week implementing a low-glycemic index, low-saturated fat diet, and physical activity. Patients were followed until delivery and perinatal outcomes were collected. According to the IOM range, patients were classified into three different groups based on total GWG: Insufficient, Adequate or Excessive. Data of women included in the LI group were compared with the remaining patients who received standard care (SC group).

Results. A total of 1874 obese women delivered in the study period. Among them, 565 (30.1%) were included in the LI group while 1309 received SC. A higher rate of women with a GWG out of the IOM was found in the SC group, while women in the LI group showed higher adequate GWG (**Table 1**). The SGA rate was frequent in the SC group and after multivariate analysis the risk for SGA was increased by insufficient GWG (OR 1.31, 95%CI 1.02–1.68) and reduced by LI (OR 0.66, 95%CI 0.43-0.98) (**Table 2**).

Conclusions. SGA risk is associated with an insufficient GWG and may be modifiable by applying early LI in pregnancies complicated by obesity.

Table 2. *Multivariate logistic regression for the likelihood of having a SGA newborn.*

	OR	95% CI	P value
Obesity classes	1.22	0.90 – 1.66	0.18
Italian place of origin	1.19	0.82 – 1.73	0.34
Lifestyle intervention	**0.66**	**0.43 – 0.98**	**0.05**
Maternal age ≥ 40 years	0.78	0.43 – 1.21	0.22
Public assistance	0.94	0.61 – 1.45	0.80
Inadequate GWG	**1.31**	**1.02 – 1.68**	**0.03**
Gestational hypertension	1.08	0.55 – 2.14	0.81

Update on treatment of cytomegalovirus infection in pregnancy: preliminary data from the regional reference center in Campania, Italy

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DOI: 10.36129/jog.2022.S52

Objective. Cytomegalovirus (CMV) is the leading cause of congenital infection. 10% of affected infants present symptoms at birth and 40% of these can develop sequelae later in life. Valaciclovir is an antiviral drug which was approved in Italy in December 2020 for the prevention and treatment of CMV fetal infection. The objective of this study was to evaluate its efficacy in preventing infection in the fetus and/or severe symptoms in affected infants.
Materials and Methods. Pregnant women with CMV infection examined ed at Federico II University (Naples) were enrolled from January 2021. According to AIFA criteria, they received 8 g of valaciclovir daily until a negative amniocentesis or until delivery in case of positive amniocentesis and/or signs of mild/moderate fetal infection. Newborns were evaluated at birth searching for CMV-DNA in a urine sample. If positive, they underwent laboratory and instrumental investigations in the first month of life to define the onset and therefore eligibility for treatment. Both symptomatic and asymptomatic infants continued periodic evaluations.
Results. Since January 2021, 16 women have been treated, without significant adverse events. Of 12 newborns, 10 were negative for congenital infection, while CMV-DNA was positive in both urine and blood samples for 2 of them. They were asymptomatic at birth and have not developed organ damage during ongoing follow up.
Conclusions. From this preliminary data, valaciclovir is a useful therapy for the prevention of fetal infection. This opportunity suggests the objective of serological screening for CMV in pregnancy to identity affected women and prevent its transmission to the fetus.

Malaria in pregnancy: multidisciplinary approach

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DOI: 10.36129/jog.2022.S53

Objective. This case highlights the utility of a multidisciplinary collaboration for good management of malaria in pregnancy, that can have several complications from miscarriage to neonatal malaria.
Materials and Methods. A 24-year-old pregnant Ethiopian woman, living in Italy for two years, developed *P. falciparum* infection in the third trimester of pregnancy after traveling to Ethiopia without receiving antimalarial prophylaxis. A three-day treatment with piperaquine tetraphosphate/dihydroartemisinin was administered, with gradual recovery and resolution of thrombocytopenia and anemia. Parasitemia was 2.5% at the end of treatment, 1.8% 10 days after and parasites were still rarely detected after 28 days. Given the clinical and laboratory recovery, treatment was not repeated. Diagnostics for placental and congenital malaria was set-up with a multidisciplinary approach.
Results. At 41+4 g.a. she delivered a male neonate by an emergency C-section for non-reassuring CTG. The Apgar score was 9-10, normal weight. Mother and newborn were fine and they were discharged in 4 days. Parasitemia in maternal blood was negative at delivery, while cord blood showed rare trophozoites. Placental examination revealed only chronic hypoxemia without evidence of parasites or malaria pigment. Peripheral blood of the newborn was tested negative for malaria at 48 hours and 14 days. At 3 months the baby is in good health, breastfed and shows regular growth.
Conclusions. Management of malaria during pregnancy may be challenging in non-endemic settings. A multidisciplinary approach and clear diagnostic procedures are needed to guide therapeutic decisions. Although placental malaria was suspected, based on detection of parasites in the cord blood, the newborn did not develop symptomatic parasitemia.

Perinatal outcome of congenital toxoplasmosis at a single centre

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DOI: 10.36129/jog.2022.S54

Objective. Prenatal screening for congenital Toxoplasmosis infection (cToxo) is part of the essential level of care in pregnancy in Italy, and its early diagnosis and treatment have allowed the reduction of cases of neonatal infections to less than 1%. The aim of our study was to evaluate such incidence in our center and to compare results from prenatal surveillance to postnatal outcome.

Materials and Methods. Retrospective analysis of cases of primary infection of toxoplasmosis observed in our hospital from 2009 to 2022. After a confirmed diagnosis on maternal serum, treatment with Spiramycine (S) or Pyrimethamine-Sulfadiazyne (PS) was started depending on the time of maternal infection, and amniocentesis was offered to detect Toxoplasma DNA by PCR. Prenatal ultrasonographic (US) surveillance every 4 weeks and postnatal evaluation of neonates to exclude infection and sequelae were performed.

Results. Of the 72 women (treatment: S - 93%, PS - 7%, 55 - 76%) underwent amniocentesis (median GA 18 weeks), with one positive case (1.8%) reported after an unrecognized infection with a late start of therapy, and one defined as doubt (1.8%) and not confirmed on the newborn. No signs of infection were detected by US in any of the 72 patients. Postnatal outcomes were available for 50 cases, all livebirths, with a median GA at delivery of 39 weeks (35-41), without evidence of cToxo or sequelae.

Conclusions. Early treatment in pregnancies with primary infection of toxoplasmosis is known to reduce risks of cTOXO, and multicenter studies should assess if amniocentesis is still necessary or should be considered only in specific cases.

COVID-19 in pregnancy may significantly affect fetal growth

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DOI: 10.36129/jog.2022.S55

Objective. Whilst most cases of COVID-19 in pregnancy evolve uneventfully, some others have a poor outcome, such as preterm birth and HDP. The effect of COVID-19 on fetal growth still has to be addressed and appears controversial. Our study aims to focus on fetal growth velocity across the trimesters in pregnancy affected with COVID-19.

Materials and Methods. This is a multicentric prospective observational study on data from COVID-19 pregnancies referred to the centers of Careggi University Hospital and "S. Stefano" Hospital in Prato from 2020 to 2022, included in the local branch of ItOSS surveillance. Fetal growth was evaluated across the three trimesters of pregnancy by abdominal circumference (AC) and expected fetal weight (EFW). Both AC, and EFW plus birthweight were used to calculate growth velocity (Vannuccini *et al*., 2017).

Results. Data from a cohort of 211 cases was collected. The majority (80%) of COVID-19 cases occurred in the third trimester. Of note, the percentage of gestational diabetes (12.3%) and preterm births (7.1%) was comparable to the general population. Mean birthweight was 3259 ± 509 g. The percentage of cesarean sections was acceptable (13.7%).

Concerning the velocity of growth, AC decreased from the second to third trimester to reach values < 10th centile in 24% of cases and < 5th percentile in 17% of cases, even in presence of 2% of hypertensive disorders (HDP). Fetal growth restriction according to Gordjin *et al*. (2015) was antenatally identified in 4.7% of cases. Fetal growth > 95th centile occurred in 5.7% of cases.

At birth, the cumulative percentage of small for gestational age newborns defined as birth weight < 2500 g resulted 5.2%. A significant percentage of newborns required NICU assistance (7.8%).

Conclusions. Regardless of the association and prevalence of preterm birth, SGA and HDP in pregnant women, fetal growth appears to be affected by COVID-19 with a higher incidence of impaired growth velocity compared to the general population.

	34 w (N=14)	35 w (N=31)	36 w (N=114)	37 w (N=9)	P value
Delivery outcomes					
Indication to delivery					0.41
Spontaneous labor	10 (71.4)	18 (58.0)	65 (59.6)	2 (22.2)	
pPROM (no suspected triple I)	3 (25.0)	9 (29.0)	39 (34.2)	6 (66.7)	
Indicated	1 (8.3)	5 (16.0)	10 (8.7)	1 (11.1)	
Labor					0.01
No labor	**4 (28.6)**	**5 (16.1)**	**26 (22.8)**	**0**	
Spontaneous	**8 (57.1)**	**20 (64.5)**	**60 (52.6)**	**2 (22.2)**	
Induced	**2 (14.3)**	**6 (19.3)**	**28 (24.6)**	**7 (77.8)**	
Mode of Delivery					**0.05**
Spontaneous vaginal	10 (71.4)	21 (67.7)	81 (71.0)	6 (66.7)	
Operative vaginal	**0**	**2 (6.4)**	**7 (6.4)**	**3 (33.3)**	
Cesarean Section	**4 (28.6)**	**8 (25.8)**	**26 (22.8)**	**0**	
pPROM to delivery interval (days)	**1 (0-1)**	**1 (0-1)**	**1 (0-2)**	**3 (2 – 3)**	**0.000**
Maternal hyperpyrexia in labor (≥38°C)	0	0	3 (2.6)	0	0.69
Antibiotic treatment	14 (100.0)	30 (96.7)	110 (96.5)	**6 (66.7)**	**0.001**
Antenatal corticosteroids					**0.01**
No administration	**12 (85.7)**	**27 (87.1)**	**105 (94.6)**	**9 (100.0)**	
Before 34 weeks	**0**	**4 (12.9)**	**4 (3.6)**	**0**	
After 34 weeks	**2 (14.3)**	**0**	**2 (1.8)**	**0**	
Tocolysis	**1 (7.1)**	0	0	0	**0.01**
Neonatal outcomes					
Birthweight (g)	**2228.8 ± 345.6**	**2605.4 ± 311.2**	**2710.4 ± 327.7**	**2871.1 ± 316.5**	**0.000**
Apgar score ≤ 7 at 5'	**2 (14.3)**	**0**	**1 (0.8)**	**0**	**0.003**
Arterial pH ≤ 7.1	0	0	3 (2.7)	0	0.71
Respiratory support	**2 (14.3)**	**1 (3.2)**	**0**	**0**	**0.000**
Neonatal sepsis	1 (7.1)	1 (3.2)	0	0	0.08
Adverse neonatal outcome*	**8 (61.5)**	**11 (36.7)**	**22 (20.4)**	**1 (12.5)**	**0.000**

Maternal and perinatal outcomes of pregnancies complicated by poxviruses infection: a systematic review and meta-analysis

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DOI: 10.36129/jog.2022.S56

Objective. To ascertain the maternal and perinatal outcomes of pregnancies complicated by poxviruses infections

Materials and Methods. Medline, Embase and Cochrane databases were searched. Maternal death, fetal and neonatal death, preterm birth and vertical transmission were observed. Sub-group analyses according to the severity of maternal infection, gestational age at infection, vaccination status and pregnancy status were also performed. Random effect meta-analyses of proportion and risk assessment were used to analyse the data.

Results. 1251 pregnancies with smallpox, 7 with monkeypox and 23 with *molluscum contagiousum*. In pregnancies affected by smallpox infection, maternal death occurred in 34.2% of the cases, miscarriage and intra-uterine fetal death in 10.2% and 26.4%. Vertical transmission was documented in 9.4% of cases. The risks of maternal death, miscarriage or preterm birth were not different when comparing infection acquired in the first, second or third trimester of pregnancy. The risk of maternal death was significantly higher in cases complicated by hemorrhagic disease. In pregnancies complicated by monkeypox infection miscarriage and intrauterine fetal demise occurred in 43.5% and 33.2% of cases. More than one third of the infected pregnancies presented fetal anomalies at birth or death. Features of the disease were observed in the fetus in 70.8% of the cases. Only two studies with molluscum contagiosum in pregnancy were included, suggested an uneventful course of the infection.

Conclusions. Pregnancies complicated by smallpox and monkeypox infection are at enhanced risk of adverse maternal and perinatal outcomes. *Molluscum contagiousum* does not seem to be associated with excess maternal or perinatal risks.

Role of fetal magnetic resonance imaging in fetuses with congenital cytomegalovirus infection

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DOI: 10.36129/jog.2022.S57

Objective. To investigate the role of fetal brain MRI in detecting anomalies in fetuses with congenital CMV infection undergoing neurosonography.

Materials and Methods. Multicenter, retrospective, cohort study involving 11 fetal medicine centers in Italy from 2012. The inclusion criteria were fetuses with congenital CMV infection diagnosed by PCR analysis of amniotic fluid, normal karyotype and MRI performed within 3 weeks from the last ultrasound examination.

Results. The analysis included 95 fetuses with a prenatal diagnosis of congenital CMV infection and normal neurosonography at first examination. The rate of structural anomalies detected exclusively at fetal MRI was 10.5%. When considering the type of anomaly, malformations of cortical development were detected at MRI in 40% of fetuses, destructive encephalopathy in 20%, intracranial calcifications in the germinal matrix in 10%, and complex anomalies in 30%. At the multivariate logistic regression analysis, only CMV viral load in the amniotic fluid > 100,000 copies / ml (OR 12.0, 95%CI 1.2-124.7, p = 0.04) was independently associated with the likelihood of detecting fetal anomalies at MRI. Associated anomalies were detected exclusively at birth and missed at both types of prenatal imaging in 3.8% of fetuses with congenital CMV infection.

Conclusions. Fetal brain MRI can detect additional anomalies in a significant proportion of fetuses with congenital CMV infection and negative neurosonography. Viral load in the amniotic fluid was an independent predictor of the risk of associated anomalies.

Prenatal predictors of adverse perinatal outcome in congenital cytomegalovirus infection: a multicenter study

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DOI: 10.36129/jog.2022.S58

Objective. To identify predictors of adverse perinatal outcome in congenital cytomegalovirus infection.

Materials and Methods. In a multicenter study fetuses with congenital CMV infection diagnosed by PCR on amniotic fluid and normal prenatal imaging at the time of diagnosis were included. Primary outcome was the occurrence of structural anomalies at follow-up ultrasound or prenatal MRI. Secondary outcomes were the occurrence of anomalies detected exclusively postnatally and the rate of symptomatic infection.

Results. 104 fetuses with congenital CMV were included in the study. Anomalies were detected at follow-up ultrasound or MRI in 18.3% (19/104) cases. Anomalies were found after birth in 11.9% (10/84) of cases and 15.5% (13/85) of newborns showed clinical symptoms related to CMV infection. There was no difference in either maternal age ($p = 0.3$), trimester ($p = 0.4$) of infection and prenatal therapy ($p = 0.4$) between fetuses with or without anomalies at follow-up. Median viral load in the amniotic fluid was higher in fetuses with additional anomalies at follow-up ($p = 0.02$) compared to those without. At multivariate logistic regression analysis, a high viral load in the amniotic fluid, defined as ≥ 100,000 copies/ mL was the only independent predictor for the occurrence of anomalies detected exclusively at follow-up ultrasound assessment or MRI, with an OR of 3.12.

Conclusions. Viral load in the amniotic fluid is a strong predictor of adverse perinatal outcome in congenital CMV infection. The results of this study emphasize the importance of adequate follow up even in case of negative neurosonography.

Monkeypox infection in pregnancy: a systematic review and meta-analysis

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DOI: 10.36129/jog.2022.S59

Objective. The main aim of this systematic review was to ascertain the maternal and perinatal outcomes of pregnancies complicated by monkeypox infection.

Materials and Methods. Medline, Embase and Cochrane databases were searched utilizing combinations of the relevant medical subject heading terms, key words, and word variants for "monkeypox" and "pregnancy". The outcomes observed were miscarriage, intra-uterine, neonatal and perinatal death, preterm birth, vertical transmission, maternal symptoms. Meta-analysis of proportion was used to analyze the data.

Results. Four studies were included. All women included in the present systematic review presented symptoms and signs of monkeypox infection. There was no case of maternal death. Miscarriage occurred in 39% (95%CI 0-89.0) while intra-uterine in 23.0% (95%CI 0-74.0) of cases. The overall incidence of late fetal and perinatal loss was 77.0% (95%CI 26.0-100), while only 23% (0-74.0) of the included fetuses survived to birth. The incidence of preterm birth prior to 37 weeks of gestation was 8.0% (0-62.0). Vertical transmission occurred in 62.0% (3.0-100) of cases. When stratifying the analysis according to gestational age at infection, fetal loss occurred in 67.0% (95%CI 9.0-99.0) of cases with first trimester and 82.0% (95%CI 17.0-100) of those with second trimester infection.

Conclusions. Monkeypox infection in pregnancy is associated with a high risk of perinatal loss and vertical transmission. The preliminary results are affected by the very small number of cases included and highlights the need for a thorough maternal and fetal surveillance in pregnancies complicated by Monkeypox infection.

Diagnostic performance of quantitative polymerase chain reaction in detecting congenital symptomatic CMV infection

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DOI: 10.36129/jog.2022.S60

Objective. To elucidate the diagnostic performance of quantitative polymerase chain reaction (qPCR) to identify fetuses with congenital CMV infection who will develop symptomatic disease.

Materials and Methods. In a multicenter study fetuses with congenital CMV infection diagnosed by PCR on amniotic fluid and normal prenatal imaging at the time of diagnosis were included. Primary outcome was diagnostic performance of qPCR in detection symptomatic CMV infection.

Results. One hundred and four fetuses with congenital CMV were included in the study. Symptomatic infection was detected in7.7% (8/104) cases. Median viral load in the amniotic fluid was higher in fetuses with additional anomalies at follow-up ($p = 0.02$) compared to those without. At multivariate logistic regression analysis, high viral load in the amniotic fluid, defined as ≥ 100,000 copies/ mL was the only independent predictor for the occurrence of anomalies detected exclusively at follow-up ultrasound assessment or MRI, with an OR of 3.12. At receiver operating characteristic curve analysis the qPCR in the amniotic fluid had an area under the curve of 0.75 (95%CI 0.69-0.82) for the detection of symptomatic infection.

Conclusions. Viral load in the amniotic fluid is a strong predictor of adverse perinatal outcome in congenital CMV infection. The results of this study emphasize the importance of adequate follow up even in case of negative neurosonography to better predict postnatal adverse outcomes of infected newborns, especially in amniotic fluid high viral load.

Presence of SARS-CoV-2 neutralizing and vaccine spike antibodies in amniotic fluid during the second trimester of pregnancy, detected by amniocentesis *(Winner of the SIMP Award, in memory of Professor Giorgio Pardi)*

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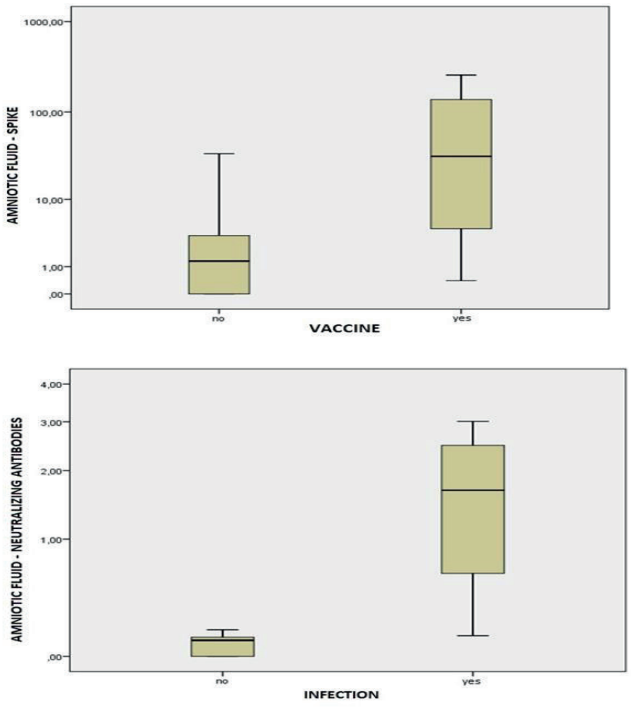
DOI: 10.36129/jog.2022.S61

Objective. Thanks to the SARS-CoV-2 vaccination, pregnant women are protected from the complications of COVID-19 infection, but the benefits of this vaccination in preventing morbidity and mortality in the fetus are not yet clear: it is not well understood if and how these antibodies cross the placenta. Indeed antibodies made after a pregnant person has received an mRNA COVID-19 vaccine have been found in amniotic fluid and umbilical cord blood at term and represent a safer method of enhancing neonatal antibody levels than administration of immunoglobulin preparation to the infant. The aim of the study is to test the presence of neutralizing SARS-CoV-2 antibodies and spike antibodies in the amniotic fluid in the second trimester of pregnancy, and then to compare the antibodies level in maternal serum and amniotic fluid to evaluate their correlation.

Materials and Methods. This cohort study took place at the Department of Obstetrics and Gynecology of Messina at the AOU Policlinico G. Martino from September 2021 to February 2022; the study consisted of 22 pregnant women who had amniocentesis in the gestational period between 15 weeks plus 6 days and 18 weeks: we analyzed serum and amniotic fluid samples of women who contracted the SARS-CoV-2 infection, or who were vaccinated against the same virus, within one year, or never infected by SARS-CoV-2 or vaccinated against it. During the amniocentesis, all patients underwent a single sample of maternal serum and of amniotic fluid to evaluate SARS-CoV-2 neutralizing antibody and S1 receptor binding domain IgG antibody levels. Inclusion criteria were pregnant women with the need to undergo amniocentesis.

Results. 22 pregnant women were enrolled in the study:10 of them were vaccinated with a mRNA COVID-19 vaccine; 12 women were not vaccinated, 4 of them had developed COVID-19 infection within one year before the collection and 2 of them developed the infection during pregnancy; the other 6 never developed the infection and have not been vaccinated, enrolled as comparators. Mann-Whitney test showed that vaccinated patients had significantly higher S1 receptor binding domain antibody levels both in amniotic fluid ($p < 0.006$) and maternal blood ($p < 0.005$) than not vaccinated women; also SARS-CoV-2 neutralizing antibody levels were higher in pregnant women who developed COVID-19 infection both in amniotic fluid ($p < 0.007$) and maternal blood ($p < 0.004$) than not vaccinated women. There was a significantly high correlation between the concentrations of spikes antibody levels in vaccinated pregnant women's serum and amniotic fluid ($p = 0.000$), and of neutralizing antibody levels in serum and amniotic fluid of women who developed COVID-19 infection ($p = 0.000$).

Conclusions. To the best of our knowledge, the analysis of amniotic fluid and serum showed for the first time that all the vaccinated pregnant women samples had SARS-CoV-2 spikes immunoglobulins both in maternal blood and amniotic fluid. There is a very high correlation between maternal blood and amniotic fluid S1 receptor binding domain antibody levels in vaccinated women: this demonstrates that there is an early transplacental antibody transfer. Also neutralizing antibodies were found in the amniotic fluid of infected pregnant women, with high correlation between concentrations.



Effectiveness and safety of prenatal valacyclovir for congenital cytomegalovirus infection

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DOI: 10.36129/jog.2022.S62

Objective. The main aim was to investigate the safety and effectiveness of prenatal valacyclovir therapy in pregnancies with maternal or congenital CMV infection.

Materials and Methods. The inclusion criteria were pregnancies with confirmed maternal CMV infection. The primary outcome was the incidence of congenital CMV infection. The secondary outcomes were symptomatic and asymptomatic infection, perinatal death, termination of pregnancy, anomalies detected at follow-up ultrasound, fetal MRI imaging or at birth, severe and mild to moderate symptoms due to congenital CMV infection, neurologic, visual, hearing symptoms and adverse events related to valacyclovir.

Results. When stratifying the analysis according to the gestational age at maternal infection, the risk of vertical transmission was significantly lower in pregnancies receiving valaciclovir following first trimester infection (pooled OR 0.30, 95%CI 0.16-0.59, I2 = 0%, p = 0.001).

Pregnancies treated with valaciclovir therapy had an increased likelihood of asymptomatic congenital CMV infection, when compared to those not receiving valacyclovir (pooled OR 2.98, 95%CI 1.18-7.55, I2 = 0%, p = 0.021), while there was no significant difference between the two groups in the risk of perinatal death (p = 0.923), termination of pregnancy (p = 0.089), anomalies detected at follow-up imaging assessment during pregnancy or at birth (p = 0.934) and symptoms due to CMV infection in the newborn.

Conclusions. Prenatal valaciclovir administration in pregnancies with maternal CMV infection reduces the risk of congenital CMV infection. Further evidence is needed to elucidate whether valaciclovir can affect the course of the infection in the fetus and the risk of adverse perinatal outcome.

Third level care experience during SARS-CoV-2 pandemic

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DOI: 10.36129/jog.2022.S63

Objective. As the SARS-CoV-2 Pandemic has widely changed pregnancy experience and assessment, the inpatient and outpatient services have had to be re-organized. Since March 2020, Careggi University Hospital (CUH) has provided a dedicated COVID-pathway: spaces for women with unknown swab status and a COVID-19 ward delivery room. The aim of this study is to analyze the inpatient and outpatient COVID-19 related activities in CUH.

Materials and Methods. We prospectively collected data from consecutive COVID-19 pregnancies referred from 2020 to 2022, included in the local branch of the ItOSS surveillance. All patients experienced COVID-19 in pregnancy at various stages of severity and gestational ages.

Results. From March 2020 to June 2022, 165 COVID-19 deliveries occurred (169 newborns), while 16 pregnant positive women were admitted without delivering. A single emergency C-section (CS) was performed because of Sars-CoV-2 related ARDS, 15 women experienced serious maternal morbidity and 5 needed ECMO. A single maternal death occurred four months after delivery (C-section). Considering ECMO supported cases during pregnancy or postpartum, the first one tested positive for COVID-19 during the second trimester. She developed ARDS and required ECMO for 38 days. She was discharged in good general conditions and a CS at term was performed following obstetric indication. The second patient developed COVID-19-related ARDS at 28 weeks of gestation and experienced a precipitous vaginal delivery at 31 weeks+6 days of gestation while on ECMO. She was discharged 1 month later in good general conditions. The third patient was an obese (BMI 38) 43-year-old woman who had performed an IVF with embryo donation; she tested positive at 38 weeks+2 days of gestation. A CS was performed because of the worsening of her condition. After the delivery she was admitted in ICU and she underwent ECMO. She died 143 days after the CS by sepsis and multiple organ failure (MOF). For all these pregnancies neonatal outcomes were positive.

No perinatal death occurred and only one baby tested positive for SARS-CoV-2 infection at nasal swab sampling (case 3). The anesthesiology team performed neuroassial analgesia intrapartum in all the positive women who needed/requested it. Monoclonal Antibodies (mAbs) have been widely used to treat mild to moderate COVID-19 outpatients (NIH and RCOG recommendations) at risk for developing severe disease. Regarding this specifical therapy, an essential role in the management of the pregnant outpatient was played by the Infectious Disease Department. All patients above 28 weeks requiring hospitalization received LMWH prophylaxis, which was administrated under 28 weeks only in presence of additional risk factors (obesity, IVF, *etc*.). All new mothers received a ten days LMWH prophylaxis. On the outpatient side, we performed 22 teleconsultations, 43 obstetric ultrasounds (including I trimester screening), 90 obstetric checks with clinical evaluation and home therapy management, 32 fetal monitoring and 47 naso-pharingeal swabs.

Conclusions. At Careggi Hospital Maternal Department an extensive re-organization of inpatient and outpatient services has been performed in order to guarantee good practice and management of all pregnant women during the SARS-CoV-2 pandemic. This was only possible thanks to a wide multidisciplinary group which enhanced every professional.

Outcome of women with COVID-19 according to vaccination status

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DOI: 10.36129/jog.2022.S64

Objective. To evaluate maternal and perinatal outcome of women with COVID-19 infection, according to vaccination status.
Materials and Methods. This was an observational retrospective study of pregnant women with COVID-19 infection who were referred to our center. Women were asked about their vaccination status, and those who had received a COVID-19 vaccination (at least one dose) were compared with those who had not (no dose at all). The primary outcome was preterm birth at less than 37 weeks of gestation.
Results. 120 women with COVID-19 infection were included in the study. 57 had no vaccination (control group); 13 had received one dose of vaccine; 28 had received two doses; and 22 had received three doses. Preterm birth at less than 37 weeks occurred in 27% of the control group and in 11% in the group of women who had received at least one dose. Also the rates of pregnancy induced hypertension and admission to neonatal intensive care unit were significantly lower.
Conclusions. Women with a completed vaccination course and COVID-19 infection have better outcomes compared to those without vaccination.

Placenta histological features in three cases of supposed SARS-CoV-2 vertical transmissions in second and third trimester of pregnancy

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DOI: 10.36129/jog.2022.S65

Objective. We described three cases of SARS-CoV-2 positive new-borns with both symptomatic and asymptomatic mothers.
Materials and Methods. Placentas were analyzed in the pathology department and showed chronic histiocytic intervillositis with presence of $CD68^+$ macrophages, syncytiotrophoblast necrosis and positivity of the syncytiotrophoblast for SARS-CoV-2 antigen or RNA.
Results. The first case dates back to March 2020, when a symptomatic COVID-19 positive patient gave birth to a healthy neonate at 37.6 weeks of gestation. Skin to skin contact was not permitted but breastfeeding with a face mask was allowed. The newborn, that remained asymptomatic throughout the entire hospital stay, resulted positive to SARS-CoV-2 immediately after birth, at 24 hours of life and after 7 days. The second was delivered at 35.1 weeks of gestation by caesarean section for non-reassuring fetal status. The mother presented with fever, cough and a positive COVID-19 swab test. The newborn resulted positive on day 7, despite not having contact with the mother. No neonatal complications were observed. The third positive mother was admitted asymptomatic to the obstetric department in September 2021 due to preterm premature rupture of membranes at 20 weeks of gestation in a high-risk twin pregnancy. At 21.4 weeks of gestation her clinical conditions deteriorated, and she delivered two stillborn fetuses: SARS-CoV-2 was detected in all tissues samples. The lung of the first fetus only showed interstitial pneumonia features.
Conclusions. We detected SARS-CoV-2 in placentas of both the second and third trimester, implying the passage of the virus through the placenta to the fetuses as the presence of SARS-CoV-2 RNA was demonstrated in swabs and foetal tissues.

Placental histological findings in COVID-19 term, preterm and metabolic disorders pregnancy

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DOI: 10.36129/jog.2022.S66

Objective. In the last two years COVID-19 infection has represented a true unknown in the management of pregnancies with maternal COVID-19 positivity. However, it has not represented a serious complication, indeed it has rarely caused premature rupture of the membrane, fetal thrombosis or postnatal complications.
Materials and Methods. Our retrospective cohort study included placental samples from 350 patients from San Pietro Fatebenefratelli Hospital collected in a period of 4 months. Inclusion criteria were COVID-19 positivity during childbirth or in the previous two months but also a pregnancy without previous COVID-19 infection. Anamnestic data were carried out for the histological study on each placenta. 59% of patients were COVID-19 positive (15% of these had other associated disorders like gestational diabetes, hypertension, fetal death, preterm birth) 26.5% were preterm and the 14,5% were high-risk pregnancy with COVID-19 negativity.
Results. The most frequently represented lesion in a COVID-19 placenta was a mild chronic deciduitis, usually absent in placentas with normal outcome. The same deciduitis was observed in gestational diabetes placentas, although less frequently. Other rare findings were patchy fibrinoid necrosis of capsular decidua, chronic villitis, umbilical cord thrombosis. Severe lesions were rare.
Conclusions. COVID-19 does not seem to have a severe impact on the health of the placenta except in rare cases in which predisposing factors coexist and determine a more serious involvement of the fetus and its appendages. COVID-19 determines a constant but mild chronic placental inflammation, that is balanced by the maternal capacity to maintain homeostasis stemming the external injuries.

Coping strategies in pregnant women with high risk pregnancies during COVID-19 pandemic

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DOI: 10.36129/jog.2022.S67

Objective. Evaluation of coping strategies in pregnant women with high risk pregnancies during COVID-19 pandemic.
Materials and Methods. This was an observational study of pregnant women with high-risk pregnancy admitted for inpatient antenatal monitoring. Women were asked to fill in the Italian version of the Coping Orientation to the Problems Experienced (COPE-NVI). The questionnaire included 5 different dimensions: 1) Social support; 2) Avoidance strategies; 3) Positive attitude; 4) Problem solving; 5) Turning to religion. We planned to evaluate the COPE-NVI score according to the different maternal or fetal complications. 100 women filled out the questionnaire and were included in the study.
Results. 37 were admitted for preeclampsia, 15 for diabetes, 5 for intrahepatic cholestasis, 14 for hyperemesis gravidarum, while 29 had severe intrauterine growth restriction requiring monitoring. The mean COPE-NVI score for social support was 31.5 ± 8.6, for avoidance strategies 25.1 ± 6.7, for positive attitude 31.7 ± 7.3, for problem solving 30.5 ± 7.5, and for turning to religion 24.9 ± 5.3. No statistically significant differences were found for the COPE-NVI score within the different maternal or fetal complications, apart for turning to religion, where the score was higher for women with preeclampsia and lower for women with intrahepatic cholestasis ($p = 0.01$).
Conclusions. Women with high risk pregnancies admitted for antenatal inpatient monitoring have a high score at coping strategies.

The post-pandemic re-organization of birth centres and its impact on perinatal asphyxia in the province of Reggio Emilia

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DOI: 10.36129/jog.2022.S68

Objective. The pandemic forced the re-organization of birth hospitals in the province of Reggio Emilia. In 2018 there were four difference birth centres, in 2021 only two out of four were still working. The OBJECTIVE of the study was to evaluate if the centralization of birth centres had worsened the stillbirth rate and perinatal asphyxia (PA) outcome during the SARS-CoV-2 pandemic period (years 2020-21) compared to the pre-pandemic period (years 2018-19).
Materials and Methods. Retrospective review of birth rate, recovery for PA rate and stillbirth rate in the province of Reggio Emilia.
Results. Statistical data showed a decrease of overall births from 2018 to 2021 (7516 newborns in 2018-19 to 6363 in 2020-21), in accordance with the national trend. The percentage of newborns in the NICU in Reggio Emilia increased from the pre-pandemic period (59.66%) to the pandemic period (83.66%). Regarding the stillbirth rate, we observed a decrease from the pre-pandemic period (3.20‰) to the pandemic period (2.36‰). As far as concerned the PA rate, the percentage showed a reduction from the pre-pandemic (0.44%) to the pandemic period (0.36%). We also observed a decrease of the hypoxic-ischemic encephalopathy (HIE) rate from 0.16% to 0.12%. Finally, three different outcomes were evaluated in patients admitted for perinatal asphyxia: mortality, brain imaging lesions and seizures. During the pandemic we observed a significant decrease in all of these (**Table 1**).
Conclusions. Centralization of birth centres did not worsen perinatal diseases as far as concerns stillbirth, PA and HIE rate. On the contrary, we observed an enhancing of patients' outcomes.

Table 1.

	Pre-pandemic (2018-2019)	Pandemic (2020-2021)
Overall birth (n)	7516	6363
NICU birth (%)	59,66	83,66
Stillbirth rate (‰)	3,20	2,36
Perinatal asphyxia rate (%)	0,44	0,36
HIE (%)	0,16	0,12
• Mortality (%)	10,00	0,00
• Brain imaging lesions (%)	36,66	26,08
• Seizures (%)	16,66	13,04

The midwife's experience in mantaining the psychoneuroendocrine balance of women in labour during the COVID-19 pandemic: a phenomenological study

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DOI: 10.36129/jog.2022.S69

Objective. Neurohormonal processes control both the physiological aspects of labor and childbirth, and contribute to the subjective psychological experiences of birth. This concept has always been underestimated in clinical practice and this became even more glaring during the COVID-19 pandemic. The aim of the study was to analyze through the experience of midwives, how they, during the pandemic, have contributed to influence and maintain the balance of the psycho-neuro-endocrine axis (PNEI).

Materials and Methods. A qualitative research study, based on the phenomenological method of Cohen on a sample of midwives from the A.O.U.I Policlinico of Bari, interviewed in September 2021.

Results. Four main themes emerged from the analysis of the interviews and "field notes": ''Woman Care'', ''Loneliness and Fear'', ''Mask and DPI'', and finally ''COVID and Contagion''. In addition, eleven subthemes were derived from these as can be seen in the table (**Table 1**). The results of the analysis showed how midwives, who have always been the main reference figures for women, newborns and couples, have worked tirelessly to ensure that women received the best possible care, covid positive or not, aware of the influence that the psycho-physical component has on the hormonal release that guides the course of the birth event.

Conclusions. As the pandemic continues, there is an urgent need to improve the care and promote a physiological birth since it is known that giving birth physiologically is a psychologically powerful experience. From this emerges the need for health care providers to become aware of the importance of maintaining the psychoneuroendocrine balance to allow women to have the most positive birth experience possible.

Table 1.

THEMES	SUBTHEMES
1 Woman care	1.1 Setup: White Zone vs Red Zone 1.2 Methods and Strategies 1.3 One to One Care
2 Loneliness and Fear	2.1 Absence vs Connexion 2.2 Being born in a video call
3 Mask and DPI	3.1 Barriers 3.2 Protection vs Well-being 3.3 Discomfort
4 Covid & Contagion	4.1 Bringing the virus home 4.2 Covid and Professional Impact 4.3 Physical impact

SARS-CoV-2 infection with mild symptoms during pregnancy and fetal outcome, experience of an Italian second level hospital

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DOI: 10.36129/jog.2022.S70

Objective. COVID-19 is a pandemic inflammatory disease where endothelial dysfunction, observed also in mildly symptomatic patients, could affect the placenta and compromise pregnancy outcome. Our aim was to study the pregnancy outcome of patients with previous SARS-CoV-2 infection contracted during gestation.

Materials and Methods. This is a retrospective study and patients were enrolled with an anamnestic interview during the puerperium. We enrolled 41 women who contracted SARS-CoV-2 infection before twenty-four weeks of gestational age; 87 who contracted the infection after twenty-four weeks of gestational age; and a control group of 159 women, who did not contract infection during pregnancy.

Results. Maternal anthropometric, anamnestic and obstetric features were similar in the three groups. There is no relevant difference between the results of the three categories examined in terms of gestational age at delivery (273.54 days *vs* 273.73 days *vs* 274.39 days, p = 0.84), mode of delivery (vaginal delivery 53.66% *vs* 58.62 % *vs* 58.49 %; operative vaginal delivery 5.88% *vs* 9.19% *vs* 8.80%; cesarean section 41.46% *vs* 32.18 % *vs* 32.71 %; p = 0.49), fetal weight at birth (3224.02 g *vs* 3276.65 g *vs* 3235.57 g, p = 0.75) admission in neonatal intensive care (0 % *vs* 2.2 % *vs* 4.4%, p = 0.30).

	Sars-Cov-2 infection <24 weeks of GA N: 41	Sars-Cov-2 infection >24 weeks of GA N: 87	Absence of Sars-Cov-2 infection during pregnancy N: 159	P value
GA at delivery (days)	273,54 (9,49)	273,73 (9,60)	274,39 (10,79)	0,84
Mode of delivery Vaginal delivery Operative vaginal delivery Cesarean section	 22 (53,66%) 2 (5,88%) 17 (41,46%)	 51(58,62%) 8 (9,19%) 28 (32,18%)	 93(58,49%) 14(8,80%) 52 (32,71%)	0,49
Neonatal weight (g)	3224,02 (396,94)	3276,65 (463,54)	3235,57(456,14)	0,75
Neonatal weight percentile	53,14 (26,14)	57,12 (28,83)	52,46 (28,40)	0,46
Admission in neonatal intensive care	0 (0%)	2 (2,2 %)	7 (4,4%)	0,30

Data are presented as Mean (SD) or n(%)

Conclusions. The SARS-CoV-2 disease with mild symptomatology, contracted during pregnancy, regardless of the gestational age at the time of infection, does not apparently impact on the fetal outcome in any significant way.

Does chronic Low Molecular Weight Heparins use during pregnancy increase the risk of postpartum hemorrhage?

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DOI: 10.36129/jog.2022.S71

Objective. To investigate the risk of postpartum hemorrhage (PPH) associated with chronic prophylactic or therapeutic use of Low-molecular-weight heparins (LMWH) during pregnancy.
Materials and Methods. A cohort retrospective study. 822 patients (LMWH group n = 411, control group n = 411) were enrolled between 2020-2022. Singleton pregnancies supplemented with LMWH, started within the first 24 weeks, proceeded until term, and suspended at least 24 hours before delivery, were included in the cohort group. Confounders were controlled by matching and logistic regression analysis. Data regarding delivery were collected retrospectively. The causes of PPH were classified using the 4 "T's" formula.
Results. 71 cases of PPH were documented in the LMWH group (17.27%) *versus* 46 in the control group (11.1%), with relative risk (RR) of 1.5435 (p = 0.0136). Severe PPH incidence was also significantly increased in the LMWH group (8.76% *versus* 4.87%) with RR of 1.8 (p = 0.0295). The prevalence of uterine atony was significantly higher in the LMWH group (73.24% *versus* 56.52%, p = 0.0026). The interval between the last dose of LMWH and delivery did not seem to influence the haemorrhagic risk.
Conclusions. LMWH chronic use during pregnancy carries an increased risk of PPH, severe PPH and uterine atony. Clinicians should balance and carefully assess the competing risks *versus* potential benefits before initiating chronic therapy in pregnant patients. Once prescribed, LMWH treatment should be considered a risk factor and active management of the third stage of labor should be promoted, even if the drug is suspended 24 hours prior to delivery.

Results

	LMWH group (N 411)	Control Group (N 411)	Relative Risk (95% CI)	P value
Postpartum Blood lose (ml)*	300 (200, 500)	300 (200, 600)		
Postpartum hemorrhage	71 (17.27%)	46 (11.19%)	1.5435 (1.093-2.179)	0.0136
Vaginal deliveries	50/240	38/240		
Elective Cesarean Section	12/124	6/124		
Urgent Cesarean Section	9/47	2/47		
Severe postpartum hemorrhage	36 (8.76%)	20 (4.87%)	1.800 (1.060-3.056)	0.0295
Uterine atony	52/411	26/411	2.000 (1.275-3.138)	0.0026
Blood transfusion	5/411	1/411	5.000 (0.587-42.612)	0.141
PPH etiology: Tone	52/71 (73.24%)	26/46 (56.52%)		
Tissue	11/71 (15.49%)	12/46 (26.09%)		
Trauma	7/71 (9.86%)	8/46 (17.39%)		
Unknown	1/71 (1.40%)	-		

*Data are expressed as median (1°, 3° IQR)

Starting a fetal surgery centre: the first year experience

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DOI: 10.36129/jog.2022.S72

Objective. Report on the first year experience on fetoscopy in a pediatric referral centre.

Materials and Methods. Between June 2021 and August 2022, 52 fetal surgery procedures were performed, including 33 fetoscopies.

Results. Fetoscopy was used to perform laser-coagulation of placental anastomosis in 18 monochorionic pregnancies with twin-to-twin transfusion syndrome (TTTS). In 15/18 cases (83%) there was the association of a severe selective fetal growth restriction (estimated fetal weight < 3rd) centile) and a ductus venosus absent/reverse a-wave, was associated). The survival rates of both and at least one twin at discharge were 33% (5/15) and 80% (12/15) respectively. Brain MRI was normal in all patients. In addition, fetoscopy was successfully performed in 8 cases with Congenital Diaphragmatic Hernia (6 left and 2 right). The balloon was removed fetoscopically in all cases except one (spontaneous deflation after 3 weeks). The median duration of the procedures was 15 min (10-30). The median duration of tracheal occlusion was 3.4 weeks (27.9-34.6). Median gestational age at delivery was 34.3 weeks (29.6-38.4). Premature rupture of membranes < 34 weeks occurred in 20% of laser and 35% of TO. No maternal complications occurred.

Conclusions. Although our cases are still limited since the center has just recently started its activities, our experience respects the required criteria for a fetal surgery center to fullfill the standards of care established in literature: specialized skills based on clinical experience, strict protocols and multidisciplinary team.

Retroperitoneal schwannoma during pregnancy: case-report and practice-based overview

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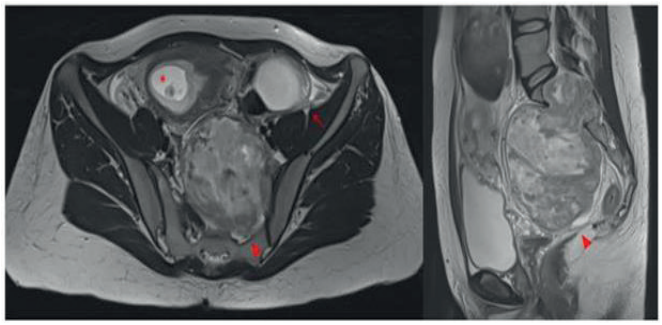
DOI: 10.36129/jog.2022.S73

Objective. Schwannomas are benign slow-growing tumors of the peripheral nerve sheaths arising from Schwann cells. During pregnancy, the routine use of ultrasound for fetal assessment has resulted in increased detection of maternal asymptomatic masses, including retroperitoneal ones. Although most of these masses are benign, the possibility of cancer must be considered.
Materials and Methods. In this report, we describe the rare case of a young woman with bilateral adnexal cysts and a presacral retroperitoneal mass diagnosed during the first trimester of pregnancy.
Results. At the 12th gestational week, she received surgery to remove ovarian tumors and to obtain a biopsy of the non-adnexal tumor. The histological examination revealed a bilateral borderline seromucinous tumor of the ovaries; the presacral mass was identified as a schwannoma. Although the dimensions of the sacral mass severely affected the quality of life of the patient, it was possible to achieve a near term pregnancy with the delivery of a healthy baby. To successfully remove the voluminous presacral schwannoma, the patient underwent neurosurgical treatment seven months after delivery.



Conclusions. Concerns regarding risk of malignancy, acceleration of tumor growth and fetal wellness may arise in healthcare practitioners after finding a schwannoma during pregnancy. Nevertheless, benign pelvic tumors do not hamper a regular pregnancy even when of great dimensions: in particular, as in our case, pelvic schwannomas are slow-growing benign tumors and do not seem to enlarge during pregnancy.

Vaccination coverage during pregnancy and factors associated with refusal

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DOI: 10.36129/jog.2022.S74

Objective. The vaccines currently recommended during pregnancy are the dTpa, the influenza vaccine, and, due to SARS-CoV-2 pandemic, the mRNA vaccine against COVID-19. The aim of this study was to evaluate vaccination coverage among pregnant women and factors associated with refusal.

Materials and Methods. 307 patients who delivered at term between March and April 2022 at Careggi Hospital answered a questionnaire about vaccines during pregnancy. The primary aim was to assess vaccination coverage and factors associated with refusal. The secondary aim was to detect differences in vaccination between Italian and foreign women.

Results. Overall, 74% of patients were vaccinated with dTpa, 82% against COVID-19 and only 33% against Influenza. Vaccination coverage for dTpa and COVID-19 was significantly higher among Italian than foreign patients (80% *vs* 51%, $p < 0.001$ and 86% *vs* 69%, $p = 0.002$, respectively). 89% of patients received recommendations for vaccines from the gynecologist, more frequently among Italians than foreigners ($p = 0.01$). The main reasons behind refusal of vaccinations were: reduced perception of the risk of disease in the case of influenza (41%), inadequate information received from the gynecologist regarding dTpa (35%), fear of side effects (63%) and of effects on the fetus (70%) from the COVID-19 vaccine.

Conclusions. Adherence to the Influenza vaccine was low because of reduced perception of the disease risks. Fear of COVID-19 disease led most of the patients to receive the vaccination. The significant difference in vaccination coverage between Italians and foreigners is likely due to less information being received by foreign patients, an example of health care disparity.

	Total population (307)	Italians (242)	Foreigners (65)	p value
Adherence to vaccines	dTPA 227 (74%)	194 (80.2%)	33 (50.8%)	<0.001
	Covid-19 252 (82%)	207 (85.5%)	45 (69.2%)	0.002
	Influenza 100 (33%)	85 (35.1%)	15 (23.1%)	0.06
Recommendations for vaccines from gynecologist	272 (89%)	220 (91%)	52 (80%)	0.014

Off-label treatment of hyperemesis gravidarum with transdermal clonidine: safety and clinical outcomes

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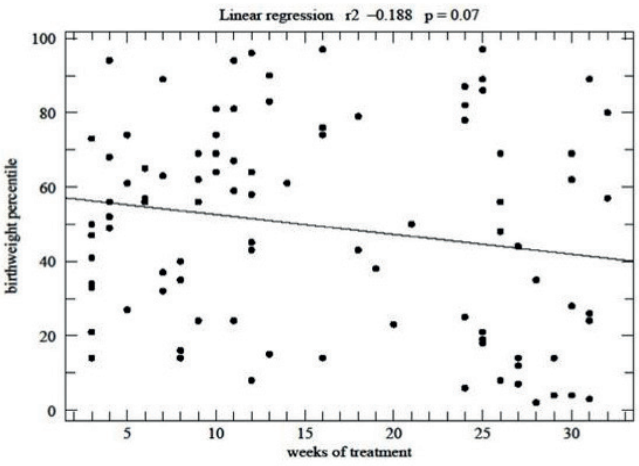
DOI: 10.36129/jog.2022.S75

Objective. Improvement of symptoms of severe persistent Hyperemesis Gravidarum (HG) with use of transdermal (TD) clonidine was described and first reported in a series of cases (Obstetric Medicine 2011) and a randomized controlled pilot study to study the efficacy was completed (BJOG, 2014). A clinical outcome database was set up under permission of the local institutional review board. Informed consent was signed by all participating women.

Materials and Methods. n = 270 women were prospectively followed throughout pregnancy until delivery after prescription of TD clonidine in the first and mid trimester for severe unresponsive HG (PUQE score at admission > 12 and no improvement with standard treatments). Median weeks at start: 10 (6-21) with a median duration of treatment of 12 weeks (1-31); 34% continued treatment until delivery.

Results. Median gestational age at delivery of the 270 women enrolled was 39 weeks with prematurity < 37 weeks in 5.6 %. Cesarean Section rate was 35%. PROM occurred in 12% of pregnancies. Median birthweight was 3260 grams (2010-4300) and median percentile for singletons 48.5; LBW newborns < 2500 grams were 8% SGA < 10th percentile occurred in 7.4%. One intrauterine fetal death and one perinatal death were reported for other causes. Prevalence of major birth defects was < 2% (mainly cardiac septal defects). Side effects were contact dermatitis (24%) and symptomatic hypotension (2%). Drop-outs: n = 6 for systemic intolerance (tiredness, fatigue, hypotension).

Conclusions. Off-label use of TD clonidine in selected cases of HG appears safe and effective in clinical practice.



Folate and vitamin D during pregnancy: association for reducing pregnancy complications

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DOI: 10.36129/jog.2022.S76

Objective. To evaluate the efficacy of supplementation with Folervid® during pregnancy.

Materials and Methods. Observational cohort of women who received daily oral supplementation of Folervid® during pregnancy starting from the first trimester of pregnancy, who were compared with a control group who did not. Folervid® contained Vitamina C 220 mg; Vitamin B12 2.5 mcg; Vitamin B6 1.4 mcg; Vitamin D 50 mcg (2,000 UI); Folate 400 mcg as 5-Methyl-tetrahydrofolate. The primary outcome was the incidence of preeclampsia.

Results. 100 women met the inclusion criteria and were included in the study. This cohort was compared with a matched control group of 100 controls.

Conclusions. Women who received Folervid® during pregnancy had significantly lower risk of preterm birth at less than 37 weeks of gestation, and first trimester abortion.

Table 1. *Maternal and perinatal outcomes.*

	Folervid ® N = 100	Control N = 100	p-value
Gestational hypertension	2%	2%	0.98
GDM	3%	4%	0.73
Preeclampsia	0%	1%	0.82
PTB <37 weeks	5	13	**0.05**
First trimester abortion	0	7	**0.05**
IUD	0	0	-
Neonatal death	0	0	-
Cesarean delivery	35%	38%	0.63

Bold face data, statistically significant

GDM, gestational diabetes mellitus; PTB, preterm birth; IUD, intrauterine feath death

Is it time to change the diagnostic thresholds for Intrahepatic Cholestasis of pregnancy?

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DOI: 10.36129/jog.2022.S77

Objective. To establish pregnancy-specific reference intervals for fasting and postprandial total serum bile acids (TSBA) levels.

Materials and Methods. A prospective cohort study of TSBA levels in healthy pregnant women. Both fasting and postprandial TSBA levels were measured in 612 women over one year (528 fasting and 377 postprandial samples). Exclusion criteria were an established diagnosis of intrahepatic cholestasis of pregnancy (ICP) or any co-existing condition of increased risk for ICP.

Results. Reference ranges were established of 4.4-14.1 μmol/L for fasting TSBA (median 7.6 μmol/L), and 4.7-20.2 μmol/L for postprandial TSBA levels (median 9.1 μmol/L). The postprandial were significantly higher than the fasting measurements, with a median increase of 1.0 μmol/L. A correlation was found between fasting and postprandial concentrations, as well as with fetal gender, parity, and the use of assisted reproductive technologies. A seasonal pattern was noticed for both fasting and postprandial levels, with the highest values in the winter season ($p < 0.01$ and 0.02, respectively).

Maternal characteristics and reference interval calculations of TSBA (fasting and postprandial)

Age (years)	34 (30, 38)	N 612
BMI (kg/m²)	22.71 (20.6, 25.6)	N 610
Gestational weight gain (kg)	12 (9, 15)	N 602
Neonatal weight (g)	3268.9 (± 466.47)	N 611
Reference fasting TSBA (μmol/L)	7.6 (6.4, 9.1)	N 528
Lower limit (95% CI)*	4.4 (4.2-4.7)	
Upper limit (95% CI)*	14.1 (12.7-15.5)	
Reference postprandial TSBA (μmol/L)	9.1 (7.1-11)	N 377
Lower limit (95% CI)*	4.7 (4.5-5.3)	
Upper limit (95% CI)*	20.2 (17.3-32.3)	

*Reference intervals were calculated using nonparametric method to account for non-normally distributed results. The lower (2.5th) and upper (97.5th) reference limits are noted with 95% confidence intervals (CI) indicated in brackets.
**Data are expressed as mean ± SD or median (1°, 3° IQR) based on their distribution

Conclusions. Normal pregnancy is a sub-cholestatic state and is associated with a physiological elevation of TSBA levels compared to non-pregnant adults, therefore a higher threshold should be considered for the diagnosis of ICP. It is suggested that the upper reference limit observed in our healthy pregnant population should be used: fasting TSBA values ≥ 14 μmol/L and postprandial TSBA values ≥ 20 μmol/L. Since the fasting TSBA value is more specific for the diagnosis, while the postprandial is important for severity assessment, we recommend measuring both, rather than obtain a random sample.

Hemodynamic evaluation and obstetric outcomes in monochorionic diamniotic twin pregnancy

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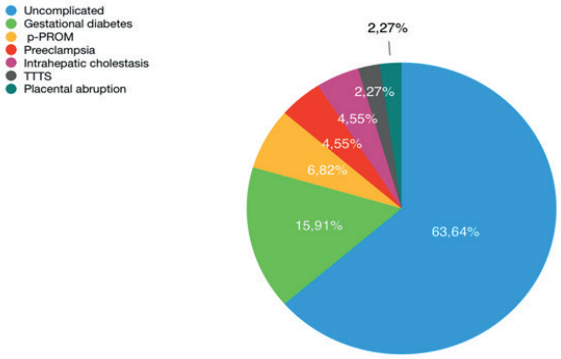
DOI: 10.36129/jog.2022.S78

Objective. The aim of the study was to evaluate the trend of maternal hemodynamics in uncomplicated and complicated monochorionic diamniotic twin pregnancies (MCDA).
Materials and Methods. 44 monochorionic diamniotic twin pregnancies were enrolled (**Figure 1**) and were subjected to a non invasive hemodynamic evaluation with USCOM method. All the pregnant women were followed until delivery.
Results. Compared to singleton pregnancies, MCDA twin pregnancies showed a higher heart rate and cardiac output and lower total vascular resistance values ($p < 0.001$) in the second trimester. On the contrary, during the third trimester the cardiac output and inotropy index were lower in MCDA twin pregnancies ($p < 0.001$) compared to singleton pregnancies. No significant differences were found from the comparison between hemodynamic values in complicated and uncomplicated MCDA, during the three trimesters.
Conclusions. Our data underline that in MCDA twin pregnancies there is a marked haemodynamic adaptation to promote a correct utero-placental perfusion, expressed by increased cardiac output and heart rate.

Figure 1.



In the third trimester, however, the cardiac output and inotropy index decrease. These conditions might be due to a mechanism of progressive exhaustion of the maternal cardiovascular system that has been subjected, in the previous trimesters, to a greater effort than normal.

Reimplantation of trophoblastic tissue on the perimetrium after laparoscopic treatment for tubal stump pregnancy: a case report

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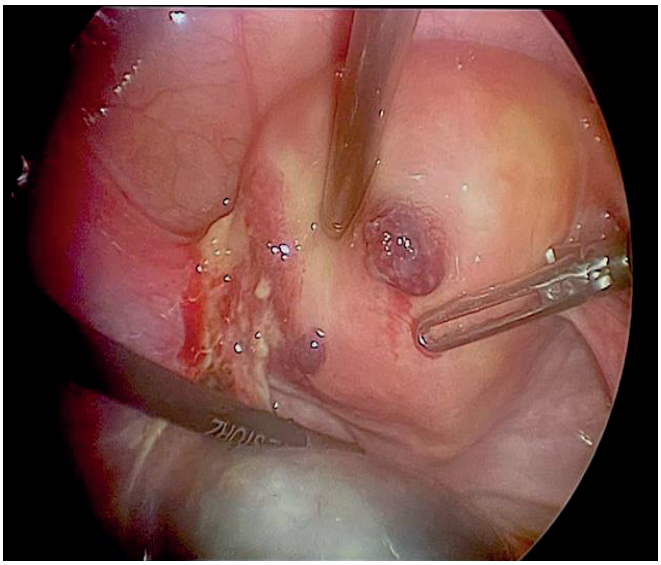
DOI: 10.36129/jog.2022.S79

Objective. Laparoscopic salpingectomy represents the best treatment for ectopic pregnancy as regards the risk of recurrences. Rarely, small residues of trophoblastic tissue in the peritoneal cavity may proliferate again, resulting in persistently elevated serum β-hcg value or recurrence of clinical symptoms. Extravillous Trophoblast (EVT) has a known proliferative, migratory and invasive capacity and the limiting mechanisms of this invasion may depend on the location of the ectopic implants. The most common sites of reimplanted trophoblastic tissue are peritoneum and omentum, while the bowel, uterosacral ligament and uterine body are rarer.
Materials and Methods. Our patient was a 36-year-old woman who underwent a laparoscopic surgery for tubal stump pregnancy. Five weeks after surgery, the patient came back to our emergency room with severe abdominal pain, asthenia and lipothymia.
Results. Ultrasound evaluation showed hemoperitoneum and CT scan reported active focal bleeding on the uterine fundus. Laparoscopy then confirmed the presence of trophoblastic tissue implanted on the uterine serosa.
Conclusions. This case describes how trophoblastic tissue left in the abdominal cavity can implant actively on a new locus. In order to avoid recurrences it is necessary to take preventive measures during surgery. Furthermore an early detection of remaining active trophoblastic tissue can be performed by dosing β-hcg value post-operatively, which should be continued until it is absent. This evaluation is always performed after conservative treatment, but it could be useful also after salpingectomy, in order to start early medical or surgical treatment.



Previous surgery for endometriosis: a further risk for obstetric complications?

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DOI: 10.36129/jog.2022.S80

Objective. A number of evidence has shown that endometriosis is associated with an increased incidence of obstetric complications, but it is still unknown if other variables related to the disease influence the outcome. Thus, the aim of the study was to evaluate whether a history of surgery represents an additional risk factor for adverse pregnancy and delivery outcome among women with endometriosis.

Materials and Methods. A retrospective observational cohort study on prospectively collected data was conducted in a single tertiary referral center for both endometriosis and high-risk pregnancy between 2019 and 2021. Women with a history of endometriosis, diagnosed either by imaging or by histological confirmation after surgery, who were followed up and delivered after singleton pregnancy were included. Women with and without previous surgical treatment for endometriosis were compared in terms of maternal characteristics, mode of conception, pregnancy management, obstetric complications, delivery and postpartum outcome, pregnancy and delivery outcome.

Results. The study population included 162 cases and 103 (63%) had 1 or more surgery for endometriosis. A high incidence of preterm births, placental disorders, gestational diabetes, caesarean section (CS) and postpartum haemorrhage (PPH) was found compared to non-endometriosis patients. However, women with a history of surgery for endometriosis had further increase of CS (47%) and PPH rate (27%) compared to those conservatively managed. No difference was found in terms of other obstetric complications.

Conclusions. Pregnant women with a history of surgery for endometriosis should be considered at high risk for peripartum and postpartum adverse outcomes.

Evaluation of the reproducibility of two speckle tracking software for the antenatal semi-automated assessment of the fetal cardiac function

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DOI: 10.36129/jog.2022.S81

Objective. Antenatal morphometric and functional evaluation of the fetal heart by means of speckle tracking technique can be performed using different software developed for the analysis of prenatally acquired ultrasound clips of the fetal heart. The objective of the study was to evaluate the reproducibility of two speckle tracking software in the antenatal semi-automated assessment of the fetal cardiac function and morphometry.

Materials and Methods. Prospective study conducted in two academic units in Italy (Parma) and Spain (Barcelona) including a non-consecutive series of non-anomalous fetuses. The evaluated speckle tracking software were TomTec-GmbH at the University of Parma and FetalHQ at the University of Barcelona.

At each participating unit, two-dimensional ultrasound clips of the four-chamber view of the fetal heart were acquired by dedicated operators. The morphometric and functional echocardiography analysis of the ultrasound clips was performed by two operators (ADT and LN), using the two proprietary software. The inter-software reproducibility of the endocardial global longitudinal strain (endoGLS) and fractional area change (FAC) of left (LV) and right ventricles (RV) and ejection fraction (EF) of LV was evaluated by the intraclass correlation coefficient (CC).

Results. 34 cases (9 from Parma and 25 from Barcelona) were included at a median gestation of 30 (22-40) weeks. Moderate-to-good reproducibility for the morphometric and functional parameters of LV was demonstrated (endoGLS 0.596, 95%CI 0.1016-0.664, $p < 0.01$; EF 0.757, 95%CI 0.513-0.879, $p < 0.01$; FAC 0.788, 95%CI 0.575-0.894, $p < 0.01$). Conversely, the morphometric and functional parameters of the RV showed no reproducibility between the two software (endoGLS 0.386, 95%CI -0.229-0.693, $p = 0.08$; FAC 0.357, 95%CI 0.357, 95%CI -0.288-0.679, $p = 0.11$).

Conclusions. This study demonstrates a fair reproducibility of the speckle tracking analysis of the morphometric and functional parameters of the LV but no inter-software reproducibility of the morphometric and functional parameters of the RV.

Comparison between commercial product of oral misoprostol and vaginal dinoprostone for induction of labor

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DOI: 10.36129/jog.2022.S82

Objective. It is known that galenic oral misoprostol is the most effective prostaglandin in terms of vaginal delivery achievement and the safest one in terms of caesarean section (CS) risk. However, there are only few data regarding the new commercial formulation. Our objective was to compare the efficacy and safety of the oral misoprostol commercial product and vaginal dinoprostone.

Materials and Methods. Monocentric, retrospective study on 186 patients with singleton term pregnancies undergoing labor induction at Careggi University Hospital, Florence, from 2020 to 2022: 93 cases received oral misoprostol commercial formulation 25-50 μg (maximum 200 μg/day), based on BMI, and 93 vaginal dinoprostone 1-2 mg (maximum 6 mg/day) or 24-hour slow-release pessary. The two groups were homogeneous for age, BMI, gestational age and parity.

Results. We observed no differences in CS rate, adverse fetal outcomes (low Apgar index, base excess, TIN admission) and uterine hyperstimulation rate. Dinoprostone was associated with a higher rate of major postpartum haemorrhage (PPH) (55% *vs* 24%, p = 0.05). Time to labor and delivery were similar, with a higher percentage of labor failed achievement in the dinoprostone group (11% *vs* 3%, p = 0.04). Consequently, dinoprostone more frequently required further induction with oxytocin than misoprostol (67% *vs* 43%, p = 0.03), whereas oxytocin augmentation rates were similar. Dinoprostone showed an increased, but not significant, tendency to hyperstimulation with abnormal fetal heart-rate.

Conclusions. Our results confirmed data regarding galenic misoprostol efficacy and safety. Indeed, misoprostol commercial formulation resulted more effective in labor induction than dinoprostone. No difference in safety was found between the two products except for major PPH.

Safety of PGE2 induction of labor: results of a multicenter observational study

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DOI: 10.36129/jog.2022.S83

Objective. Induction of labor with dinosprostone is associated with an increased risk of disseminated intravasascular coagulation (IDC) in women aged ≥ 35 years and in pregnancy at gestational age (GE) ≥ 40 weeks. The AIFA note of July 21 emphasizes the risk of tachysystole associated with the use of dinoprostone. The primary objective of this study was to evaluate the prevalence of IDC in patients older than 35 years or that are ≥ 40 weeks of GE. The secondary objective was to evaluate the safety of induction of labour (IOL) with dinoprostone (PGE2) in this class of patients.
Materials and Methods. A multicentre, retrospective, observational study on 1486 singleton pregnancies who underwent IOL with PGE2 (either vaginal gel or slow-release insert). Data regarding maternal demographics, medical and obstetrical history, and pregnancy outcome were collected. Statistical significance was evaluated through chi-square test.
Results. IDC occurred in 0 patients. Tachysystole occurred in 79 patients (5.3%); of these, 14 (0.9%) needed treatment and 27 (1.8%) underwent emergency caesarean section. 41 (2.8%) babies were born with a cord pH ≤ 7.1 and 20 (1.3%) with a 5th minute Apgar ≤ 7. Maternal age ≥ 35 years was significantly associated with treated tachysystole. GE ≥ 40 weeks was significantly associated with tachysystole and 5th minute Apgar ≤ 7.
Conclusions. IDC is a rare occurrence. The prevalence of PGE2-related tachysystole and its consequences is higher in patients who are older than 35 years or GE ≥ 40 weeks. Research should be encouraged regarding pharmacokinetics and pharmacodynamics in pregnancy, particularly at an advanced age, given the differences recorded in physiological response to drugs.

Induction of labor in high-risk nulliparous women with unfavorable cervix: retrospective study

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DOI: 10.36129/jog.2022.S84

Objective. The aim of the study is to evaluate the success rate, safety and time to delivery for induction of labor (IOL), with the use of dinoprostone 10 mg controlled-release vaginal insert or by the Foley balloon method, in the case of high-risk pregnancy nulliparous women with Bishop score < 4.
Materials and Methods. A retrospective study of 229 women who underwent IOL, either with dinoprostone or by the Foley balloon method. In the first instance, if labor had not been successfully induced after the removal of the dinoprostone, oxytocin was administered. As for the second group, the bishop score was re-evaluated after foley removal and patients continued the induction with dinoprostone (if Bishop < 6) or Oxytocin (if Bishop > 6). After dinoprostone removal and no labor, oxytocin was administered. The Caesarean section (CS) rate, along with demographic characteristics and fetal and maternal complications were recorded. Time to delivery was tracked.
Results. The CS rate was superimposable between groups (37.56% *vs* 34.37%, p = 0.88). The BMI of women who underwent CS was significantly higher, 27.30 *vs* 26.52, p = 0.012. Time to delivery was statistically lower in the dinoprostone group (26.82 h), as opposed to the Foley group (48.25 h) (p < 0.0001). No differences in complications (p = 0.3).
Conclusions. The CS rate was superimposable in both groups. A higher BMI was the only significant risk factor for CS. Starting with dinoprostone resulted in a significantly shorter induction, with the same maternal-fetal outcomes. There is no need therefore to prolong the induction and raise maternal stress levels, as this will not yield better outcomes.

Labor induction with misoprostol (Cytotec) *versus* dinoprostone (Propess)

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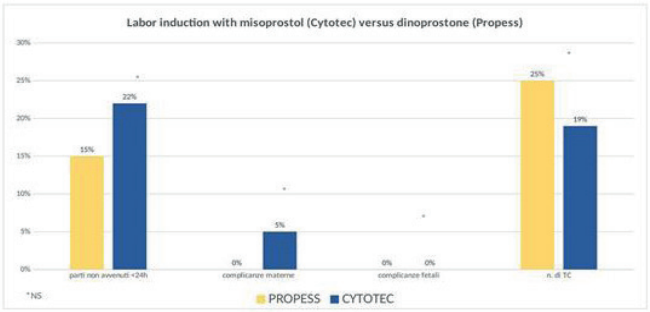
DOI: 10.36129/jog.2022.S85

Objective. To compare and assess the efficacy and the safety of both oral and local prostaglandins for induction of labour (IOL).
Materials and Methods. This was a single-centre prospective cohort study, conducted at San Filippo Neri Hospital. Data were collected through a clinical panel we developed. 164 women at term were recruited between November 2021 and August 2022; 93 of them underwent IOL through either oral or local prostaglandins alone. 73 women received oral prostaglandins (misoprostol). 20 received vaginal prostaglandins (dinoprostone). Bishop score was unfavourable in both groups (< 4). The primary outcome measured was caesarean deliveries. Secondary outcomes were time from induction to vaginal delivery and measures of maternal and neonatal safety.
Results. Oral and local prostaglandins showed similar efficacy and safety. The overall cesarean section rate was 19% for the first group and 25% for the second. Mean time from induction to vaginal delivery was 15 h for both groups. Maternal complications were detected in 4 patients of the first group: 2 PPH, 2 retained placenta. No fetal complications occurred during our study: Apgar score was > 7 in all newborns and intensive care treatment was never required. The major indication for caesarian section following IOL was non-reassuring CTG.
Conclusions. Overall, both oral and local prostaglandins proved to be safe IOL, and their efficacy can be considered comparable. Even though no statistical significance can be assessed, caesarean section rate was lower in those patients treated with oral prostaglandins.



Labor induction with misoprostol 25 μg *versus* misoprostol 50 μg in patients with term premature rupture of membranes

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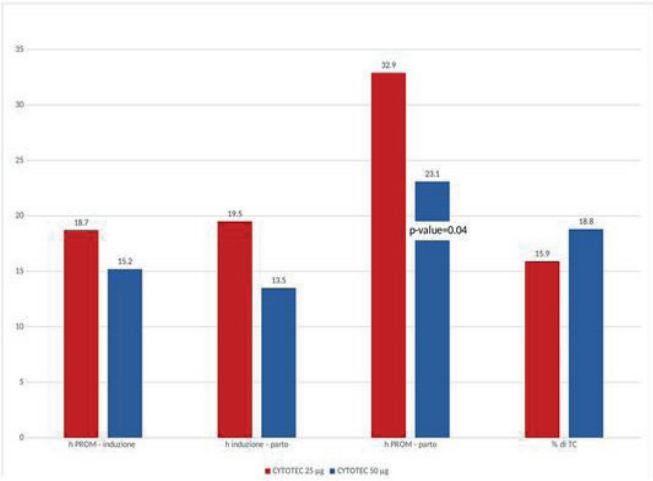
DOI: 10.36129/jog.2022.S86

Objective. To compare two groups of patients with premature rupture of membranes (PROM) that underwent induction of labor (IOL) with misoprostol 25 μg and misoprostol 50 μg, respectively.

Materials and Methods. We conducted a single-center prospective cohort study in the gynecological unit of San Filippo Neri. Data were collected from 11/2021 to 08/2022 through a questionnaire. 167 patients with PROM were recruited. In 88 women spontaneous delivery occurred. 79 underwent IOL through misoprostol, which was administered according to two different protocols: 63 patients received misoprostol 25 μg, 16 received 50 μg. Outcomes were the time between PROM and delivery, between PROM and induction and between induction and delivery. Secondary outcomes were the rate of cesarean section and its indications.

Results. There was no statistically significant difference in the two groups in mean time between PROM and induction (P-value = 0.3772) and between induction and delivery (P-value = 0.2193). The mean time from PROM to delivery was significantly lower in the second group (P-value = 0.0435). There was no significant difference in the rate of caesarean section in the two groups (P-value = 0.78). There was no registration of Apgar Index < 7 at the 5th minute.

Conclusions. The comparison of the two groups showed similar efficacy and safety in both IOL schemes. However, the time between PROM and delivery appears to be shorter in patients induced with 50 μg misoprostol. This scheme has also proven to be positive for patients because of the lower number of CTG and administrations that allows women to rest more.



Vacuum assisted delivery: comparison between two groups (prolonged second stage of labour and non reassuring CTG)

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DOI: 10.36129/jog.2022.S87

Objective. The main purpose of assisted vaginal birth is to accelerate childbirth with minimal maternal and neonatal morbidity. The main indications for vacuum use are the non-reassuring cardiotocography and a prolonged second stage of labour.

Materials and Methods. We conducted a retrospective cohort study of pregnant women at term who delivered by vacuum (Kiwi OmniCup) from 2013 to 2019. Clinical data were collected from the 'assisted vaginal birth record' and analysed using chi-square test (significance: P-value < 0.05).

Results. The prevalence of assisted vaginal birth with vacuum from 2013 to 2019 was 7.3% (358/4900). The indications were: non reassuring CTG (224 cases: 62.6% - Group A) and prolonged second stage of labour (134 cases: 37.4% - Group B). As expected, epidural analgesia, neonatal weight > 4000 g and nulliparity were more frequent in patients with a prolonged second stage of labour.

In this group also the use of oxytocin, a normal CTG, three or more pulls, an application time ≥ 10 min. and blood loss ≥ 1000 ml were significantly more frequent.

Moreover, in group B there was a trend of Kristeller and episiotomy. There were 14 cases of 3rd and 4th degree perineal tears (3.9%), all with episiotomy with no differences between the groups.

There were also no differences regarding head station, the occiput posterior position, cup detachment and thick meconium.

Despite the importance of abdominal palpation in 1/5^{ths} it was performed only in 198 cases (55.3%).

In two cases, one per group, vacuum failed, with a subsequent caesarean.

An Apgar score < 7 at 5' was recorded in 5 infants, all in group A.

Operative Vaginal Delivery	Non reassuring fetal heart rate Group A	Prolonged second stage of labor Group B	Total	P Value	OR (CI 95% OR)
Cases N° (%)	224 (62,6)	134 (37,4)	358 (100)		
Nulliparous women (%)	164 (73,2)	118 (88,0)	282 (78,7)	0.001	*0,37 (0,20-0,67)*
Epidural analgesia (%)	38 (17,0)	37 (27,6)	75 (20,9)	0.01	*0,53 (0,32-0,89)*
Station of the head -1 (%)	11 (5,0)	4 (3,0)	15 (4,2)	0.37	*1,67 (0,52-5,38)*
Station of the head 0/+1 (%)	92 (41,0)	68 (50,7)	160 (44,7)	0.07	*0,67 (0,44-1,04)*
Station of the head +2/+3 (%)	121 (54,0)	62 (46,3)	183 (51,1)	0.15	*1,36 (0,88-2,09)*
Occiput posterior position (%)	57 (25,4)	43 (32,0)	100 (27,9)	0.17	*0,72 (0,45-1,15)*
Oxytocin infusion (%)	123 (54,9)	119 (88,8)	242 (67,6)	< 0.001	*0,15 (0,08-0,27)*
*CTG Normal (%)	6 (2,7)	93 (69,4)	99 (27,6)	< 0.001	*0,01 (0,005-0,03)*
*CTG Indeterminate (%)	81 (36,1)	37 (27,6)	118 (33,0)	0.09	*1,48 (0,93-2,36)*
*CTG Abnormal (%)	137 (61,2)	4 (3,0)	141 (39,4)	< 0.001	*51,1 (18,2-143,4)*
Meconium stained liquor (%)	65 (29,0)	27 (20,1)	92 (25,7)	0.06	*1.62 (0,97-2,70)*
Three or more pulls (%)	85 (37,9)	78 (58,2)	163 (45,5)	< 0.001	*0,43 (0,28-0,67)*
Application time ≥ 10 min. (%)	30 (13,4)	40 (29,8)	70 (19,5)	< 0.001	*0,36 (0,21-0,62)*
Cup detachment (%)	51 (22,7)	25 (18,6)	76 (21,2)	0.35	*1,28 (0,75-2,19)*
Kristeller manoeuvre (%)	41 (18,3)	36 (26,8)	77 (21,5)	0.05	*0,61 (0,36-1,01)*
Mediolateral episiotomy (%)	190 (84,8)	123 (91,8)	313 (87,4)	0.05	*0,50 (0,24-1,02)*
3th an 4th degree vaginal tears (%)	9 (4)	5 (3.7)	14 (3.9)	0.89	*1,08 (0,93-1,20)*
Birth weight > 4000 g. (%)	4 (1,7)	13 (9,7)	17 (4,7)	0.001	*0,16 (0,05-0,53)*
Blood loss ≥ 1000 ml (%)	5 (2,2)	12 (8,9)	17 (4,7)	0.004	*0,23 (0,08-0,67)*

*ACOG and National Institute of Child Health and Human Development

Conclusions. Our data show that we should expect different outcomes based on indications for assisted vaginal birth. Vacuum delivery performed by experienced operators result in safe outcomes for the mother and the baby. Abdominal palpation is scarcely used, the ultrasound assessment may be helpful for new operators.

Is it possible to predict the success of TOLAC? *(Winner of the SIMP Award, in memory of Professor Carlo Romanini)*

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DOI: 10.36129/jog.2022.S88

Objective. The aim of this study was to determine antenatal factors, which may predict vaginal birth and uterine defects after a ceasarean section.

Materials and Methods. His retrospective observational study conducted at Policlinico Casilino from June 2019 to July 2022 using data obtained from medical records, included women with a single pregnancy with cephalic presentation at gestational age of > 35 weeks who had previously undergone one lower segment cesarean delivery and who had attempted trial of labor after cesarean delivery (TOLAC).

Results. Our study enrolled 360 women who obtained the TOLAC consensus. 208 (57.78%) had a successful vaginal birth. A total of 7 (1.94%) uterine dehiscences and no uterine ruptures were registrated. A successful vaginal birth was significantly correlated with lower (Body-Mass Index) BMI (23.23 *vs* 25.89, p < 0.0001); previous vaginal birth (13.46% *vs* 3.29% p = 0.0005) and fewer interpregnancy months interval (55.7 *vs* 66, p = 0.01) while a decreased VBAC rate was observed in those with induction of labour (37.02% *vs* 50%, p = 0.02) and recurrent indication (arrest disorder, cephalopelvic disproportion) of prior ceasarean section (25.48% *vs* 36.18%, p = 0.0291). Uterine dehiscence was significantly correlated with a lower uterine segment (LUS) thickness (1.7 *vs* 2.2, p = 0.02), lower full LUS thickness (3.3 *vs* 3.7, p = 0.0043) and higher neonatal weight (3701 *vs* 3263, p = 0.0001). Neonatal weight results the only independent variable for the uterine dehiscence (AUC 0.917), thus the independent variables regarding the success of vaginal birth include lower BMI and previous vaginal birth. Furthermore, a logistic regression analysis was performed, as described on **Table 1**.

Conclusions. These significant variables could be used to accurately predict individual success rates of TOLAC during prenatal counselling.

Table 1.

	ROC	p	OR	AUC
Vaginal Birth				
BMI	cut off ≤23.2335	**<.0001**	3,30	0.645
Previous vaginal birth		**0.0005**	4.57	0.551
Induction of labour		**0.02**	0.5878	0.565
Interval between labours (months)	cut off <40.77	**0.009**	1,81	0.569
Reccurent indication of prior C-section	0.603	**0.0291**	0.554	0.501 to 0.606
Dehiscence				
LUS thickness	cut off ≤1.8	**0.02**	7,95	0.713
Full LUS thickness	cut off ≤3.5	**0.01**	6.80	0.723
Weight of birth	cut off >3440	**0.0001**	28	0.828

Shoulder dystocia: a preventable obstetric emergency?

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DOI: 10.36129/jog.2022.S89

Objective. The aim of the study was to evaluate the maternal risk factors and the neonatal outcomes in women whose delivery was complicated by shoulder dystocia.

Materials and Methods. We retrospectively reviewed data charts of all deliveries complicated with shoulder dystocia from January 2019 to December 2021 in our hospital. We analysed prepartum maternal risk factors (diabetes and BMI > 30), intrapartum risk factors (operative vaginal delivery, induction of labour, Kristeller manoeuvre, expulsive phase lasting more than 60 minutes) and obstetrical manoeuvres used at the delivery. We also analysed the neonatal outcomes (pH, Apgar score, NICU admission, neonatal sequelae).

Results. 63 women were included in the study. Twenty (30%) did not have any risk factors, 43 (70%) had at least one risk factor while 24 had only intrapartum risks. Ten out of 63 (15.8%) neonates experienced brachial plexus palsy and 11 were admitted to NICU (17.4%). Of these 11 newborns, 3 deliveries (27%) had no prenatal risk factor, 8 (73%) had at least one and 3 had intrapartum risk factors. Eight (72%) of these newborns were delivered with the Jacquemier manoeuvre. Three neonates out of the 20 deliveries without risk factors were admitted to NICU (15%) as well as 3 out of the 24 with intrapartum risk factors (12.5%) and 1 out of the 9 with intrapartum and prepartum risk factors (11.1%).

Conclusions. There are still a considerable portion of deliveries which are complicated by shoulder dystocia that cannot be foreseen. In order to manage these events staff must be trained to face emergency settings with simulations and updates.

Maternal hemodynamic evaluation in anemic patients: a useful tool to possibly prevent maternal-fetal complications

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DOI: 10.36129/jog.2022.S90

Objective. During pregnancy there is a physiological reduction in the hemoglobin value which is the expression of a discrepant increase between the plasma volume and the increase in erythrocyte mass. The purpose of the study was to evaluate the maternal haemodynamics of anemic patients, highlighting any correlations with adverse maternal-fetal outcomes.
Materials and Methods. We enrolled 78 anemic patients, with Hb levels below 10.5 g/dL, who underwent a non-invasive hemodynamic evaluation using USCOM at hospital admission. The different parameters were compared with a control group characterized by normal Hb.
Results. Anemic patients showed higher HR, TFc, INO, CO and lower RVS, CI than patients with normal values of Hb, as a sign of hyperdynamic circulation (**Table 1**); while Delivery of Oxygen was the same in both groups.
Conclusions. Anemic patients have an hyperdynamic hemodynamics characterized by higher cardiac output and lower systemic vascular resistances, guaranteeing a delivery of oxygen comparable to controls despite the low hemoglobin levels. Furthermore, shear stress associated with hyperdynamic circulation could favor endothelial damage, explaining the worsening of maternal-neonatal outcomes, in particular the risk of postpartum hemorrhage.

Table 1.

	Hb <10,5 g/dL (n=78)	Hb>10,5 g/dL (n=78)	p-value
Gestational Age	39,2 ± 1,9	38,9 ± 1,5	0,3
DO_2	1006,5 ± 443,3	994,5 ± 404,5	0,87
HR	92,8 ± 17,7	85,1 ± 12,8	0,002
CO	8,7 ± 2,4	7,6 ± 1,2	<0,01
RVS	830,8 ± 158,7	924,5 ± 149,2	<0,01
CI	3,9 ± 1,1	4,3 ± 0,7	0,007
TFc	389,5 ± 34,5	375,3 ± 29,9	0,007
INO	1,7 ± 0,4	1,4 ± 0,2	0,0001
PAS	110,2 ± 12,5	114,1 ± 8,9	0,03
PAD	69,7 ± 9,9	71,6 ± 7,4	0,176
SV	86,2 ± 20,1	91,2 ± 15,6	0,08
PKR	22,8 ± 11,7	20 ± 6,4	0,07

Maternal hemodynamic in twin pregnancy at 20-24 weeks as a predictor of IUGR and gestational hypertensive disorders: a prospective study

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DOI: 10.36129/jog.2022.S91

Objective. Twin pregnancy is a risk factor for gestational hypertensive disorders (GHD) and intrauterine growth restriction (IUGR). Cardiac function assessment plays a key role in identification of a singleton pregnancy at risk of developing GHD or IUGR. Maternal hemodynamics show pronounced changes in twin pregnancies. The aim of our study was to evaluate the predictive capacity of hemodynamic assessment to identify twin pregnancies at risk. We compared maternal hemodynamics at 20-24 weeks' gestation between complicated and uncomplicated twin pregnancies also taking into consideration chorionicity.

Materials and Methods. We enrolled 63 monochorionic (MC) and 55 dichorionic (DC) twin pregnancies and we assessed maternal hemodynamics. All cases were followed up until delivery in order to identify patients who would develop selective IUGR, GHD or IUGR of both twins. ANOVA test was used for pairwise comparison. ROC analysis was used to test predictive capacity.

Results. MC who developed sIUGR did not show any difference with an uncomplicated pregnancy. On the contrary, pregnancy with GHD/IUGR showed higher SVR, hypodynamic circulation and reduced LVEDV. SVR > 1123 d.s.cm^{-5} (AUC 0.88), PKR > 19 (AUC 0.86) and LVEDV £ 163 mm^3 (AUC 0.84) showed a significant predictive capacity to identify MC who would develop GHD/IUGR.

We did not show any differences in cardiac function between complicated and uncomplicated DC pregnancies.

Conclusions. MC twins showed a significant cardiovascular effort to sustain the pregnancy request. Pregnancies with reduced preload, high resistance and hypodynamic circulation have a higher risk of developing GHD/IUGR and the evaluation of maternal cardiac function shows significant predictive capacity.

Monochorionic				
	No complications N: 40	sIUGR N: 15	GHD/IUGR N: 8	P value
SVR	863.65 (189.62)	916.73 (173.62)	1154.25 (161.37)	<0.01[a,b]
CO	8.31 (1.71)	8.00 (1.93)	6.94 (1.23)	0.12
INO	2.04 (0.42)	2.06 (0.68)	1.86 (0.39)	0.61
PKR	18.97 (6.68)	20.73 (6.80)	30.12 (7.95)	<0.001[a,b]
LVEDV	165.70 (18.39)	159.27 (20.73)	143.12 (13.99)	<0.01[a]
Dichorionic				
	No complications N: 35	sIUGR N: 12	GHD/IUGR N: 8	P value
SVR	936.60 (165.99)	1020.25 (92.43)	1040.75 (165.66)	0.11
CO	7.51 (1.41)	6.92 (0.87)	6.72 (1.14)	0.18
INO	1.86 (0.34)	1.81 (0.24)	1.71 (0.29)	0.49
PKR	20.66 (5.75)	21.42 (2.87)	22.50 (4.87)	0.64
LVEDV	168.77 (19.15)	168.75 (14.59)	157.25 (20.67)	0.27

Delivery mode in women with congenital fetal heart disease (CHD)

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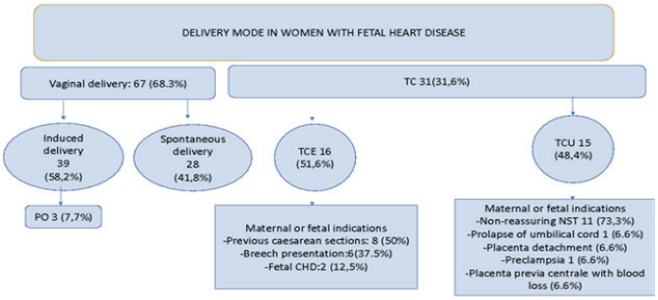
DOI: 10.36129/jog.2022.S92

Objective. The aim of this study is to evaluate the impact of delivery mode on neonatal birth outcomes in women with fetal CHD.

Materials and Methods. We retrospectively reviewed the data charts of patients who delivered in our Hospital between 1st January 2019 to June 2022 with antenatal diagnosis of CHD. Data were collected from obstetrical ward databases and delivery room records. We analyzed maternal characteristics, CHD type, delivery mode as well as fetal outcomes in terms of mean weight, mean pH, Apgar scores and intubated fetuses at birth.

Results. 98 women were included with prenatal diagnosis of TGA (10/98 10.2%%), TOF (8/98 8.1%), CoA (9/98 9.1%) pulmonary and aortic valve stenosis (6/98 6.1%), right or left heart hypoplasia (9/98 9.1%), other CHDs of lower frequency (56/98 57.1%). Vaginal deliveries accounted for 67 (68.3%) of the total. Spontaneous labor with normal vaginal delivery was 41.8% (28/98). In 39 (58.2%) women labor was induced with only 3 cases of operative vaginal delivery (7%). The rate of cesarean deliveries was 31 (31.6%): 15 (48.4%) urgent and 16 (51.6%) elective. Of 98 neonates 5 (5.10%) were intubated at birth, 2 born by vaginal delivery, 2 by urgent cesarean, and 1 by elective cesarean. Neonatal mortality rate was 3.06%: 1 TGA, 1 CHD associated with malformative syndrome and 1 left heart hypoplasia.



Conclusions. Safe vaginal delivery can also be obtained in women with prenatal diagnosis of severe CHD with no effect on neonatal outcomes.

Obstetric outcome in pregnant women with heart disease, a tertiary care center hospital experience in light of ESC guidelines

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DOI: 10.36129/jog.2022.S93

Objective. Women with heart disease have an increased risk of obstetric and fetal events, which peaks during labor. The aim of this study was to evaluate pregnancy outcomes of cardiopathic patients followed in a tertiary care hospital in terms of delivery outcome (mode of delivery, rate of cesarean sections and postpartum bleeding) compared to a control group.

Materials and Methods. A retrospective study was conducted at Careggi University Hospital between 2019 and 2021, comparing a cohort of 157 cardiopathic patients (218 pregnancies) to 2662 controls delivered in the same period.

Results. Our population was divided according to mWHO classification of maternal cardiovascular risk: 73 class I, 51 class II, 24 class II-III, 8 class III, 1 class IV. Of 218 pregnancies, 150 were candidated for vaginal delivery, which was successful in 116 patients (77.3%). Although the rate of medical induction resulted similar between the groups, the indication for induction in most of the study group (66.6%) was the cardiac disease alone. Rate of emergency cesarean sections of cardiopathic patients was not higher compared to the control group and were all performed following obstetrical indications. Elective cesarean section was performed for heart disease in 20 cases (29.4%). The difference between the rate of elective cesarean section for other indications was not significant. No differences were found in the rate of postpartum haemorrage.

Conclusions. Our data confirm that vaginal delivery is affordable in most cases and suggest that a close follow up in a tertiary hospital allow similar outcomes to that of the general population to be reached.

General or neuraxial anesthesia: what is best choice for red code cesarean section?

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DOI: 10.36129/jog.2022.S94

Objective. Red code (RC) cesarean section (CS) is an obstetrics emergency performed for immediate risk for the life of the woman or the fetus. We have assessed the role of anesthesia on obstetrics and perinatal outcomes in patients who underwent RC CS.

Materials and Methods. A multicenter retrospective cohort study in four maternity units including all cases of RC CS between January 2018 and December 2021. We collected medical and surgical reports, intrapartum fetal heart rate monitoring. Patients who underwent analgesia during labor were excluded. Outcomes were related to the anesthesiology technique utilized (general anesthesia - GenA *versus* neuraxial anesthesia - NeuraxA). Retrospective audits were performed by an expert obstetric team for assessment of appropriateness of indications for RC CS.

Results. From a total of 168 RC CS (3.5% of deliveries), 122 (72.4 %) cases were included. GenA (45.1%) was compared with NeuraxA (54.9%). While GenA was associated with a shorter decision-to-delivery interval (DDI) (p = 0.028) and better umbilical artery (UA) pH (p = 0.005), it was related to a greater blood loss (p = 0.006), UA base excess (BE) < -16 mmol/L (p = 0.013) and need for neonate reanimation (p = 0.028).

Moreover, on multivariate analysis, only appropriateness of indication for RC CS (p = 0.003) and GenA (p = 0.008) were independently related to a worse neonatal UA BE, while DDI was not significant (p = 0.53).

Conclusions. NeuraxA seems the preferential type of anesthesia during CR CS, because GenA is related to worse perinatal outcomes in terms of UA BE and neonatal reanimation and greater maternal blood loss.

	NEURAXIAL ANESTHESIA	GENERAL ANESTHESIA	MISSING	P-VALUE
Number of cases	67 (54.9%)	55 (45.1%)	0	/
Maternal anamnesis				
Maternal Age	32.49 (SD ± 5.8)	33.2 (SD ± 5.7)	0	0.503
BMI at delivery	28.2 (SD ± 4.3)	28.0 (SD ± 4.2)	18	0.844
Previous CS	6	10	4	0.133
Cefalic presentation	57	47	4	0.407
Comorblity	18	11	0	0.375
Gestational age at delivery	38.5 (SD ± 2.3)	37.4 (SD ± 4.7)	0	0.110
CS indications				
Sentinel event	25	24	4	0.478
Appropriateness	41	45	4	0.014
Timing				
Decision-to-incision interval (min)	19.08 (SD ± 11.6)	15.78 (SD ± 9.0)	5	0.089
Decision-to-delivery interval (min)	24.03 (SD ± 12.4)	19.31 (SD ± 10.7)	4	0.028
Maternal outcomes				
Blood loss (mL)	453.73 (SD ± 280.7)	725.47 (SD ± 726.4)	6	0.006
Blood trasfusion	0	3	4	0.053
Surgical complications	8	4	4	0.389
Neonatal outcomes				
UA pH	7.14 (SD ± 0.15)	7.22 (SD ± 0.16)	7	0.005
UA BE < 12	6	11	7	0.084
UA BE < 16	1	7	7	0.013
UA lactates > 7	11	11	11	0.601
Apgar score at 5min < 7	13	11	4	0.934
Neonatal reanimation	17	24	5	0.028
Neonatal inubation	10	12	5	0.301
Neonatal ICU access	9	15	4	0.056
Hypothermia	2	3	5	0.480

Trial of labor after caesarean section (TOLAC): the role of an early counselling in the choice of the mode of delivery

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DOI: 10.36129/jog.2022.S95

Objective. The Caesarean section (CS) rate and consequent short- and long-term complications especially in case of elective repeated CS (ERCS) continues to rise globally, therefore, in absence of contraindications, TOLAC should be proposed. Our aim was to evaluate possible factors influencing maternal choice of the mode of delivery and to investigate possible strategies to improve the TOLAC rate.

Materials and Methods. Monocentric retrospective cohort study on 482 women with one or more previous CS or myomectomy, delivered at Careggi University Hospital, Florence in 2021. We selected, as the study population, 301 women with only one previous CS eligible to TOLAC according to Italian guidelines.

Results. Out of 301 cases, 120 (40%) chose TOLAC. The success rate of vaginal birth after caesarean (VBAC) and maternal and neonatal outcomes were consistent with the literature. Comparing TOLAC *vs* ERCS group, no differences were found in terms of maternal characteristics or pregnancy complications influencing women's delivery choice, except for a history of previous vaginal delivery or VBAC. However, all women in the TOLAC group received an adequate counselling, whereas in the ERCS group only 62% were informed. Furthermore, the median gestational age at the first counselling was 34 weeks, even though patients informed earlier were more likely to prefer TOLAC to ERCS.

Conclusions. Despite the known advantages of VBAC, education and awareness on TOLAC is still poor. In order to reduce the CS rate, fully comprehensive and accurate counselling should be offered early during pregnancy and a dedicated team should be guaranteed for a standardized medical practice.

Maternal and neonatal outcomes based on appropriateness of indication and timing of surgery in red code caesarean section: a multicentre retrospective study

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DOI: 10.36129/jog.2022.S96

Objective. A red code (RC) cesarean section (CS) is an emergency for maternal and/or fetal life. We evaluated maternal and neonatal outcomes in a series of RC CS, in relation to the level of maternal unit, indications and surgical times.

Materials and Methods. Multicentre retrospective study in 2 second-level university hospitals and 2 first-level community hospitals on all women who underwent RC CS between 2018 and 2021. An independent team of experts performed retrospective audits to assess appropriateness of indications, procedures and outcomes.

Results. Among the 25065 deliveries, 4783 were CS (19.1%), 168 of which (3.5%) were RC. The most frequent indication was non-reassuring fetal heart rate tracing (41.7%). Two indications were independently associated with worse perinatal outcomes: umbilical artery lactate > 7 mmol/L (P 0.023) and base excess (BE) ≥ 16 mmol/L (p = 0.016). Rates of appropriate indications were higher in the second-level hospitals (80.2% *vs* 65%, p = 0.036), as were rates of neonatal intubation (p = 0.001) and neonatal ICU admission (p = 0.001). Appropriate indications for RC CS correlated with higher maternal blood loss (p = 0.02), lactate values > 7 mmol/L (p = 0.001) and neonatal resuscitation (p = 0.02). After correcting for the appropriateness of indications, the time between decision and delivery (DDI-mean 21.0 minutes) was not associated with worse neonatal outcomes.

Conclusions. The DDI is not significantly associated with neonatal outcomes, as opposed to the appropriateness, which is associated with worse outcomes. First level maternal units guarantee safety comparable to second-level, but with lower rates of appropriate indications.

	APPROPRIATES	INAPPROPRIATES	MISSING	P-VALUE
Number of cases	119 (70.8%)	45 (26.8%)	4 (2.4%)	/
Maternal anamnesis				
Second-level hospitals	65	16	4	0.036
Maternal Age	32.8 (SE 0.5)	33.3 (SE 0.8)	4	0.599
BMI at delivery	28.8 (SE 0.5)	27.5 (SE 0.7)	22	0.168
Previous CS	14	8	4	0.315
Comorbility	25	10	4	0.834
Gestational age < 37	27	6	4	0.274
CS indications				
Fetal heart rate alterations	44	24	4	0.075
Sentinel event	49	13	4	0.206
Timing				
Decision-to-incision interval (min)	15.4 (SE 0.9)	20.4 (SE 1.7)	5	0.006
Decision-to-delivery interval (min)	19.4 (SE 1.0)	25.7 (SE 1.8)	4	0.002
Maternal outcomes				
Hospitalization post-CS (days)	4.6 (SE 0.3)	4.5 (SE 0.4)	6	0.900
Blood loss (mL)	636.3 (SE 54.2)	418.9 (SE 44.2)	6	0.019
Blood transfusion	9	0	5	0.064
Surgical complications	2	2	5	0.305
Neonatal outcomes				
UA pH	7.160 (SE 0.015)	7.241 (SE 0.018)	11	0.002
UA BE > -12	14	2	9	0.2
UA Lactates > 7	39	4	16	0.001
UA pO_2 (mmHg)	19.4 (SE 1.4)	16.5 (SE 1.6)	34	0.259
UA pCO_2 (mmHg)	60.6 (SE 2.1)	57.2 (SE 2.5)	20	0.365
Apgar score at 5 min < 7	25	5	4	0.178
Neonatal reanimation	45	7	5	0.008
Neonatal intubation	21	3	5	0.086
Neonatal ICU access	28	2	4	0.030
Hypothermia	6	1	5	0.675

Qualitative research for the analysis and evaluation of obstetrical assistance to immigrant women in labor and delivery: the woman's point of view

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DOI: 10.36129/jog.2022.S97

Objective. To analyse, through the experience of the women interviewed, the impact that the migratory experience has had on them in the context of pregnancy and childbirth, and the quality of the obstetric care received during labor and childbirth.
Materials and Methods. For this study, a qualitative methodology was adopted known as Cohen's phenomenology. The study was conducted in the period between January 2022 - March 2022 recruiting a sample of 11 immigrant women at the Policlinico of Bari and the Società Cooperativa Sociale OASI 2 "San Francesco Onlus".
Results. From the analysis of the interviews, five main themes emerged: "Migration", "Memory", "Assistance to immigrant women", "The language barrier", "Loneliness". The stories uncovered the basic needs that bring every woman together during pregnancy and childbirth and the cultural aspects, bringing out the impact of migratory trauma. The women reported that they had received good obstetric care, defining the image of a midwife as the one who "stands beside". However, several difficulties emerged, from the language barrier to loneliness, burdened by the restrictions imposed by the COVID-19 pandemic.
Conclusions. It emerged from the interviews that the preparation of the midwife in the transcultural field is essential in order to be able to provide appropriate and personalized assistance. The goal of health workers is to create a mental attitude of openness towards confrontation and knowledge, and suspension from judgment. It is important to approach the life of immigrant women and tear down barriers, embracing the possibility of other narratives of body, health and disease.

MAIN THEMES	SUB-THEMES
1. Migration	1.1. "My history…is too much…is no good"
2. Memory	2.1. Attitude of closure vs attitude of openness
	2.2. Memory of the birth
	2.3. Memory of the culture
3. Assistance to immigrant women	3.1. Obstetrical assistance in Italy
	3.2. Country of origin vs country of arrival
	3.3. "They are not…God"
4. The language barrier	4.1. Cultural mediator
	4.2. Language skills of health professionals
5. Loneliness	5.1. Distance from the family
	5.2. Mother-son relationship
	5.3. Host community

Ultrasound assessment of the head flexion in occiput posterior fetuses and prediction of rotation to occiput anterior

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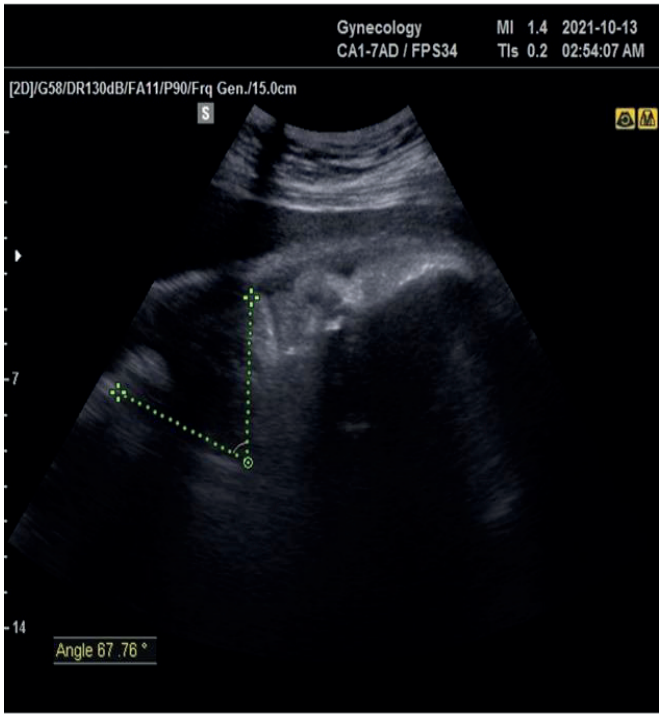
DOI: 10.36129/jog.2022.S98

Objective. To evaluate the relationship between the fetal attitude in fetuses in occiput posterior (OP) at full cervical dilatation and the chance of rotation to occiput anterior (OA) at birth.
Materials and Methods. Single centre prospective observational study including women with uncomplicated labour and OP position at full cervical dilatation. Eligible cases were submitted to intrapartum ultrasound to confirm the OP and to evaluate the degree of flexion (CCA). At time of delivery, occiput rotation was checked. The primary outcome was delivery in OA position. The secondary outcome was to evaluate the reproducibility of the CCA measurement.
Results. 73 women were included (vaginal delivery was recorded in 80.8%). Rotation to OA position at birth was associated with narrower CCA compared to the cases with persistent OP (44+20 *vs* 62 ± 22 degrees, $p < 0.01$). The optimal CCA cut-off value discriminating between cases that rotated *versus* those that did not was 51.5 degrees. This was associated with: 67.3% sensitivity, 79.2% specificity, 97.5% PPV and 48.5% NPV. ICC analysis showed excellent intra- and inter-observer reproducibility of the CCA (0.963, 95%CI 0.910-0.985, $p < 0.01$ and 0.887, 95%CI 0.755-0.948, $p < 0.01$).
Conclusions. Within an unselected cohort of women with fetus in OP position at full cervical dilatation the CCA is associated with an increased chance of rotation to OA position at birth. High intra- and inter-observer agreement of the CCA measurement is demonstrated.



The efficacy of non clinical interventions to reduce the cesarean section rate

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DOI: 10.36129/jog.2022.S99

Objective. Cesarean delivery (CD) could be complicated by several morbidities such as higher risk of postpartum cardiac arrest, ematoma, hysterectomy, major puerperal infection, anesthetic complications, venous thromboembolism and hemorrhage requiring hysterectomy. Moreover, the risk of severe maternal morbidity is generally higher in women with an unplanned cesarean birth during labor than in those with a scheduled prelabor cesarean birth. We aimed to evaluate the effect of a composite non-clinical intervention to reduce the CD rate in our Clinic.

Materials and Methods. We retrospectively reviewed the delivery charts in our center from January 2021 to April 2022. We collected maternal and neonatal data until the delivery.

Results. During the pre-intervention period, the CD rate was 24%, and after the intervention started, it was 18% ($p < 0.05$). The cases with an Apgar score < 7 had a significantly lower birthweight than the controls (2090.48 ± 918.09 *vs* 3110.21 ± 372.69, $p < 0.05$). No severe adverse outcomes were observed after the implementation of the non-clinical interventions.

Conclusions. Non-clinical interventions can achieve a safe reduction of CD. However, greater effort should be made to more accurately identify prelabour high-risk fetuses such as small for gestational age fetuses to allow adequate labor management.

Causes of stillbirth in Emilia-Romagna: a prospective cohort study

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DOI: 10.36129/jog.2022.S100

Objective. This study aims to assess the frequency of Stillbirth (SB) causes, in preterm and term pregnancy. Their identification could help to reduce SB rates and improve perinatal outcomes in subsequent pregnancies.

Materials and Methods. We conducted a prospective cohort study in Emilia-Romagna. For each SB (≥ 22 weeks of gestation or ≥ 500 g) between January 2014 to June 2021 (n = 854), the same diagnostic workup was performed and a clinical record was completed. Causes of perinatal death were classified according to a modified ReCoDe classification in eight subgroups (**Table 1**), then subdivided in early preterm, late preterm and at term SB.

Results. Out of 854 SB, 601 (70.4%) occurred preterm, 253 (29.6%) at term. Total SB rate was 3.6 per 1000 births (854/232.907). Overall, placental pathology (31.4%), fetal pathology (16.3%) and unexplained causes (21.4%) were the most represented causes. Placental pathology and fetal pathology were more frequent in preterm groups, while infections were more frequent in the early preterm group. Umbilical cord accidents were higher at term *versus* both preterm groups. Finally, unexplained stillbirth had a significant rise at term (**Table 1**). Moreover, late IUGR were significantly represented in SB at term (n = 13, 5%).

Conclusions. Placental pathology is the principal cause in every group while maternal disorders are less impacting, possibly due to antenatal care. However, fetal pathology at term is still incident, namely for suboptimal diagnosis/management of late IUGR fetuses. One in four of term SB remains unexplained.

Table 1. *Causes of death according to gestational age classes (< 32 weeks, 33-36 weeks, > 37 weeks).*

Causes of death	GA ≤ 32 (N=401)	GA 33-36 (N=200)	GA ≥ 37 (N=253)	P value
Fetal pathology	72 (17.9)	43 (21.5)	24 (9.5)	**<0.001**
Umbilical cord accidents	30 (7.5)	25 (12.5)	56 (22.1)	**<0.001**
Placental pathology	131 (32.7)	77 (38.5)	60 (23.7)	**0.003**
Unexplained	77 (19.2)	37 (18.5)	69 (27.3)	**0.03**
Infections	52 (13.0)	10 (5.0)	23 (9.1)	**0.008**
Maternal disorders	24 (6.0)	5 (2.5)	9 (3.6)	0.10
Intrapartum asphyxia	9 (2.2)	0	5 (1.9)	0.11
Others	6 (1.5)	3 (1.5)	7 (2.7)	0.46

Impact of a lifestyle intervention on stillbirth and other adverse perinatal outcomes in a cohort of obese women *(Winner of the SIMP EUBRAIN Award, in memory of Claudio Bastia)*

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DOI: 10.36129/jog.2022.S101

Objective. Obesity is a well-known risk factor for several adverse perinatal outcomes. This study evaluates if a lifestyle intervention (LI) started early in pregnancy, has a benefit, namely in preventing stillbirth (SB).

Materials and Methods. This is a prospective cohort study including singleton obese women (BMI ≥ 30) delivered at a tertiary hospital between 2016 and 2020. A group of them was randomly referred to an *ad-hoc* clinic for LI (LI group). The program started at the 9-12th week implementing a low-glycemic index, low-saturated fat diet (total intake 1500 kcal/d), and physical activity. Follow-up was granted until delivery. The remaining received standard care (SC group) in public and private settings. Perinatal outcomes were collected. Student t-test, chi-squared test, and multivariate logistic regression were performed.

Results. A total of 14,849 deliveries occurred in the study period, and 1963 (13.2%) were considered obese. Among them, 654 (33.2%) entered the LI program. Gestational diabetes and preterm birth did not differ between groups, while severe obesity and hypertensive disorders were higher in the LI group (**Table 1**). Antepartum SB (5.1/1000) was more frequent in the SC group, in particular the SB risk increased with each class of obesity (OR 2.58, 95%CI 1.13-5.86), while it was reduced in those who received LI (OR 0.10, 95%CI 0.01-0.79). On the other hand, a low Apgar score was more frequent in the LI with respect to the SC group (p = 0.001).

Table 1. *Maternal characteristics and perinatal outcomes.*

	Standard Care (N=1309)	Lifestyle intervention (N=654)	P value
Maternal characteristics			
Mean age	**36.5 ± 5.6**	**34.8 ± 5.7**	**0.000**
Nulliparity	435 (33.2)	245 (37.5)	0.06
Country of origin			**0.005**
Italy	**686 (52.4)**	**387 (59.2)**	
Others	**623 (47.6)**	**267 (40.8)**	
Ethnicity			**0.000**
Caucasian	**709 (54.1)**	**473 (72.3)**	
African	**251 (19.1)**	**95 (14.5)**	
Maghrebian	**290 (22.1)**	**60 (9.2)**	
Others	**59 (4.5)**	**26 (4.0)**	
Low Education level (≤8 years)	673 (51.4)	353 (54.1)	0.32
Obesity classes			**0.000**
Class I	**971 (74.2)**	**381 (58.3)**	
Class II	**257 (19.6)**	**164 (25.1)**	
Class III	**81 (6.2)**	**109 (16.7)**	
Care providers			**0.000**
Public (family centers)	**960 (73.4)**	**521 (79.6)**	
Private (Gynecologist)	**349 (26.6)**	**133 (20.3)**	
Gestational Diabetes Mellitus	401 (30.6)	219 (33.5)	0.41
Gestational Hypertension	**89 (6.8)**	**70 (10.7)**	**0.000**
Preterm Birth (<37 weeks)	96 (7.3)	53 (8.1)	0.51
Perinatal Outcomes			
Birthweight	3334.8 ± 578.8	3322.4 ± 596.2	0.65
Macrosomia (>4000g)	130 (9.9)	62 (9.5)	0.37
Need for resuscitation	11 (0.8)	7 (1.1)	0.26
Apgar 5' ≤ 7	**53 (4.0)**	**35 (5.3)**	**0.001**
Stillbirth	**9 (0.7)***	**1 (0.1)#**	**0.05**

* Five cases were related to placental insufficiency, three to infections, and one to a congenital anomaly.
# Placental abruption

Conclusions. An early intervention through LI program can prevent antepartum SB among obese women. Further randomized controlled trials are required to prove this effect.

Fetal sex and external cephalic version success

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DOI: 10.36129/jog.2022.S102

Objective. This study aims to assess the role of fetal sex on the success and failure rate of the external cephalic version (ECV) in breech fetuses. Secondary outcomes were fetal presentation in labor and mode of delivery.

Materials and Methods. This cross-sectional study examined live birth certificates from 2003 through 2020 from US states and territories that implemented the 2003 revision. A total of 149,671 single pregnancies with information about ECV success or failure were included. The outcome was ECV success/failure, while the primary exposure was fetal sex. Other known factors associated with the outcome were also considered.

Results. There were 96,137 (64.23%) successful ECV procedures. After adjusting for possible confounding factors, the female sex was associated with an increased ECV failure (OR 1.08, 95%CI 1.03-1.13, $p < 0.05$). Additional significant risk factors for ECV failure were high pre-pregnancy BMI, nulliparity, and small for gestational age fetuses. Younger maternal age, black and American Indian and Alaska Native race categories were significantly protective factors against ECV failure. The prevalence of vaginal delivery in successful ECV was significantly higher in female compared to male fetuses (73.18% *vs* 70.06%, $p < 0.05$).

Conclusions. The present results found the female fetal sex to be negatively correlated to ECV success but positively correlated to a vaginal birth in the case of ECV success. These findings can potentially improve the knowledge about factors involved in the ECV procedure, allowing more informed counseling for women undergoing this procedure.

Pregnancy outcomes subsequent to stillbirth: a single tertiary-care center experience

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DOI: 10.36129/jog.2022.S103

Objective. Currently, there is little evidence to guide clinical management of pregnancies after stillbirth. Our study aims to evaluate the pregnancy outcome in women with a previous stillbirth, by applying a standardized protocol for etiologic investigations and subsequent treatment of the underlying etiology.

Materials and Methods. A retrospective cohort study on a group of 100 women with history of stillbirth was performed. All patients were followed up in their subsequent pregnancies (n = 153) in a tertiary university hospital, between 2005 and 2021. During the preconception period causes of stillbirth were investigated and a correction of modifiable risk factors was encouraged. Data about pregnancy management, obstetric complications, mode of delivery and neonatal outcomes were collected.

Results. The analysis of previous stillbirths revealed that, by using the ReCoDe classification, the most common identifiable cause of death was fetal growth restriction (21%) whereas 15.8% of stillbirth was unexplained. Out of 153 subsequent pregnancies, 131 (85.62%) resulted in live births; no cases of stillbirth recurrence occurred. The most common obstetric complication was gestational diabetes (21.4%). The mean gestational age at delivery was 38 weeks with a mean birth weight of 2886.63 g.

Conclusions. Our experience is encouraging as it reflects a good outcome in terms of live birth rates in the subsequent pregnancies, with no cases of recurrence. These results are probably due to an extensive preconception evaluation with a multidisciplinary approach, essential for improving maternal and fetal outcomes aimed at minimizing the risk of recurrence of stillbirth.

Pregnancy outcomes of subsequent pregnancies		N
Pregnancies after stillbirth *Total 153*	One pregnancy	64 (42.1%)
	Two pregnancies	25 (16.4%)
	Three or more pregnancies	11 (7.2%)
Pregnancy outcomes *Total 153*	Live birth	131 (86.27%)
	Early miscarriage	15 (9.8%)
	Late miscarriage	7 (4.57%)
Method of delivery *Total 131*	Spontaneous vaginal delivery	38 (29%)
	Vaginal delivery, Induced labor	35 (26.7%)
	Urgent C-section	17 (12.98%)
	Elective C-section	41 (31.3%)
Indication for elective C-section *Total 41*	Prior C-Section	33 (80.5%)
	Breech Presentation	3 (7.3%)
	Maternal pathology	2 (4.8%)
	Maternal request	2 (4.8%)
	Placenta previa	1 (2.4%)
2° and 3° trimester complication *Total 131*	Gestational diabetes mellitus	28 (21.4%)
	Early preterm delivery	16 (12.2%)
	Fetal growth restriction	10 (7.6%)
	Intrahepatic cholestasis of pregnancy	5 (3.8%)
	Hypertensive disorders	8 (6.1%)

Stillbirth at term: a regional prospective case-control study over the 8-year period

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DOI: 10.36129/jog.2022.S104

Objective. Intensified efforts to identify the risk factors for stillbirth (SB) are needed to reduce its rate. The aim of the study is to assess the risk factors for SB in late pregnancy.

Materials and Methods. This is a prospective case-control study conducted in Emilia-Romagna (Italy) on pregnant women at ≥ 37 weeks referred to the Obstetric Units from 2014 to 2021. The case group consisted of all cases of SB; the live births in the same period were included in the control group. We compared the information about risk factors for SB and conducted a descriptive analysis about the cause of SB according to the modified Re.CoDe. classification.

Results. From 2014 to 2021, the SB rate in Emilia-Romagna was 3.27 per 1000 births. The risk factors significantly associated with SB at term were maternal foreign origin, high education level, overweight, a previous SB, and low neonatal weight. There was no association between the two groups regarding the other risk factors analysed (**Table 1**). 26.1% of SB remained unclassified. The more frequent causes of death were placental (23.7%) and umbilical cord pathology (22.2%). Infections, foetal and maternal pathology were responsible for a smaller number of cases (9.3%, 8.9% and 3.5% respectively). The main causes in the last two categories were IUGR and diabetes (12 and 8 cases respectively).

Conclusions. Our study confirms what has already been described in literature. The detection rate of late IUGR and the management of pregnancy with diabetes, overweight and a previous SB need to be improved to prevent SB at term.

Table 1.

	Stillbirths		Live births				
	257		246177				
Risk factors for stillbirth	**N°**	**%**	**N°**	**%**	**RR**	**95% CI**	**p value**
Maternal age (years)							
<35	162	63,0%	161668	65.7%		Reference	
≥35	94	36,6%	84257	34,2%	1.07	0.91-1.26	0.4076
Missing	1	0,4%	252	0,1%			
Education (years)							
≤8	52	20,2%	83657	34,0%		Reference	
>8	174	67,7%	162520	66,0%	1.17	1.09-1.25	0,0005
Missing	257	100,0%	246177	100,0%			
Country of origin							
Italy	136	52,9%	156443	63,5%		Reference	
Others	121	47,1%	88801	36,1%	1.30	1.14-1.48	0,0003
Missing	0	0,0%	933	0,4%			
Smoking habit							
No	210	81,7%	204784	83,2%		Reference	
Yes	36	14,0%	36501	14,8%	0.97	0.72-1.31	0,8290
Missing	11	4,3%	4892	2,0%			
Parity							
0	123	47,9%	122832	49,9%		Reference	
≥1	133	51,8%	123345	50,1%	1.04	0.92-1.17	0,5543
Missing	1	0,4%	0	0%			
Previous SB							
No	125	94,0%	123345	98,5%		Reference	
Yes	8	6,0%	1822	1,5%	4.13	2.11-8.10	<0,0001
Type of pregnancy							
Single	250	97,3%	242544	98,5%			
Multiple	5	1,9%	3633	1,5%	1.33	0.56-3.17	0,5210
Missing	2	0,8%	0	0%			
In vitro fertilization pregnancy							
No	251	97,7%	237015	96,3%		Reference	
Yes	6	2,3%	6263	2,5%	0.91	0.41-2.00	0,8083
Missing	0	0,0%	2899	1,2%			
Pre-pregnancy BMI							
<25	155	60,3%	172479	70,1%		Reference	
≥25	82	31,9%	69462	28,2%	1.21	1.01-1.44	0,0452
Missing	20	7,8%	4236	1,7%			
Gestational weight gain (IOM rec.)							
Adequate	78	35,0%	93212	44,3%		Reference	
Inadequate	115	51,6%	112955	53,6%	1.09	0.97-1.22	0,1807
Missing	30	13,5%	4450	2,1%			
Birthweight centile (INeS Chart)							
SGA	48	18,7%	21105	8,6%	2.14	1.66-2.57	<0,0001
AGA	187	72,8%	199501	81,0%		Reference	
LGA	15	5,8%	25567	10,4%	0.65	0.40-1.06	0.0782
Missing	7	2,7%	4	0%			

Is CTG after term useful to avoid stillbirths?

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DOI: 10.36129/jog.2022.S105

Objective. To establish a possible link between intrauterine fetal death in fetus > 36 weeks in low risk pregnancies and the use of antepartum CTG.
To evaluate the correct timing of first access to GAT (ambulatory for full-term pregnancy) for patients with a low-risk pregnancy (currently at about 37-38 weeks after telephone evaluation).
To assess medical checks (at present at 40 week+1 day and 41 week+1 day with eco office TA and CTG) and timing of induction of labor after term.
Materials and Methods. We selected all patients with a low-risk pregnancy afferent to the Gynecology and Obstetrics Department of the University of Chieti, from 1st June 2018 to 31st August 2022 from 37-38 weeks of pregnancy. After a first check at 38 week we planned a medical check at 40 week+1 day and 41 week+1 day with eco office TA and CTG. Then from 1st June 2018 to 31st August 2022 patients were selected from hospital discharge records using Code v271 (stillborn). Women with low risk pregnancy who received a diagnosis of intrauterine fetal death after 36 weeks were included.
Results. 5103 Deliveries, 33 stillborn (0.64%), 9 over 36 weeks (27%), no one after 40 weeks, only 6 with no comorbidities (18%).
Conclusions. Retrospectively we observed that intrauterine fetal death happened for the majority of cases in women who had not logged in to GAT before 36 weeks of pregnancy.
Should we anticipate GAT access? Are two antepartum CTG in low-risk pregnancies enough for fetal well-being surveillance? We need to evaluate if a change in management is required.

Endouterine fetal death and its impact on the living of the woman and of the couple: a phenomenological study

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DOI: 10.36129/jog.2022.S106

Objective. Stillbirth affects nearly 2 million babies every year. According to the major scientific societies, fetal intrauterine death is the death of a fetus beyond 22 weeks of gestation during pregnancy or childbirth. The aim of the study is to analyze the impact of the event on the experience of the couple by analyzing any psycho-emotional and social repercussions and the relation with the COVID-19 pandemic.

Materials and Methods. A qualitative survey, conducted with phenomenological methodology according to Cohen. The study focuses on individual, semi-structured interviews administered to a sample of ten women with an intrauterine fetal death between January 2020 and September 2021 who gave birth at the U.O.C of Obstetrics and Gynecology of the A.O.U.C Policlinico di Bari.

Results. Four main themes emerged from the analysis of the interviews: "memory", "bereavement", "healthcare workers" and "change". Afterwards thirteen sub-themes were extrapolated and analyzed as can be seen in the table (**Table 1**).

Conclusions. It emerged that post-loss bereavement has an impact on many aspects of the future life of women and couples that does not end at the time of discharge from the hospital. Greater awareness is needed on the subject for women, operators and those around them; more information and training, both human and theoretical. It is essential to live this experience with your partner as injured parties in equal measure and this should always be possible, even during a pandemic like the one caused by COVID-19. The couple should be psychologically supported throughout the bereavement process starting from hospitalization.

Table 1.

THEMES	SUB-THEMES
1. THE MEMORY	1.1. Everything was fine
	1.2. The belly: a safe place?
	1.3. Childbirth: meeting or rejection?
	1.4. Covid and loneliness
2. THE BEREAVEMENT	2.1. The pain belongs to everyone
	2.2. Sine causa
	2.3. And the psychologist?
3. HEALTHCARE WORKERS	3.1. Communication and management
	3.2. Training
	3.3. Differences in treatment
4. THE CHANGE	4.1. The woman from before will never come back
	4.2. The relationship with the partner
	4.3. The context

Follow up of PAS (placenta accreta spectrum) disorders treated with conservative management

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DOI: 10.36129/jog.2022.S107

Objective. PAS consists of several grades of abnormal myometrium invasion. The incidence is constantly increasing and is nowadays a major cause of peri-partum hysterectomy with related maternal morbidity. Recently our standard strategy has become a conservative surgery with the aim of reducing short and long-term complications. The aim of the study was to estimate the time of reabsorption of the placental residue left in the uterus and long-term follow-up.

Materials and Methods. A prospective monocentric study on 15 confirmed PAS enrolled from 2019 to 2022 at Careggi University Hospital, Florence, who underwent conservative surgery with placental residue left in the uterus. Follow-up consisted of ultrasound or magnetic resonance imaging until complete reabsorption.

Results. The average age was 40.3 years and 50.3% had performed an *in vitro* fertilization (IVF).

The major risk factor for PAS resulted placenta previa (87%). 27% had undergone a previous caesarean section and 67% other uterine surgery.

Only two patients underwent a delayed hysterectomy.

In three cases embolization was required for haemorrhage. Four patients showed infective complications, solved with antibiotics.

The range time of reabsorption of the residue was 21-150 days (mean 93 days) proportional to the starting size and to the grade of PAS.

Conclusions. Our study confirms a low incidence of major complications in PAS treated with conservative surgery. Clinical and radiological follow-up is effective for management and identifies the onset of complications early on. The time of reabsorption is reasonable and well tolerated by patients. Further studies are necessary to support this post-partum management and to find the best post-operative follow-up.

Cases	Starting size of residue (mm)	Estimated Blood Loss (mL)	Embolization	Blood transfusion (units)	Timing of imaging	Timing of reabsorption (days)	Complications	Type of complication
1	70	400	No	0	monthly MRI and US	150	None	-
2	35	2300	No	2	monthly MRI and US	60	Yes	fever, no major complications
3	41	800	No	0	monthly US	30	None	-
4	20	1500	No	0	missing data	missing data	Yes	fever, no major complications
5	40	300	No	0	every 2 months, US and MRI	90	None	-
6	50	2200	Yes	0	monthly US	not applicable	Yes	delayed hysterectomy due to fever and anemia
7	65	1500	No	0	monthly MRI	not applicable	Yes	delayed hysterectomy due to fever, hematuria and anemia
8	40	1200	No	0	monthly MRI and US	130	None	-
9	20	700	No	0	missing data	missing data	None	-
10	65	2000	Yes	3	every 2 month, US and MRI	150	Yes	fever, no major complications
11	40	600	No	0	monthly MRI and US	ongoing	None	-
12	30	400	No	0	missing data	missing data	None	-
13	20	1050	No	0	every 2 month, US	ongoing	None	-
14	20	1700	No	0	every 2 month, US	120	None	-
15	10	2500	Yes	2	monthly US	21	None	-

Placental expression of Tryptophan degradation enzymes and Angiotensin (1-7) in physiological pregnancies delivered at term

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DOI: 10.36129/jog.2022.S108

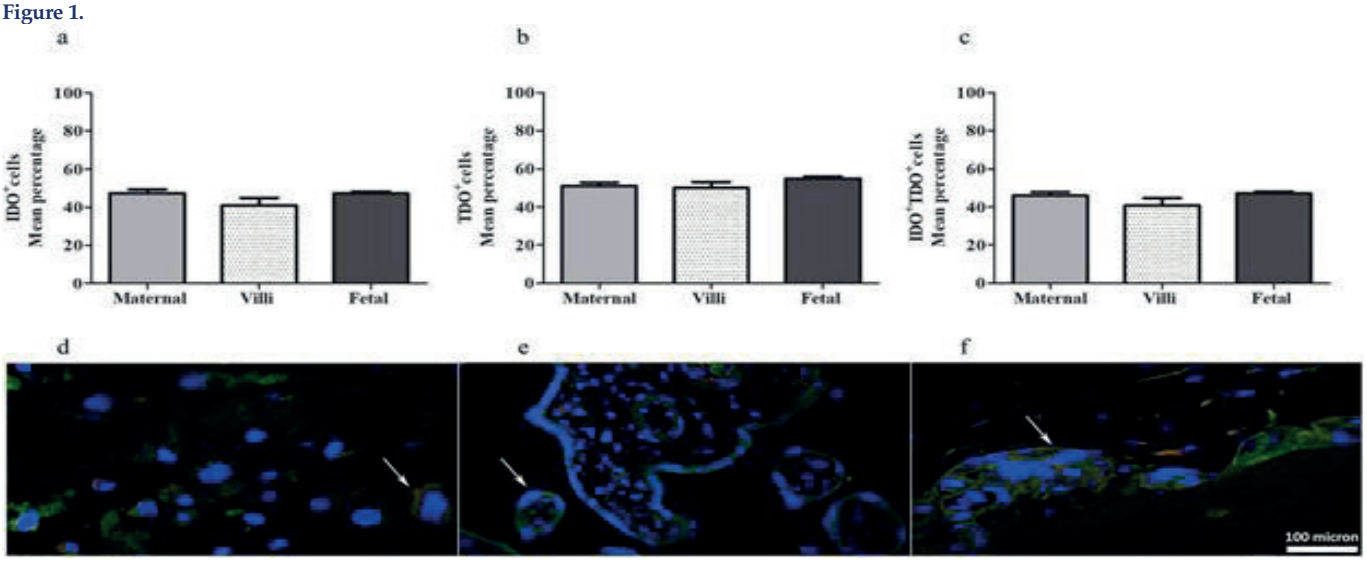
Objective. The objective of this study is to characterize the placental expression of Indoleamine 2,3-dioxygenase (IDO) and tryptophan 2,3-dioxygenase (TDO), two key enzymes for tryptophan degradation in the placenta, that is crucial for immune tolerance during pregnancy, and to investigate TDO co-expression with Angiotensin(1-7), a protein with anti-inflammatory properties.

Materials and Methods. Prospective observational study on 20 singleton physiological pregnancies delivered vaginally at term. Fresh placental tissue was collected immediately after delivery. Placental TDO mRNA expression was assessed by Real Time PCR and TDO, IDO and Ang(1-7) localization was evaluated by immunofluorescence analyses. The expression of the enzymes in different areas of the placenta was compared using univariate and multivariate analyses.

Results. TDO mRNA was expressed in the maternal and fetal sides of the placentas. TDO protein was localized in the maternal and fetal sides and in the villi and it was co-expressed with IDO in over 40% of cells at these sites (**Figure 1**). The percentage of TDO^+ and IDO^+ cells was influenced by maternal pre-gestational smoking and newborn weight ($p < 0.05$). There was a strong correlation between the percentage of TDO^+ and IDO^+ cells in the villi (Pearson 0.86, $p < 0.01$). TDO^+ cells also expressed Angiotensin(1-7), with a higher percentage in the fetal side and in the villi compared to the maternal surface ($p < 0.0001$).

Conclusions. TDO is localized in placental tissue and is often co-expressed with IDO in all placental sites and with Angiotensin(1-7) in the villi and fetal side.

Figure 1.



Placenta previa: evaluation of cervical length as a predictor of caesarean section before 34 weeks

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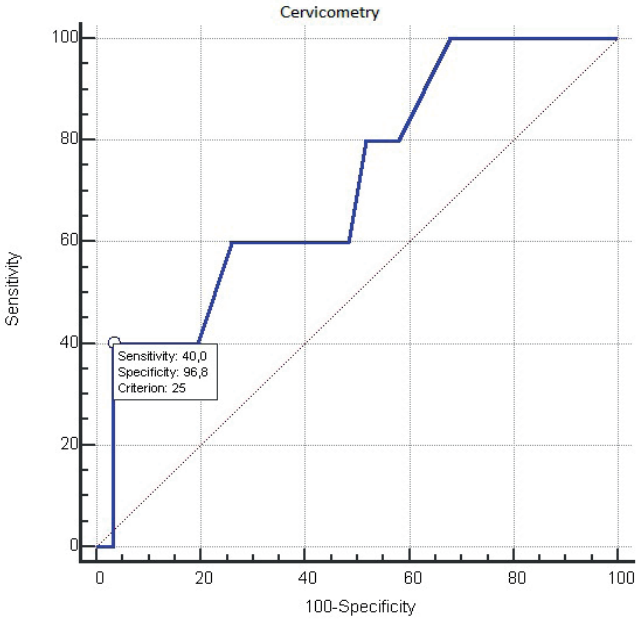
DOI: 10.36129/jog.2022.S109

Objective. Placenta previa carries significant maternal and fetal complications, that can be effectively prevented by early identification and proper follow-up in specialized centers, and by performing a scheduled caesarean section, sometimes with a multidisciplinary team. Ultrasound assessment by a qualified operator is recommended in these cases.
The aim of the present study is to evaluate the cervical length as a predictor of caesarian section before 34 weeks in women with placenta previa.
Materials and Methods. 36 pregnant women were involved in this study. Cervicometry by transvaginal ultrasound was performed between 30 weeks+1 day and 34 weeks, according to a standardized technique. 31 patients underwent caesarean section after 34 weeks (group A - 86.11%) and 4 patients before or at 34 weeks (group B – 13.89%). ROC curve analysis was performed to test the sensitivity and specificity of cervical length and emergency caesarean sections before 34 weeks.
Results. Cervical length proved to be a moderately accurate predictor of emergency caesarean sections before 34 weeks (AUC 0.716, 95%CI 0.542-0.853). Patients with cervical length < 25 mm have an increased risk of caesarean section before 34 weeks (OR 20.00, 95%CI 1.97-291.08).
Conclusions. The cervicometry is not the unique prognostic factor of caesarean section before 34 weeks, but its evaluation could be useful in women with placenta previa in order to prevent obstetric complications.



A case report of placenta accreta spectrum (PAS): magnetic resonance and ultrasound evaluation for the diagnosis and management

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DOI: 10.36129/jog.2022.S110

Objective. Placenta accreta spectrum (PAS) disorders represent conditions of abnormal adherence of the placenta, which increase risk of severe hemorrhage and maternal morbidity and mortality.
We present a case of central placenta previa and vaginal bleeding during gestation in which a concomitant use of MRI and Ultrasound allowed minimization of peripartum risks through a tailored management.
A 46 year old woman gravida 2 with a previous cesarean section was referred to ultrasound evaluation at 28 and 31 weeks for vaginal bleeding. A central placenta previa with anterior development classified as PAS1 was diagnosed. The MRI was assessed at 33 weeks. It described thinning of the myometrium in the right lateral inferior site with placental bulging, so there was a concordance between the two techniques for staging the pregnancy as a PAS1, with moderate risk of bleeding during delivery. Two hospitalizations for vaginal bleeding occurred. We decided for a hysterectomy at 34 weeks.
Materials and Methods. We performed Ultrasound scan using three-dimensional Ultrasound (SAMSUNG HERA) technique and MRI.
Surgical techniques and postpartum diagnosis were made according to FIGO consensus guidelines on placenta accreta spectrum disorders.
Results. The histological findings confirmed a PAS disorder with FIGO grading 3.
Conclusions. The reported case provides a clear example of how two complementary evaluations by MRI and ultrasound can rightly stage a pregnancy at risk of PAS disorders and correctly customize the management of delivery to minimize hemorrhage in post-partum avoiding major maternal risks.

Vein of Galen aneurysmal malformation: from fetal diagnosis to perinatal management and long term follow up. A multidisciplinary paradigm for the diagnosis and treatment of a rare and challenging disease

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DOI: 10.36129/jog.2022.S111

Objective. Vein of Galen aneurysmal malformation (VGAM) is a high-flow, low-resistance arterovenous malformation of the choroidal arterial system. It represents the most frequent congenital intracranial vascular malformation with an incidence of about 1 in 25,000 deliveries. VGAM results from the abnormal persistence of the median prosencephalic vein of Markowski, which normally involutes by the 11th week of gestation. Morbidity and mortality rates are still high despite a progressive improvement in pathophysiological understanding of the disease and treatment strategies. The diagnostic and therapeutic pathways are complex and based on a multidisciplinary approach, incorporating neuroradiological definition of the lesion, neonatal and pediatric intensive care support, and endovascular treatment (EVT). Few centers worldwide regularly take care of patients with VGAM from fetal diagnosis to long term follow-up and the current literature does not provide sufficient data to define many controversial aspects of this complex condition.

Materials and Methods. Several specialities are involved in the care of patients with VGAM at Gaslini Children's Hospital (IGG VGAM Team): Genetics, Perinatal Pathology and Medicine, Fetal and Pediatric Cardiology, Neurology, Neonatal and Pediatric Intensive Care, Interventional Radiology and Neuroradiology. A diagnostic and treatment paradigm was applied in a case series including all newborns with VGAM admitted to the Neonatal and Pediatric Intensive Care Unit between 2009 and 2021. Main scopes of the multidisciplinary approach in our Institution were: to define the genetic background of VGAM; to study fetal and neonatal ultrasound, echocardiographic, and neuroradiological features and identify prognostic factors; to apply specific intensive care strategies for neonates with VGAM and severe CHF and optimize treatment pathways (palliation, EVT, medical treatment); to define and overcome treatment challenges in endovascular treatment; to study specific pathological features secondary to VGAM: brain damage, lung and heart pathological changes secondary to AV shunt and overflow; to manage pregnancy, delivery, perinatal period and follow up with counseling and family support; to plan a multidisciplinary long term follow up with evaluation of outcomes (functional outcome and quality of life).

We here present a summary of the IGG VGAM Team experience from 2009 to 2022.

Results. Treatment, prognostic factors, and main outcomes are described in **Table 1**. Intensive care support and endovascular treatment prevented refractory cardiac and multiorgan failure in the neonatal period. Overall survival of treated patients was 87% (27/31) and good neurological outcome in survivors was 77%.

Conclusions. The complexity of VGAM pathophysiology requires a multidisciplinary approach in a tertiary care center with specific experience and competencies. Morbidity and mortality rates remain high in newborns; however, the mortality rate in our population was lower than the ones reported in the literature (30-60%). The neuroradiological and hemodynamic risk factors identified are consistent with those described by other authors. International key-experts' collaboration and data sharing are mandatory to finding appropriate answers to the challenges in the diagnosis and treatment of VGAM. The IGG VGAM Team is promoting an international registry through a network of leading researchers in this field to advance research and knowledge, and ultimately improve outcomes.

Table 1.

Total number of patients enrolled at Gaslini Children's Hospital	45
Number of patients enrolled in the neonatal period • inborn (prenatal diagnosis) • outborn (postnatal diagnosis)	38 33 5
Patients treated in the neonatal period	20 (53%)
Patients treated beyond the neonatal period	11 (29%)
Total EVTs • neonatal EVTs	68 28
EVTs/patient	0-8
Patients with EVT complications • newborns • children	11/31 (35%) 10/20 (50%) 1/11 (9%)
Neonatal mortality • procedure related • palliation for congenital severe cerebral damage	8 (21%) 4 (10.5%) 4 (10.5%)
Functional outcome Good overall performance or mild disability • total • survivors	 60% 77%
Factors associated with adverse outcome • neuroradiological • hemodynamic	 - sagittal superior sinus stenosis - jugular bulb stenosis - arterial pseudofeeders - heart failure - right to left PDA shunt
IGG VGAM Team Silvia Buratti, Marisa Mallamaci , Andrea Moscatelli, Elisabetta Lampugnani, Giulia Tuo, Mariasavina Severino, Francesco Pasetti, Andrea Rossi, Lucio Castellan, Marco Pavanello, Gianluca Piatelli, Valeria Capra, Dario Paladini, Francesca Buffelli, Ezio Fulcheri	

EVT: endovascular treatment. PDA: persistent ductus arteriosus

Early neonatal determinants and neurological outcome in the first three years of life of newborn undergoing hypothermic treatment: a single center prospective study

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DOI: 10.36129/jog.2022.S112

Objective. Therapeutic hypothermia (TH) is the gold standard treatment for hypoxic-ischemic encephalopathy (IIE) affecting mortality and neuro-behavioral disability. The objective of this study was to identify early markers (in the first days of life) of subsequent neurological outcome in neonates undergoing TH in order to individualize the post neonatal follow-up and counselling with parents.

Materials and Methods. Neonates who received hypothermic treatment (according to the recommendations of the SIN 2012) from 2014 to 2021 at NICU "Federico II" were included in a register and followed prospectively for the first 3 years. Determinants of severity of clinical conditions in the first days of life were recorded (pattern of aEEG at enrollment and after hypothermic treatment, seizures, inotropic treatment, pathological MRI according to Okereafor). Such determinants were related to psychomotor development (Hammersmith and Griffiths tests) performed during the follow-up in the first 3 years of life by means of not parametric (Spearmann Rho coefficient) and linear regression analysis (level of significance set as $p < 0.05$).

Results. 38 infants were included in the register. The aEEG pattern at enrolment was correlated with neurological outcome as Hammersmith at 12 months (rs -0.412, $p = 0.026$); there was correlation between normalization of the aEEG within 72 h and neurological outcomes at 12 and 24 months (rs -0.551, $p = 0.008$; rs -0.551, $p = 0.008$, respectively). Seizures showed the best correlation with abnormal Griffith scales at 12 months (rs -0.634, $p = 0.000$); treatment with both dopamine and dobutamine had the stronger correlation with abnormal Hammersmith score at 12 (rs = 0.556, $p = 0.002$) and 24 months (rs = 0.490, $p = 0.021$); abnormal MR was the best predictor of psychomotor retardation at 24-months according to Griffith scales (rs 0.770, $p = 0.00$).

Conclusions. The failure of normalization of aEEG, seizures and pathological brain MRI are the main factors associated with an unfavorable long-term neurological outcome. Moreover, we showed that inotropics treatment during hypothermia may represent an early predictor of abnormal neurological long term outcome.

Sexual dimorphisms in retinopathy of prematurity following complete vs incomplete antenatal corticosteroid prophylaxis

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DOI: 10.36129/jog.2022.S113

Objective. This study sought to assess sexual dimorphisms in retinopathy of prematurity (ROP) occurrence following 12 mg (incomplete course) *versus* 24 mg (complete) of betamethasone prophylaxis in preterm infants.
Materials and Methods. This study is a retrospective single-center cohort analysis including neonates born between 24 and 34 weeks of gestation from 2001 to 2019. The study population was divided into two groups according to neonatal sex. The primary outcome was ROP occurrence, and the main covariate was complete *vs* incomplete antenatal corticosteroid (CCS) prophylaxis.
Results. The study population included a total of 995 single pregnancies exposed to a complete (803) or incomplete (192) CCS prophylaxis. The female population comprised 467 (46.93%) newborns, and the males were 528 (53.07%). The prevalence of ROP was 20.34% (95/467) in the female population and 18.18% (96/528) in males ($p = 0.388$).
In the female population in the complete CCS group, there was a significantly lower prevalence of ROP, 17.88% (69/386) *vs* 32.10% (26/81) in the incomplete CCS group ($p < 0.05$). No significant differences were observed in the male population between complete CCS (18.23%, 76/417) and incomplete CCS (18.02%, 20/111). In multivariate logistic regression analysis the complete CCS prophylaxis was significantly protective for ROP in females (OR 0.37, 95%CI 0.19-0.72, $p < 0.05$). While, in the male population, it was not (OR 1.01, 95%CI 0.59-1.75, $p = 0.960$).
Conclusions. Preterm female fetuses will benefit from a complete CCS course to reduce the ROP occurrence, but males will not.

Introducing the speech therapist in the Neonatology Unit: an innovative way to support breastfeeding in healthy newborns even during COVID-19 pandemic

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DOI: 10.36129/jog.2022.S114

Objective. The aim of the study was to intercept early problems and difficulties in onset and stabilization phases of breastfeeding, in a population of healthy full-term newborns - during the COVID-19 pandemic - through a Clinical Governance Project, supported by the Department of Neonatology and Pediatrics, which introduced a speech therapist, as part of the professional team acting synergistically with neonatologists, pediatricians, pediatric nurses, midwives and gynecologists.

Materials and Methods. Over a period of two months (2020), n = 72 newborns, 38 males and 34 females, were recruited (mean age:1.3 days) in the Departments of Neonatology and Obstetrics and Gynecology of Castelli Hospital, ASLRM6. Lingual frenulum neonatal screening (Martinelli, 2015) was administered to all the newborns and the frenulum was classified as normal, doubtful or impaired. Breastfeeding difficulties were evaluated and speech therapist counseling was performed, to support early onset and stabilization of breastfeeding.

Results. Lingual frenulum screening resulted normal in 36 (50%), doubtful in 20 (28%) and impaired in 16 (22%) of total newborns. An alteration of both lingual and upper labial frenulum was found in 16 (22%) of the newborns studied. n = 23 newborns (32%) showed alterations able to hinder breastfeeding: these cases were successfully managed by helping the mothers to change the breastfeeding position, adopting a "rugby hold" position.

Conclusions. According to our preliminary results, speech therapist counselling, in the critical COVID-19 pandemic, allowed early detection of lingual frenulum alterations, and their impact on the onset of breastfeeding. We found that altered lingual frenulum was associated with breastfeeding difficulties: in these patients, speech therapist intervention resulted useful in managing early breastfeeding problems.

Sudden unexpected postnatal collapse (SUPC): analysis of two neonatal deaths in the same family

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DOI: 10.36129/jog.2022.S115

Objective. In our study we focus on 2 SUPC-attributed neonatal deaths which occurred in the same family.
SUPC is a rare, difficult to identify event, so it is essential to draw the scientific community's attention to this condition in order to reach a correct diagnosis through a multidisciplinary approach.
Furthermore, there is currently no relevant scientific data which links SUPC to specific genetic disorders.
Materials and Methods. Our first case regards a full-term newborn with a 10-minute from birth 10-point Apgar score who, at 24-hours of age, suddenly developed severe respiratory distress associated with bradycardia and acidosis. Despite all resuscitation efforts, the baby did not survive.
One year later, her two-day old sister also died, in very similar circumstances.
In both cases, an autopsy and all relevant laboratory investigations were carried out.
Results. On the basis of such tests, the first baby's cause of death was determined to be SUPC.
In addition, when searching for significant pathogenic mutations for cardiomyopathies, a gene variant in the NKX2-5 gene of uncertain pathogenic significance was identified.
Conclusions. The two cases of SUPC that have occurred in this family call for the continuation and in-depth genetic analysis of the parents as well; this could make it possible to identify a possible correlation, as yet undocumented, between SUPC and gene mutations.

Congenital syphilis in the twenty-first century: an area-based study

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DOI: 10.36129/jog.2022.S116

Objective. The resurgence of syphilis and the subsequent risk for newborns has been described worldwide, however European data on this congenital infection is lacking. We report the activity of a multidisciplinary specialized unit which assists a large area in Southern Italy.

Materials and Methods. A retrospective cohort study was conducted at the Perinatal and Pediatric Infectious Disease Units of the Federico II University in Naples, enrolling all newborns and children referred from January 2010 to June 2022 exposed to *Treponema pallidum* in utero and/or congenitally infected.

Results. A total of 323 patients were included in the analysis. Twenty (6.2%) received a diagnosis of confirmed congenital syphilis (CS) and one died. Fifteen CS cases had typical clinical features. The number of referred neonates tripled after 2017 while the rate of late maternal diagnoses did not significantly differ. When compared with mothers of exposed infants, mothers of CS cases were younger (25 ± 7.2 *vs* 29.9 ± 6 years, $p = 0.041$), had less previous pregnancies (0.64 *vs* 1.11, $p = 0.044$) and had received a diagnosis of syphilis at a later stage of pregnancy (86% *vs* 20%, from the third trimester or later, $p < 0.001$). Appropriate maternal therapy is protective against vertical transmission (-1.2, 95%CI -1.4, -1, $p < 0.001$). Paternal syphilis status was known in 36% of cases.

Conclusions. CS has still a significant impact. Prevention should be implemented towards specific maternal risk profiles. A specialized unit is the preferable model to improve surveillance and healthcare for this neglected population.

Hemodynamic assessment of Levosimendan use in a newborn with vein of Galen aneurismatic malformation

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DOI: 10.36129/jog.2022.S117

Objective. Vein of Galen aneurismatic malformation (VGAM) is a rare congenital anomaly which can be present during the neonatal period with high output heart failure. Medical management of VGAM-related hemodynamical status is complex and challenging.

The aim of this study was to gain reliable data about hemodynamic changes after Levosimendan use in one patient with VGAM.

Materials and Methods. Hemodynamic parameters indicative of cardiac preload, afterload, contractility and tissue oxygen delivery were systematically collected and analyzed offline before and after 48 hours from Levosimendan infusion. MostCare-Up® relies on pressure recording analytical method (PRAM) and analyses beat-by-beat arterial waveform.

Near-Infrared Spectroscopy (NIRS) measures regional cerebral and splanchnic tissue oxygen saturation (rSO_2c and rSO_2s).

Results. The female baby had a prenatal diagnosis of VGAM and was born preterm (33+2 GA) due to fetal heart failure. Postnatal heart failure was treated with continuous infusion of diuretics (etacrynic acid, up to 0.2 mg/kg/h), milrinon (0.75 mcg/kg/min) and Levosimendan at 8 hours of life after discontinuation of milrinon.

Use of Levosimendan determined significant changes in the hemodynamic status; we recorded significantly higher systolic, diastolic and dicrotic arterial pressure, higher Cardiac Index (CI) and a significant increase in DO_2I (total amount of oxygen delivered to the tissues per minute).

NIRS and rSO_2c/rSO_2s values were not significantly different before and after treatment protocol (**Table 1**).

Conclusions. This is the first case report exploring hemodynamic changes after Levosimendan treatment in a patient with VGAM. We observed a significant improvement of arterial pressure values, CI and global oxygen delivery within 48 hours after treatment.

Table 1.

	Before levosimendan	*After 48hours since levosimendan infusion*	*p-value*
Systolic pressure	52.0 (49.0 - 54.0)	64 (60.0 – 66.0)	<0.0001
Diastolic pressure	25.0 (24.0 – 27.0)	38.0 (34.0 – 44.0)	<0.0001
Dicrotic pressure	24.0 (23.0 – 26.0)	30.0 (28.0 – 31.0)	<0.0001
Pulse rate	155 (148 – 159)	154 (135 – 158)	0.0004
dP/dt	0.82 (0.77 – 0.87)	0.68 (0.64 – 0.98)	<0.0001
CI	2.05 (1.94 – 2.29)	2.90 (2.53 – 3.04)	<0.0001
PPV/SVV	0.96 (0.67 – 1.20)	0.69 (0.36 – 1.19)	<0.0001
DO2I	354 (334 – 403)	495 (431 – 518)	<0.0001
Cerebral rSO2	0.48 (0.41 – 0.53)	0.51 (0.45 – 0.56)	0.6857
Renal rSO2	0.31 (0.22 – 0.46)	0.62 (0.49 – 0.72)	0.1143

Neurodevelopmental outcomes of infants with Vein of Galen aneurismatic malformation

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DOI: 10.36129/jog.2022.S118

Objective. Vein of Galen aneurismatic malformation (VGAM) is a rare congenital anomaly characterized by an arteriovenous shunting of the choroidal system draining into the vein of Galen forerunner. Reliable long-term data on neurodevelopmental outcome are still lacking.

Our objective is to report developmental functioning assessed through The Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III) in patients with VGAM.

Materials and Methods. We conducted an observational retrospective study collecting medical data from the electronic medical records during the study period April 2020-April 2022.

Developmental outcome was assessed using three domains (cognitive, language, motor) of Bayley-III Scales at 6 months of age.

Results. A total of 3 infants with VGAM (100% male, 0% female) were included in the study.

Bayley-III Scales were performed at a mean age of 6.6 months (**Table 1**).

No decrease in cognition (Mean Mental Developmental Index: 100) and language domains (Mean Language Score: 105) was detected in our cohort.

We were able to detect a decrease in motor skills in 1 patient (33.3%) showing a motor Development Index of 73 at 6.6 months of age.

Conclusions. Infants with VGAM may display poorer motor development at 6 months.

Our study emphasizes the relative importance of Bayley-III Scores to be routinely used in a clinical setting to assess the development of children with VGAM.

Early identification of delay is critical to improve early intervention in order to minimize impairment.

Table 1.

	Age(days) at first embolization	Age(days) at second embolization	Age(months) at Bayley-III evaluation	Bayley-III Cognitive Score	Bayley-III Motor Score	Bayley-III Language Score
Case 1	10	17	6.6	90	73	103
Case 2	30	Not performed	6.3	95	91	106
Case 3	42	Not performed	6.9	115	91	106

Relationship between admission temperature and risk of cerebral palsy in infants admitted to Special Care Unit in a low resource setting: a retrospective single-center study

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DOI: 0.36129/jog.2022.S119

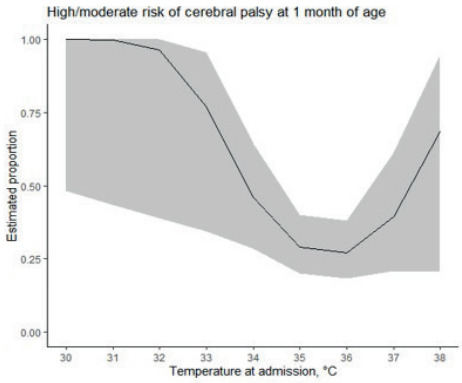
Objective. Deviations from normothermia affect early mortality and morbidity, but the impact on neurodevelopment of the survivors is unclear. We aimed to investigate the relationship between neonatal temperature at admission and the risk of cerebral palsy (CP) at one month of age in a low-resource setting.

Materials and Methods. This retrospective study included all inborn neonates admitted to the Special Care Unit of Tosamaganga Hospital (Tanzania) between 1 January 2019 and 31 December 2020. The neurological examination at one month of age was performed using the Hammersmith method. The relationship between the admission temperature and the risk of CP was investigated using logistic regression models, with temperature modeled as the non-linear term.

Results. High/moderate risk of CP was found in 40/119 (33.6%) of the neonates at one month of age. A non-linear relationship between the admission temperature and moderate/high risk of CP at one month of age was found. The lowest probability of moderate/high risk of CP was estimated at admission temperatures of between 35 and 36 °C, with increasing probability when departing from such temperatures.

Conclusions. In a low-resource setting, we found a U-shaped relationship between the admission temperature and the risk of CP at one month of life. Expanding the analysis of the follow-up data to 12-24 months of age would be desirable in order to confirm and strengthen such findings.

Figure 1. *Estimated proportion of high/moderate risk of cerebral palsy at 1 month of age. Shaded areas represent bootstrap 95% confidence intervals.*



Genetic insight in vein of Galen aneurysmal malformation

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DOI: 10.36129/jog.2022.S120

Objective. The vein of Galen aneurysmal malformation (VGAM) is a rare alteration of the cerebrovascular development resulting from fistulous communication between Markowski's vein and deep choroidal arteries. The deriving aneurysmal formation is the most common non-cardiac cause of high-output heart failure in newborns. Despite the advances in interventional neuroradiology designed for embolization procedures, infant mortality remains high.

An obstacle in the improvement of care is the limited understanding of the pathophysiological and genetic basis of VGAM.

The aim of our study is to analyze genetic mutations to drive appropriate genotype-phenotype correlations that may impact on the therapeutic approach.

Materials and Methods. From April 2020 to April 2022 at the Bambino Gesù Pediatric Hospital in Rome we observed 11 newborns diagnosed with VGAM, 9 identified during the prenatal period. All the neonates had chorioid morphology, 9 underwent embolization, 3 died during the first month of life. Genetic investigations were obtained in 8 out of 10 patients.

Results. In our cohort, 2 patients showed a heterozygosis mutation in the family of NOTCH genes (NOTCH3 and NOTCH4) with maternal segregation pattern. These genes are known in the literature as signal regulators in morphogenesis and vascular remodelling process during the embryonic period. The NOTCH genes mutations in murine models are associated with cerebral arteriovenous malformations.

Conclusions. The identification of a VGAM could represent a recommendation for postnatal genetic study and counseling for future pregnancies, even if the genes that might be involved show incomplete penetrance and variable expressivity.

Impact of quality improvement bundle on neonatal mortality in a district hospital in Tanzania

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DOI: 10.36129/jog.2022.S121

Objective. The poor quality of care received by mothers and neonates in many limited resource countries represents a main determinant of newborn mortality. Small and sick hospitalized newborns are the highest-risk population, and they should be one of the prime beneficiaries of quality-of-care interventions. This study aimed to evaluate the impact on neonatal mortality of quality improvement interventions which were implemented at Tosamaganga Council Designated Hospital, Iringa, Tanzania, between 2016 and 2020.

Materials and Methods. A retrospective comparison between pre- and post-intervention periods was performed using the chi-square test and Fisher's exact test. Effect sizes were reported as odds ratios with 95% confidence intervals.

Results. The analysis included 5742 neonates admitted to the Special Care Unit (2952 in the pre-intervention period and 2790 in the post-intervention period). A decrease in mortality among infants with birth weight between 1500 and 2499 g (overall: OR 0.49, 95%CI 0.27-0.87; inborn: OR 0.50, 95%CI 0.27-0.93) was found. The analysis of cause-specific mortality showed a decrease in mortality for asphyxia (OR 0.33, 95%CI 0.12-0.87) among inborn infants with birth weight between 1500 and 2499 g.

Conclusions. A quality improvement intervention was associated with decreased mortality among infants with birth weight between 1500 and 2499 g. Further efforts are needed to improve prognosis in very-low-birthweight infants.

Cerebral injury in monochorionic twins complicated with twin anemia-polycythemia sequence

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DOI: 10.36129/jog.2022.S122

Objective. Twin polycythemia sequence anemia (TAPS) is a rare complication of monochorionic (MC) pregnancies, which can occur after laser surgery for twin-twin transfusion syndrome (TTTS) or spontaneously. Management of this condition is still a matter of debate, in order to avoid demise or brain injury (BI) of both donor (anemic) and recipient (polycythemic) twin. The aim of our study is to evaluate the rate of pre- and post-natal brain injury and to define risk factors for these lesions.
Materials and Methods. Prospective study from 2006 to 2022 of MC twins complicated by TAPS, defined by US evaluation of Middle cerebral artery Doppler, and confirmed by placental evaluation after delivery, along with hematologic evaluation of twins. For each case fetal and/or neonatal magnetic resonance (MR) was considered. Management options were laser surgery, intrauterine transfusion (IUT) of donor twin, selective feticide, or preterm delivery (PD), tailored to each case.
Results. From the 50 pregnancies (100 twins) included, BI was found in 9 (9%), 6 donors (1 neonate) and 3 recipients, all neonates. Types of BI were: 2 intraventricular hemorrhage (IVH) grade 4, 1 IVH grade 3, 3 periventricular leukomalacia, 1 IVH grade 1, 1 mild parenchymal damage. **Table 1** shows an analysis of the variables.

Conclusions. Brain lesions in TAPS twins can develop before and after birth, especially in donors, with no evidence of any risk factor. An international randomized trial is ongoing to assess the best management option, and the report of such cases might help to identify a diagnostic work-up.

Table 1.

	Cases without brain lesions (N=91)	Cases with brain lesions (N=9)	p
TAPS			*0,9*
spontaneous	49 (53%)	5 (55%)	
post laser	42 (46%)	4 (44%)	
Treatment			*0,7*
Expectant management	45 (49%)	3 (33%)	
Laser	28 (30%)	4 (44%)	
IUT	3 (3%)	1 (11%)	
Preterm delivery	11 (12%)	1 (11%)	
Selective feticide	2 (2%)	-	
TOP	2 (2%)		
Stage TAPS			*0,8*
I	18 (19%)	2 (22%)	
II	48 (52%)	4 (44%)	
III	16 (17%)	2 (22%)	
IV	9 (10%)	1 (11%)	
Twin TAPS status			*0,29*
Donor	44 (48%)	6 (66%)	
Recipient	47 (51%)	3 (33%)	
GA at diagnosis	21,5 (16-33)	21 (19-31)	*0,37*
GA at delivery *	33 (27-38)	28 (24-36)	*0.17*

Neurodevelopmental outcomes of children with prenatal diagnosis of isolated vermian hypoplasia

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DOI: 10.36129/jog.2022.S123

Objective. Magnetic resonance (MR) helps in the definition of malformations when posterior fossa anomalies are suspected. What is still under debate is how to counsel parents about less severe conditions. The aim of our study was to evaluate neurodevelopmental (ND) outcomes of children with isolated vermian hypoplasia.

Materials and Methods. Prospective study of children born with a confirmed diagnosis of vermian hypoplasia, prenatally evaluated at our centre from 2009 to 2021. All fetuses underwent MR, amniocentesis was offered to investigate molecular and standard karyotype. Neurological follow-up was performed using age-appropriate developmental tests (GRIFFITHS II, WPPSI-III, WISC-IV) or by submitting a questionnaire to cases living far from our centre.

Results. 31 pregnancies were included, of which 9 (29%) were terminated on parental request: MR autopsy and pathologists confirmed the findings. 22 cases were considered for ND evaluation: fetal MRI in 21 (95%), and amniocentesis in 13 (59%) were performed. Six cases were lost at postnatal follow-up; 5 had syndromic features (Noonan, Turner, Joubert, X-linked disorder, one still under genetic investigation); one was post haemorrhage. 10 cases were defined isolated: the ND outcome at scholar age was normal in 4 children (40%), mildly impaired in 4 (40%) and moderately impaired in 2 (20%), one diagnosis of autism spectrum disorder and one moderate learning disability.

Conclusions. Although tending towards a favourable prognosis, there is a fair variability of neurological outcomes when cerebellar vermian hypoplasia is isolated, which should be considered in parental counselling. Long-term follow-up is necessary to detect scholar age motor and language outcomes.

Mo.Mi.C.K. - Mother's Milk in chronic kidney disease: a case-control study

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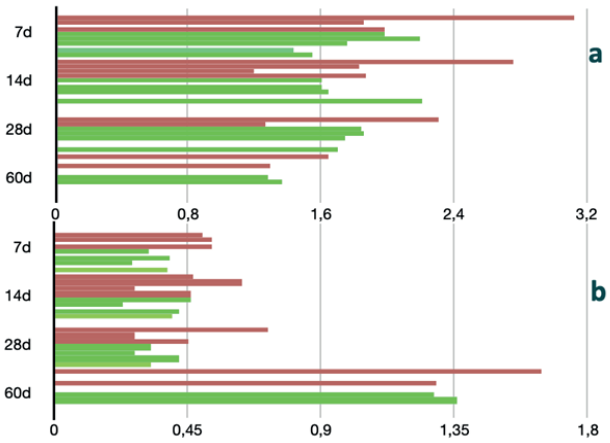
DOI: 10.36129/jog.2022.S124

Objective. Chronic kidney diseases are widespread amongst obstetric patients.
Breastfeeding is the reference normative standard for infant feeding and nutrition.
Nevertheless, we lack evidence regarding how CKD affects human milk composition and clinicians often discourage breastfeeding in nephropathic women.
To evaluate milk composition and nutritional adequacy in mothers affected by CKD.
Materials and Methods. Six pregnant nephropathic women followed in the CKD centre of Sant'Anna Hospital, were recruited from February 2021 onward and each paired with two controls. Milk was collected on the 7th-14th-28th-60th day post-delivery. At ISPA laboratories quantification and characterization of protein and non-protein nitrogen content was performed by using Dumas and OPA method. Auxological and neurodevelopmental follow-up of infants was performed at 40 weeks and 3 months of age using NBAS. Linear mixed models analyses was conducted to compare milk composition.
Results. 5 cases and 10 controls were recruited. Of the 5 cases, 3 presented CKD stage 3 and 2 presented nephrotic syndrome. Of the 5 infant-cases, 3 received exclusive breastfeeding, 2 mixed feeding.
A preliminary comparison of milk showed that there were non-significant differences regarding nitrogen and protein content between cases and controls. The non-protein nitrogen content was higher in nephropathic patients, and positively related with their serum creatinine and urea levels. Infants showed appropriate growth and neurobehavioral development. No adverse effects of the higher non-protein nitrogen content were clinically detected.
Conclusions. This pilot study suggests that breastmilk of women affected by CKD maintains adequate nutritional and biological properties. Therefore, breastfeeding should be encouraged.

Figure 1. *Milk protein nitrogen content (a) and non-protein nitrogen content (b) (in g//100 ml) in cases (brown) and controls (green) at 7-14-28-60 days post-delivery.*



Interhospital transport and intraventricular hemorrhage

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DOI: 10.36129/jog.2022.S125

Objective. Intraventricular hemorrhage (IVH) is a leading cause of mortality and morbidity in the preterm infant. Data in current literature are conflicting about the causal relation between IVH and inter-hospital transport. The aim of this study was to clarify the inter-hospital transport role in IVH onset.
Materials and Methods. Retrospective search of preterm IVH cases recovered in Gaslini NICU between 2012 and 2021.
Results. Total cases were 639. Inborn were 522, outborn 117. Median inborn gestational age was 29+5 weeks, 31 weeks in outborn. Inborn median birth weight was 1200 g, outborn 1440 g. Cesarean section was performed for 72.2% inborn and for 65.8% outborn. The median Apgar score at 5 minutes was 8 in both. IVH was detected in 21% of inborn and in 23% of outborn. Considering preterm < 30 weeks, IVH was found in 29% of inborn and in 41% of outborn. Association between outborn status and IVH lacked statistical significance (OR 1.07, p = 0.77), even considering only preterm < 30 weeks (OR 1.65, p = 0.14).
Conclusions. The aim of this study was to compare IVH occurrence in inborn *versus* outborn patients. Our data suggest that transport during the first hours of life of preterm babies could play a role in IVH onset. Several factors related to transport (difficulty of maintaining body temperature, delay in medical interventions and travel-related trauma) could influence the onset of hemorrhage. Although the small sample size did not allow a statistical Significance, our data suggest the importance of maternal transfer to tertiary perinatal centers to allow optimization of perinatal management.

Neurophysiological studies in infants with Vein of Galen aneurismatic malformation (VGAM): Bambino Gesù Children Hospital experience in the last two years

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DOI: 10.36129/jog.2022.S126

Objective. Vein of Galen aneurysmal malformation (VGAM) is a rare cerebral vascular congenital anomaly due to intracerebral arteriovenous shunt across the remnant of an embryological structure, known as Markowski's vein, affecting less than one birth in 25,000.

VGAM represents the most frequent cerebral vascular anomaly in the pediatric population.

Our goal was to evaluate neurophysiological features such as sensitive, visive and auditive responses in newborns with VGAM.

Materials and Methods. In the past two years, from April 2020, at Bambino Gesù Pediatric Hospital in Rome, we have taken in 11 neonates with VGAM, 9 of them with prenatal diagnosis. We have subjected them to non-invasive neurophysiological exams including sensory evoked potentials (SEP). These are recorded from the central nervous system following stimulation of sense organs and include somatosensory (SSEP), visual (VEP) and brainstem auditory evoked potentials (BAEPs).

Results. In our cohort SSEP gave pathological findings in 6 neonates, specifically we found asymmetric responses in 5 patients and a total lack of response in one of them. Visual evoked potentials were altered in 3/8 while BAEPs resulted asymmetric in only one in 8 patients.

Conclusions. VGAM remains one of the most challenging vascular anomalies in pediatric patients, clinically and therapeutically. They have a higher risk of poor long-term outcome in terms of neurological development and neurophysiological impairment.

In our opinion a complete neurophysiological functions assessment is essential to begin a personalized rehabilitation treatment.

Perinatal diagnosis of congenital urogenital sinus abnormality

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DOI: 10.36129/jog.2022.S127

Objective. Anomalies of the urogenital sinus, which is a transient feature of early human embryological development, are rare birth defects that most commonly occur within the context of congenital adrenal hyperplasia. These anomalies are characterized by the confluence of the urethra and vagina that creates a common channel; in this anomaly, the urogenital tract and the anorectal canal drain through separate perineal orifices. Urogenital sinus abnormalities commonly present as pelvic mass, hydrometrocolpos or ambiguous genitalia. Here, we report the case of a female newborn with congenital urogenital sinus abnormalities diagnosed soon after birth.

Materials and Methods. This female newborn was delivered at 38 weeks gestational age by vaginal delivery. Pregnancy was unremarkable, however prenatal ultrasound revealed the presence of an abdominal mass of unknown origin. At delivery, the Apgar score was 8 at 1 minute and 9 at 5 minutes of life. Birth weight was 2890 gr (10-25th percentile). Based on the prenatal ultrasound finding, the presence of urogenital sinus abnormality was first hypothesized. Family history was negative for congenital malformations and disorders.

Results. By employing many postnatal imaging modalities (pelvic ultrasound, cystourethrography and genitography), the urogenital sinus abnormality was confirmed and the patient underwent surgery.

Conclusions. Given the normal adrenal function, the non-ambiguous genitalia and the absence of associated syndromes or malformations, we assume that the urogenital sinus abnormality of this patient can be ascribed to an arrest of normal cloacal development.

A case of Pallister-Killian Syndrome in a newborn

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DOI: 10.36129/jog.2022.S128

Objective. Pallister Killian syndrome (PKS), a rare disorder caused by tissue-limited mosaicism tetrasomy of chromosome 12p, has a typical dysmorphic pattern: macrosomia, coarse facies, hypertelorism, small nose with long philtrum, V-shaped upper lip, low set ears, frontotemporal alopecia and pigmentary skin anomalies. Seizures and developmental delay, cardiac defects, diaphragmatic hernia, renal/anal malformations may be associated.
Materials and Methods. We report the case of a newborn with multiple congenital malformations, later diagnosed with PKS.
Results. A female baby was born from vaginal delivery at 41 weeks of gestational age. Pregnancy was unremarkable. Apgar score was 8 at 1 minute and 9 at 5 minutes. Weight at birth: 4030 g (95th percentile). On neonatal examination, hypertelorism, ogival palate, a white hair wisp, ulnar fingers deviation and anteriorly displaced anus with perineal fistula were observed. A few hours after birth, she showed severe respiratory distress, with development of persistent pulmonary hypertension, requiring intubation and ventilatory support with conventional and non-conventional systems. Antibiotics therapy was started for neonatal sepsis. A gradual improvement in the respiratory function and sepsis resolution allowed ventilator support to be interrupted. Brain MRI and encephalic ultrasound were normal. Abdominal ultrasound and MRI documented the presence of a cystic lymphangioma and multiple bilateral ovarian cysts. Unilateral hydronephrosis was also diagnosed. Genetic karyotype allowed the diagnosis of PKS: mos47,XX,i(12)(p10)[1]/46,XX[99].
Conclusions. Phenotypic and cytogenetic variability of PKS, with lack of correlation between tetrasomic cells proportion and disease severity, may be challenging for diagnosis. A detailed physical examination is mandatory for early suspicion and diagnosis.

A first experience of neonatal cerebral ultrasound in the Central African Republic

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DOI: 10.36129/jog.2022.S129

Objective. The Teaching Paediatric Hospital in Bangui (CHUPB) is the only referral paediatric hospital for the 4,500,000 habitants: 18,940 admitted infants in 2021, 1511 new-born, 583 weighing > 2500 g.
Neonatal seizures (NS) are common at CHUPB and asphyxia neonatorum is the main diagnosis. In the first 6 months of 2022, from the 880-new-borns admitted, 100 at term had seizures in a context of neonatal encephalopathy (NE), often associated with infection/sepsis.
Before cUS use, diagnosis was NE in 44% of cases (associated with infection in 20% and with sepsis in 16% of cases). 28% died (71.42% after 24 hours).
Materials and Methods. In June 2022, the ONG "Doctors with Africa CUAMM" organised a 2 week training course on cUS, for the paediatricians and medical residents. After this a trained paediatrician performed cUS under supervision (the images were sent to AO).
cUS were performed in 30 at term new-borns with seizures and low Apgar score, with an ESAOTE machine, 5Mhz convex probe.
Results. cUS and clinical diagnosis are summarized on **Table 1**.
Conclusions. cUS has led to a significant diagnostic improvement to allow the early detection of congenital or other non-hypoxic-ischemic (HI) causes of NE and informs regarding the timing of HI injury.
cUS has proven to be not only a diagnostic device but a way to increase a neurological culture and to encourage an exchange with obstetricians; in our experience not all NE originate at the time of delivery.

Table 1. *cUS Diagnosis.*

Normal	11
Arterial infarcts	3
Cerebral malformations	3
Abscess /hemorrhages	1
Oedema	10
Basal ganglia thalami lesions	1
Congenital infections	1

Impact of small for gestational age and bronchopulmonary dysplasia on neurodevelopment at 2 years in preterm infants of less than 32 weeks

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DOI: 10.36129/jog.2022.S130

Objective. To evaluate the impact of small for gestational age (SGA) status and bronchopulmonary dysplasia (BPD) on cognitive neurodevelopmental score (COG) at 2 years (Y) in preterm infants with a gestational age (GA) of less than 32 weeks (W).

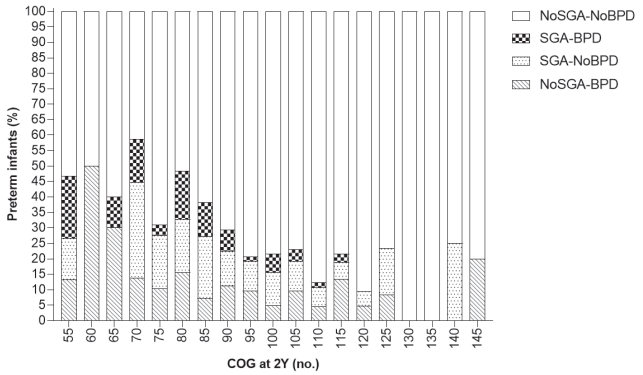
Materials and Methods. Preterm infants with GA between 24.0-31.6W, admitted to the NICU from January 01, 2006 to December 31, 2019, with a neurodevelopmental assessment at 2Y were studied. Outborn and congenital malformations were exclusion criteria. Infants with a birth weight below the 10th centile according to the Italian growth charts were classified as SGA, whereas others as NoSGA.

BPD was defined according to the physiologic definition. SGA with BPD (SGA-BPD), SGA without BPD (SGA-NoBPD), and NoSGA with BPD (NoSGA-BPD) were GA- and gender-matched with NoSGA without BPD (NoSGA-NoBPD). COG at 2Y was assessed using Bayley-III test.

Results. We screened 1336 infants, 812 met the inclusion criteria and were analysed: 47 SGA-BPD (6%), 97 SGA-NoBPD (12%), 79 NoSGA-BPD (10%), and 589 NoSGA-NoBPD (72%). COG at 2Y was lower in SGA-BPD, SGA-NoBPD and NoSGA-BPD compared to NoSGA-NoBPD (86.2 ± 14.1, 92.1 ± 15.9, 91.1 ± 16.3, and 97.3 ± 15.4, p < 0.001, respectively; **Figure 1**). This result was confirmed in the GA- and gender-matched pairs (SGA-BPD *vs* NoSGA-NoBPD: -11 ± 21, p = 0.001; SGA-NoBPD *vs* NoSGA-NoBPD: -5 ± 23, p = 0.026; NoSGA-BPD *vs* NoSGA-NoBPD: -5 ± 21, p = 0.044).

Conclusions. SGA status and BPD were independently associated with a reduced COG at 2Y in preterm infants of less than 32W. Neurodevelopment at 2Y may benefit from combined prenatal and neonatal strategies to reduce the incidence of SGA and BPD in preterm infants.

Table 1.



Neonatal seizures in the pediatric teaching hospital in Bangui: epidemiology, etiologies and outcome

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DOI: 10.36129/jog.2022.S131

Objective. The highest incidence of seizures is noted in the neonatal period. It affects 1.5-3.5 per 1000 live births. The etiologies are diverse and it constitutes the most frequent marker of cerebral injury.
To describe the profile of neonatal seizures managed in a hospital setting in a low income country.
Materials and Methods. A single-center, cross-sectional, descriptive study was conducted over a 6-month period (January to June 2022). Newborns with seizures upon admission or during hospitalization were included.
Results. Out of 770 newborns admitted, 100 presented seizures; a hospital frequency of 12.98%. The sex ratio was 1.5 and the mean age was 3.2 days. Among the mothers, those under 25 years represented 59% and 54% were primiparous. Antenatal cares were poorly attended in 70% of cases. In 29% of cases, no antenatal care was performed. The mothers lived in rural areas in 13% of cases. Fifty-nine percent of newborns were sent from a hospital. Twenty-nine percent of transfers were medicalized. Forty-five percent of seizures were observed upon admission and 55% occurred in the ward. Tonic seizures were observed in 45% of cases. Status epilepticus were observed in 47% of cases. The main etiologies were: hypoxic-ischemic encephalopathy (44%), neonatal infection (20%) and sepsis (16%). Death was noted in 28% of which 71.42% (n = 28) after 24 hours.
Conclusions. Neonatal seizures are common at CHUPB. Asphyxia and neonatal infection are at the origin. Reducing the frequency of seizures requires strengthening antenatal care and monitoring delivery.

Michelin Tire Baby (MTB) Syndrome: a case report

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DOI: 10.36129/jog.2022.S132

Objective. Michelin Tire Baby syndrome (MTBS) is a rare and heterogeneous disorder characterized by multiple and redundant skin folds, which can be isolated or associated with other phenotypic anomalies. We report the case of a newborn who immediately captured our attention because of his appearance.

Materials and Methods. A full-term male was born in our department with a birth weight of 3.590 kg (0.57 SDS). Clinical examination revealed multiple, asymmetric and deep skin folds involving forearms, legs and lower eyelids (right > left) (**Figure 1**). These folds did not seem to cause any physical discomfort to the newborn. In addition, hypertrichosis, micrognathia, low-set ears and a thin, down-turned border of the upper lip were observed (**Figure 1**). Cardio-respiratory, abdominal and neurological examinations were unremarkable. There was no family history of similar phenotypic anomalies.

Results. Considering such clinical findings, an array-CGH was performed and it did not show significant pathogenic gain or loss. The following genetic counseling clinically diagnosed MTBS, in relation to the typical cutaneous involvement, and concluded that, in the absence of other clinical signs, evolution is generally benign and skin folds tend to disappear over time. However, the baby's DNA was sent for further targeted genetic analysis, still in progress.

Conclusions. This clinical case underlines the importance of neonatal physical examination to ensure a timely diagnostic and therapeutic approach. Our patient presented multiple skin folds and facial dysmorphism but a normal systemic and neurological examination. However, since MTBS may be associated with later neurological involvement, a regular follow-up is recommended.

Figure 1.

Who needs a second dose of exogenous surfactant?

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DOI: 10.36129/jog.2022.S133

Objective. To identify prenatal and postnatal risk factors associated with surfactant redosing in preterm infants.
Materials and Methods. A retrospective single-center study including infants with respiratory distress syndrome (RDS) born from 24.0 to 31.6 weeks of gestation and admitted to the NICU from January 01, 2004 to 28 February, 2021. Hypertension in pregnancy (HIP), antenatal corticosteroids, GA (weeks), gender, year of birth, small-for-gestational-age (SGA), histological chorioamnionitis, time to first surfactant dose (hours), SpO_2 to FiO_2 ratio before surfactant administration, 100 or 200 mg/kg as surfactant initial dose and early onset sepsis were tested as risk factors for surfactant redosing.
Results. From a total of 1615 admissions, 662 infants were treated with exogenous surfactant: 462 (70%) could be managed with a single dose and 200 (30%) received more than one dose (25.5% two doses and 4.5% three doses). Risk of redosing was higher for infants born to mothers with HIP (OR 3.95, p = 0.000), for SGA infants (OR 3.93, p = 0.000) and when the initial surfactant dose was 100 mg/kg (OR 4.56, p = 0.000). Infants with higher GA, with delayed first surfactant administration and milder RDS, had a reduced risk of redosing (**Table 1**). Infants who received multiple surfactant doses had a significantly higher rate of bronchopulmonary dysplasia (44% *vs* 16%, p = 0.000) and mortality (16% *vs* 4%, p = 0.000), as well as longer duration of respiratory support than patients that received one dose (192 | 108-403 | *vs* 24 | 10-119 |, p = 0.000).
Conclusions. HIP and SGA were associated with the need for surfactant redosing. Early detection of prenatal risk factors would be desirable to improve the short and long-term respiratory outcome of very preterm babies.

Table 1. *Logistic regression models of prenatal and postnatal risk factors of surfactant redosing.*

	Exp (B)	95% CI	Sign.
SGA [a]	3.93 [a]	2.36 – 6.57	0.000
HIP [b]	3.95 [b]	2.49 – 6.29	0.000
Antenatal corticosteroids [a,b]	0.95 [a]	0.45 – 1.99	0.889
	0.91 [b]	0.43 – 1.90	0.798
GA (weeks) [a,b]	0.85 [a]	0.77 – 0.95	0.003
	0.83 [b]	0.75 – 0.92	0.001
Year of birth [a,b]	0.94 [a]	0.88 – 1.01	0.077
	0.94 [b]	0.88- 1.01	0.082
Age at first surfactant dose (hours) [a,b]	0.92 [a]	0.88 – 0.95	0.000
	0.92 [b]	0.88 – 0.95	0.000
SFR before first surfactant dose [a,b]	0.995 [a]	0.992 – 0.997	0.000
	0.994 [b]	0.992 – 0.997	0.000
Surfactant dosing of 100 mg/kg [a,b]	4.56 [a]	2.47 – 8.41	0.000
	4.61 [b]	2.49– 8.53	0.000
EOS [a,b]	1.16 [a]	0.55 – 2.45	0.706
	1.38 [b]	0.65 – 2.96	0.406

[a] indicates variables included in the regression model (a) with Hosmer-Lemeshow Test of 0.898
[b] indicates variables included in the regression model (b) with Hosmer-Lemeshow Test of 0.701

EOS, Early Onset Sepsis; GA, Gestational Age; HIP, Hypertension in Pregnancy; SGA, Small for Gestational Age; SFR, SpO_2 to FiO_2 ratio.

A neonatal report of iliac artery aneurysm

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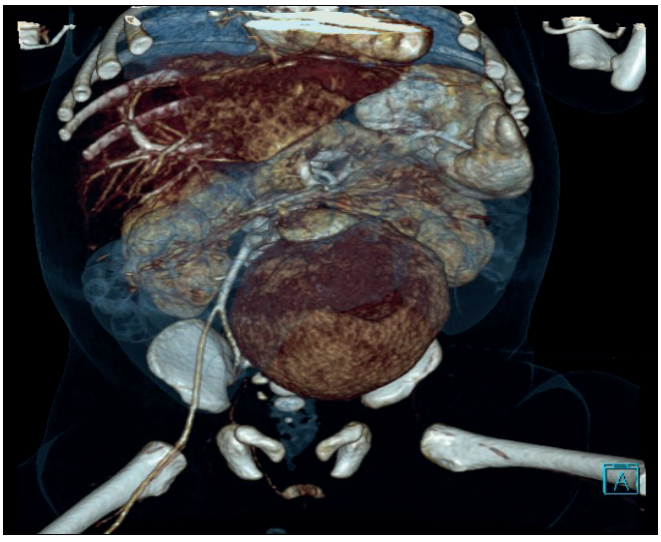
DOI: 10.36129/jog.2022.S134

Objective. Aneurysmal disease of major arteries represents a life-threatening event with a mortality of up to 30% among newborns. Its occurrence is mostly related to connective tissue disorders, infections, vasculitis, and trauma; idiopathic aneurysms can also be observed. The abdomen is the most common site of aortic aneurysm. Considering the limited number of cases observed in pediatric patients, to date there is no consensus for the management of arterial aneurysm in children. Notably, only twelve cases of isolated congenital iliac artery aneurysms have been reported, with four cases diagnosed in the neonatal period.

Materials and Methods. A 14-day-old boy, after having repeated the neonatal screening for a suspected acetyl-carnitine deficiency, was noted to have slight paleness and anemia. An abdominal mass was detected in the median hypogastric area, which appeared to have a taut-hard consistency, to be poorly mobile, and painful to palpation.

Results. A computerized tomography angiogram revealed a saccular aneurysm originating from the common left iliac artery, with maximum axial dimensions of 5.5 × 6.4 cm, which was promptly and successfully treated with surgical repair.

Conclusions. This case report emphasizes the importance of clinical evaluation in newborns and timeliness in the management of similar life-threating events. Indeed, considering the high mortality associated with this condition, an early diagnosis is fundamental to guarantee prompt treatment. However, the extreme variability of the clinical picture, the rarity of radiological findings, and the peculiar difficulties related to surgical repair in neonates make it a real medical challenge.



Perinatal outcomes in anemic fetuses after intrauterine transfusion

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DOI: 10.36129/jog.2022.S135

Objective. Intrauterine transfusion (IUT) is a procedure performed in fetal anemia derived from maternal alloimmunization, infections (parvovirus B19 and cytomegalovirus (CMV)), single demise of monochorionic (MC) twin or other causes. The aim of our study was to evaluate perinatal outcomes in all pregnancies which underwent IUT in our center.
Materials and Methods. Cases referred from 2009 to 2022 with a suspicion of fetal anemia based on Doppler ultrasound (US) of the middle cerebral artery peak systolic velocity (MCA-PSV) above 1.5 multiples of the median (MoM), underwent fetal blood sampling (FBS) to assess fetal hemoglobin values. A calculated amount of RH negative concentrated red blood cells (RBC) was transfused in the same site until fetal anemia was corrected. US monitoring 1 and 7 days after IUT, and, in case of suspected brain lesion, fetal magnetic resonance (MR) were performed. Elective delivery was an option in case of persistent anemia after 34 weeks. Postnatal follow-up comprehensive of obstetrical and perinatal outcomes was collected.
Results. During the study period, 59 pregnancies complicated by fetal anemia underwent a total of 97 IUT (**Table 1**).
Termination of pregnancy followed two cases of surviving MC twins with brain damage demonstrated at MR, which, alongside with two cases of newborns with sequelae (1 from CMV, 1 after maternal alloimmunization) accounted for 7% of cases.
Conclusions. IUT is a safe procedure with low rate of obstetrical complications in expert hands and higher survival rates and better post-natal outcomes in immune anemic fetuses when compared to other conditions.

Table 1.

	Total (59)	Alloimmunization (21)	Infections (16)	Single demise MC Twins (10)	Other (12)	p
GA IUT (wks)	25.21+/-4.00	27.20+/-4.25	23.31+/-3.19	23.05+/-3.34	26.06+/-3.26	.001
IUD < 48 H	4/59 (7%)	0/21 (0%)	2/16 (12%)	1/10 (10%)	1/12 (8%)	NS
MIscarriage	0/59 (0%)	0/21 (0%)	0/16 (0%)	0/10 (0%)	0/12 (0%)	NS
TOP	2/59 (3%)	0/21 (0%)	0/16 (0%)	2/10 (20%)	0/12 (0%)	NS
pPROM	0/59 (0%)	0/21 (0%)	0/16 (0%)	0/10 (0%)	0/12 (0%)	NS
PD < 32 wks	18/59 (30%)	7/21 (33%)	2/16 (12%)	3/10 (30%)	6/12 (50%)	.001
GA (wks)	33.05+/- 4.89	31.97+/- 2.75	36.49+/- 4.84	32.92+/- 6.32	30.87+/- 5.06	.001
Livebirth	53/59 (90%)	21/21 (100%)	14/16 (87%)	7/10 (70%)	11/12 (92%)	.001
NND	5/59 (8%)	2/21 (9%)	0/16 (0%)	0/10 (0%)	3/12 (25%)	.001
Birthweight (g)	2227+/- 897	2038+/- 591	2492+/- 946	2409+/- 1374	2085+/- 848	NS
NDI	2/59 (3%)	1/21 (5%)	1/16 (6%)	0/10 (0%)	0/12 (0%)	NS

Meningoencephalitis and intraventricular devices: when intravenous therapy is not enough

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DOI: 10.36129/jog.2022.S136

Background. M. was a full-term boy, born via emergency C-section because of a not reassuring cardiotocographic trace.

Case presentation. At 12 hours of life, he presented seizures. A lumbar puncture was performed, and the cerebrospinal (CSF) fluid was positive for *Listeria monocytogenes*. Brain magnetic resonance imaging (MRI) showed dilation and thrombosis of the transverse sinuses, with evidence of tetraventricular hydrocephalus and ventriculitis.

At 11 days of life, due to the worsening dilation of ventricles, the child was transferred to our Neonatal Intensive Care Unit (NICU). Intravenous antibiotic therapy (ampicillin and gentamicin) was administered for 21 days, with the resolution of the infectious episode.

Due to progressive ventricular dilation, an intraventricular Rickham reservoir was inserted, to ensure CSF removal when necessary.

Subsequently, he suffered from *Klebsiella pneumoniae* sepsis with meningoencephalitis.

Even with prompt starting of antibiotic therapy with Meropenem and Amikacin, to which the bacterium was sensitive, and the replacement of Rickham reservoir, it was not possible to eradicate the CSF infection. Only after the objective of ceftazidime/avibactam therapy and the initiation of intravenous and intrathecal therapy with colistin, the patient recovered. The long-term outcomes of the infection were severe with a worsening cystic hydrocephalus, which made CSF removal very difficult, and a severe impairment of the sensory, motor, and visual pathways.

Conclusions. Due to the absence of randomized studies, intrathecal antibiotic therapy cannot be used as a routine treatment. However, it can promptly address the therapeutic failure of intravenous antibiotic therapy, especially in patients with intracerebral devices in which infectious eradication is particularly difficult.

A rare case of patent urachus in association with a giant cystic of the umbilical cord

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DOI: 10.36129/jog.2022.S137

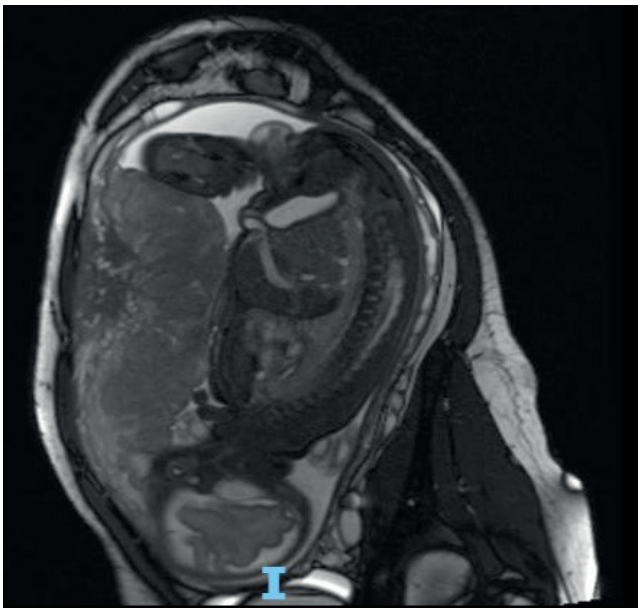
Background. Patent urachus (PU) results from a failure in the closing of the remnant of the allantois constituting a connection between the bladder and umbilicus, which occurs in 1-2 babies in 100,000 births.

Case presentation. A 26-year-old female patient was referred at 21 weeks of gestation. Ultrasound (US) detected the presence of an extra-abdominal cystic formation of 22.7 × 23.8 mm, communicating with the fetal bladder and surrounded by the umbilical vessels. No genitourinary tract anomalies, nor abdominal wall defects were found at US controls. Fetal MR (**Figure 1**) was performed at 32 weeks and a diagnosis of allantois cyst and patent urachus was made. A full- term male weighing 2940 g was born by vaginal delivery. Neonatal findings confirmed a patent urachus with urine leak and circumferential erythema but normal genitalia with no alterations in the infra-abdominal wall or pubic bone diastasis. Urinary infection occurred in II postnatal day and cystography was performed once the infection was resolved confirming communication with the bladder. A plastic reconstruction of the dome of the bladder and resection of the urachus was completed at 20 days-of-life.

Patient was discharged after 6 days with transurethral catheter left in place, lately removed in outpatient clinic after 4 days. US performed at six months showed a normal bladder with no pelvic dilation.

Conclusions. Prenatal diagnosis of PU is rare, sometimes difficult due to its rarity, but usually with good outcomes. PU must be differentiated from other more complex causes of cord cysts.

Figure 1.



Minor dysmorphic features in a newborn: an unexpected diagnosis

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DOI: 10.36129/jog.2022.S138

Objective. We present a clinical case of a female newborn, caucasian, of nonconsanguineous parents. The pregnancy was characterized by the findings of IUGR and bilateral renal pyelectasis at 36 weeks of gestation. Delivery was spontaneous at term. The birth weight was 2440 g (< 3rd centile), length 46 cm (4th centile), head circumference 32 cm (6th centile). The clinical evaluation revealed minor dysmorphisms, such as wide anterior and posterior fontanelles, down slanting palpebral fissures, high nasal root, bulbous nasal tip, large mouth, wide auricles, left foot talus valgus and right foot varus supinated, clinodactyly in the fourth and fifth toes.
Materials and Methods. We analysed the clinical data of the patient and researched similar cases in literature. Diagnostic investigations included medical visits, ultrasounds and genetic testing.
Results. The echocardiography showed septal atrial defect and septal ipo-dyskinesias, whereas transfontanellar and abdomen ultrasounds were normal. Array- CGH revealed the presence of a pathogenetic duplication in 9p24.3p21.2.
Conclusions. Although rare, trisomy of the short arm of chromosome 9 is one of the most common autosomal structural anomalies in newborns, also known as Rethorè syndrome. To date, different cases have been reported in literature, characterized by similar craniofacial dysmorphisms, limb anomalies, delayed mental and psychomotor development. The phenotype may be variable, depending on the size of the chromosomal abnormalities and the different genes involved, such as DOCK8 (important in immunology) and KINK1 (in oncology). Genetic studies should be extended to the child's parents to identify the source of any balanced translocation and the risk of recurrence.

Identification and management of newborns at risk of infection in ASST Brianza: focus on neonatal sepsis

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DOI: 10.36129/jog.2022.S139

Objective. Neonatal sepsis is the leading cause of mortality and morbidity in the newborn (0.3-2‰ live births). Many maternal and neonatal risk factors predispose to sepsis. Prognosis depends on early diagnosis and treatment. The evaluation of the correlations between maternal clinical presentation, placental damage and neonatal outcome in women/infants with risk factors of early onset sepsis (EOS).

Materials and Methods. Retrospective observational cohort study on 240 women and their newborns with risk factors for EOS born in 2021 in ASST Brianza (newborn 3367), whose placentas were sent for histological examination. In order to identify neonatal infections and EOS, maternal risk factors (such as Triple I) and neonatal characteristics were assessed; Kaiser score was calculated.

Results. Out of 3367 newborns, one case of EOS and 63 cases of neonatal infection were reported, of which 27 (43%) were identified by antenatal risk factors with placental exam. The **Table 1** summarises their characteristics. At multivariate analysis, intrapartum fever and Apgar score at 5 min were independently associated to neonatal infection. Comparing the diagnostic performance of prenatal Kaiser score and Triple I as predictive tests of EOS: Triple I has higher sensitivity and VPN than the Kaiser score (89% *vs* 29%, 98% *vs* 90%); Kaiser score has higher specificity, VPP and diagnostic accuracy than Triple I (90% *vs* 60%, 27% *vs* 22%, 83% *vs* 61%).

Conclusions. By integrating prenatal risk with clinical evaluation of the newborn, the Kaiser score is useful for identifying infants who need antibiotics. Shared protocols can promote placental exam and observation strategies optimizing diagnosis of infection and reducing antibiotic use.

Table 1. *Maternal/neonatal characteristics and their significance: comparison between healthy infants (n = 213) and infants with infection (n = 27).*

Maternal risk factors	p-value
GBS +, duration of ROM ≥18 hours, inadequate antibiotic prophylaxis, leukocytosis	>0,05 (n.s.)
Intrapartum fever	<0.0001
Suspected Triple I (with fever ≥38°C)	<0.0001
Histological confirmation of Triple I	<0.0001
Meconium-stained amniotic fluid	0.0486
Maternal tachycardia	<0.0001
Maternal CRP ↑	0.0002
Kaiser score ≥0,65	0.0251
Neonatal characteristics	
Gestational age, FHR monitoring type 2-3, cord-blood acidosis, feeding problems, impaired glycemia, resuscitation at birth	>0,05 (n.s.)
Fetal tachycardia	0.0033
Respiratory distress	0.0433
Use of respiratory support	0.0168
Impaired muscolar tone and/or reflexes	0.0110
Abnormal skin color	<0.0001
Neonatal CRP ↑	<0.0001
Neonatal leukocytosis	0.0014

Perinatal asphyxia or postnatal vasospasm, that is the question

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DOI: 10.36129/jog.2022.S140

Objective. After a normal course pregnancy, a 41-week boy presented an unexpected depression at birth. Invasive ventilation was needed, and a 3-7 Apgar was scored. The cord arterial blood showed a Ph of 6.9 and a BE of -17. Intubation was discontinued within the first hour of life and hypothermia treatment was not indicated, according to Italian guidelines. At 30 hours of life, the baby manifested a sudden desaturation, diffuse cyanosis, and deep pallor in his right arm. The clinical presentation resolved gradually in 4-6 minutes. Cerebral ultrasound (cUS) and MRI scans were conducted (T0). 24 hours later, a clonic seizures cluster was seen, involving the left side. T1 cUS and MRI scans followed.

Materials and Methods. T0 scans and T1 scans were conducted respectively at day 2.5 (after cyanosis) and day 7.

Results. T0 cUS showed an intense hyper-echogenicity in subcortical biparietal fields. T0 MRI resulted negative for perinatal stroke or sinus venous thrombosis. In T1 cUS examination, periventricular echogenicity became normal, but cortical highlighting was seen in the same areas. T1 MRI detected pre-rolandic cortical ischaemic injuries bilaterally, and a post-rolandic cortical ischaemic injury on the right side.

Conclusions. Bilateralism and lesions pattern at MRI oriented us towards sub-acute hypoxic-ischaemic aetiology, rather than cerebral vasospasms or multiple embolisms. The cyanosis and pallor were probably a subtle seizure manifestation. Brain ultrasound showed the injured areas involvement earlier than MRI, likely due to the venous outflow engorgement in subcortical fields, after a post-ischaemic hyper-perfusion.

Prevention of negative late neurodevelopmental outcomes of prematurity: a case series of interventions on ex premature children early screened for adverse neurodevelopmental outcomes

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DOI: 10.36129/jog.2022.S141

Background. Prematurity-related negative outcomes are changing due to the widespread improvement of neonatal care. Preterm infants survive at earlier stages without major brain lesions, so that concerns about their negative neurodevelopmental outcomes have therefore shifted to a long-term perspective, that implies early screening to change adverse developmental and behavioral trajectories.

Case presentation. We present a case series of 6 out of 51 ex-premature children (and their follow-up after 6 months) screened at early stages (6-36 months of corrected age) and tested positive for neurodevelopmental and behavioral problems.

Conclusions. Indication for treatment and on-site interventional programs are discussed as well as parental, prenatal, intrapartum and neonatal risk factors associated with their clinical outcome.

Full-term newborns physiological visual skills: evolution during the first 48 hours of life

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DOI: 10.36129/jog.2022.S142

Objective. Full-term newborns show visual skills that include recognition of black and white or colored contrasts, target seeking, fixation and a certain degree of visual acuity. The aim of this study is to examine the evolution of visual skills in the first 48 hours of life in physiological newborns born at term.
Materials and Methods. One hundred physiological infants (mean gestational age 39.6 ± 1.4 weeks, mean birth weight 3359 ± 396 g) were assessed, divided in two populations: 50 newborns (27 males, 23 females) examined at 24 ± 2 hours of life, and other 50 newborns (25 males, 25 females) examined at 48 ± 2 hours of life. The visual assessment battery developed by Ricci *et al*. was used. The evaluation includes: ocular movements assessment (spontaneous behaviour and in response to a target), fixation and seeking skills of black and white target, recognition of a red and yellow target and visual acuity skills (Teller cards).
Results. Comparing the assessments performed at 24 and 48 hours of life, we observed a statistically significant increase in the share of neonates able to complete vertical tracking (25% increase, $p < 0.05$), to discriminate stripes (39% increase, $p < 0.05$) and to keep attention at distance (44% increase, $p < 0.05$).
Conclusions. Our study shows an evolution of the visual performance in a short time of 24 hours, not dependent on the functional exercise. The role of environmental stimulations contributing to the early visual experience in this process needs to be further investigated. Assessment of visual function should be part of the standard newborn neurological examination.

Perinatal stroke in NICU: a single-center experience

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DOI: 10.36129/jog.2022.S143

Objective. Perinatal stroke is an important cause of acquired brain injury in neonates. The goal of our study was to describe perinatal stroke cases observed in our department in a 10 year period.

Materials and Methods. In our department we have the opportunity to perform brain MRI on every neonate with neurological symptoms (seizures, apnoea, change in consciousness, *etc.*). In order to identify cases of perinatal stroke we retrospectively reviewed brain MRI of neonates born or transferred shortly after birth to our department from March 2012 to July 2022, with the type of stroke registered.

Results. Out of 468 infants with neurological symptoms, 58 had perinatal stroke. 28 patients (48.3%) presented an arterial ischemic stroke: in 8 cases the strokes were multiple, and in another 4 they were accompanied by punctate white matter lesions. In 17 cases (29.3%) the stroke had a venous origin: in 10 thrombosis of cerebral sinuses was present, and in 4 of them thalamic and intraventricular haemorrhage (IVH) could be seen; other 3 cases were associated with vascular malformations. The remaining 13 cases (22.4%) were haemorrhagic strokes, with 6 cases of parenchymal haemorrhage, 5 cases of IVH and 2 cases with association of both. Eighteen infants were born at our Institute, while 40 infants were transferred from other centres: 25 from the Liguria Region and 15 from the rest of Italy.

Conclusions. According to our experience, venous and haemorrhagic strokes could be more frequent than described, and this could be important considering treatment options available.

Role of antenatal steroids in brain development of VLBW infants

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DOI: 10.36129/jog.2022.S144

Objective. Antenatal corticosteroids are widely used in pregnancies at risk of preterm birth, but their role in brain development is debated. The aim of this study was to define the effect of a complete antenatal steroid course (cASC) on prematurity-related brain lesions, brain growth and neurodevelopment at 3 years of age in VLBW infants.

Materials and Methods. All VLBW patients admitted to our NICU in a 5-year period with brain MRI at term-equivalent age were included and their clinical data were registered. MRI scans were reviewed to identify white matter lesions (WML), intraventricular hemorrhage (IVH), and cerebellar hemorrhage (CBH). Biparietal width (BPW) and trans-cerebellar diameter (TCD) were measured and total maturation score (TMS) was calculated. Frequency of brain lesions, brain metrics and values of Griffiths Scale at 3 years of age were compared between patients with and without cASC.

Results. Out of 389 infants, 295 (76%) received cASC. In univariate analysis, cASC was associated with lower frequency of IVH (23% *vs* 37%, p = 0.008), bigger TCD (51.4 mm *vs* 49.4 mm, p = 0.027) and lower frequency of pathologic developmental score at 3 years (15.2% *vs* 26.8%, p = 0.04). In multivariate analysis cASC remained significantly associated with lower rates of IVH (p = 0.0327) and bigger TCD (p = 0.034), while the association with outcome at 3 years was not significant. No correlations were observed between ASC and TMS.

Conclusions. Complete antenatal steroid course can be beneficial for brain development as it is associated with lower rates of IVH and bigger cerebellum. A trend for the positive effect on neurodevelopment requires further studies.

Intracranial hemorrhages in full-term newborns: nosological and etiological insights in a large monocentric cohort *(Winner of the SIMP EUBRAIN Award, in memory of Sir John William Little for his fundamental study of 1862)*

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DOI: 10.36129/jog.2022.S145

Objective. Intracranial hemorrhage (ICH) is a pathological accumulation of blood within the cranial vault. Complications during delivery remain the most relevant risk factor. The use of Susceptibility Weighted Imaging (SWI) MRI represents the most sensitive diagnostic technique.
The aim is to find associations in a large cohort of babies as SWI has been pioneered and introduced into daily practice since 2012 at Gaslini Children's Hospital.
Materials and Methods. We enrolled children born at GA ≥ 37 week, showing neurological signs within 28 days of life who underwent brain SWI-MRI between 2012 and 2022 and were diagnosed an ICH. In these subjects, we registered the site of hemorrhage, the total maturation score of the brain (TMS), and perinatal history.
Results. 103 newborns were analysed out of 209 scanned for symptoms (total of 1200 MRI of term neonates). Median TMS 12. 78.6% were born by VD, 15.3% needed the use of vacuum. ICH was more frequently detected in VD if compared to the CSs ($p = 0.04$). A subdural hemorrhage was detected in 54, subarachnoid in 7, subpial in 4, intraparenchymal in 25, IVH in 39, posterior cranial fossa (PCF) in 53. PCF ($p = 0.02$) and subarachnoid ($p = 0.04$) were most detected in case of vacuum. IVH was associated with a lower TMS ($p < 0.001$).
Conclusions. The most frequent form of ICH was subdural. VD represented a significant risk factor for all ICHs. Vacuum was accompanied by increased PCF hemorrhages. The association between IVH and a lower TMS suggests that immature structures may favor this form, commonly due to choroid plexus bleeding at term of gestation.

The enigma of defining "symptomatic" CMV babies according to neuroradiological findings

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DOI: 10.36129/jog.2022.S146

Objective. Brain Magnetic Resonance Imaging (MRI) is not widely used as a gold standard for categorizing minor abnormalities (like diffuse excessive hypersignal signal intensities, DEHSI) as a sign of late in pregnancy CMV infections highlighting inflammation of white matter. We consider DEHSI as a sign of CMV "symptomatic" infections together with germinolytic pseudocysts as we cannot exclude that these babies may develop long-term neurological sequelae. Our analysis aims to track the prevalence of these abnormalities and observe our attitude in offering drug treatment.
Materials and Methods. This was a retrospective cohort study of CMV infections referred between 2012 and 2022.
Results. We included 54 full-term infants; 34/54 (62.9%) were defined "symptomatic" and offered antiviral treatment. Severe brain abnormalities were present in 11/34 of symptomatic newborns (32.3%), while in the remaining 23/34 cases (67.6%) only mild abnormalities were detectable. Minor neuroradiological changes were in 24% (13/54) of newborns as the sole sign of disease moving us to offer treatment. Antiviral treatment was accepted by parents in only 3 of the aforementioned 13 cases. Overall, antiviral therapy was performed in 17/34 symptomatic cases (50%).
Conclusions. We showed a surprisingly high number of babies "named" symptomatic for CMV infections thanks to the mild US or MRI detectable brain abnormalities. We remain uncertain of the reasons for the high number of parents not accepting antiviral therapy. We believe we should offer antiviral treatment via a multicenter prospective trial with different groups of "symptomatic" babies, one based on US compared to MRI to diagnose mild abnormalities (respectively germinolytic pseudocysts *vs* DEHSI).

Origin of the intraventricular haemorrhage (IVH) in preterm infants: germinal matrix or choroid plexus?

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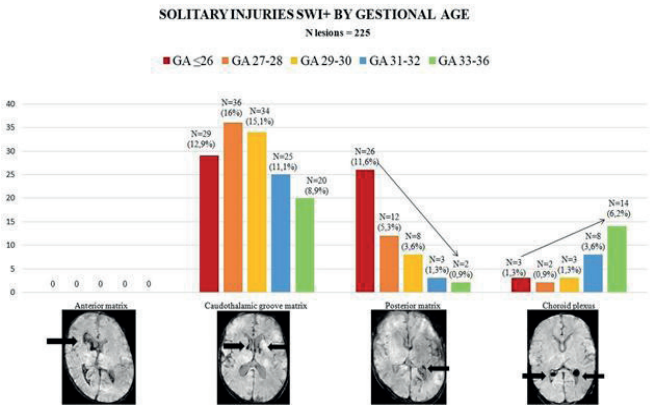
DOI: 10.36129/jog.2022.S147

Objective. We know IVH can originate from the germinal matrix (GMH-IVH) or the choroid plexus (CP-IVH). GMH-IVH has been widely studied via ultrasound and MRI in the most premature babies while no guidelines related to CP-IVH diagnosis are available with any of the neuroradiological techniques. Our aim is to investigate MRI findings able to differentiate GMH-IVH from CP-IVH.

Materials and Methods. 181 babies with IVH out of a total of 1018 preterm (< 37 weeks of GA) studied with cerebral MRI at term equivalent age (TEA) between 2012-2022 were enrolled. Conventional MRI and Susceptibility-Weighted Imaging (SWI), so far, the most sensitive to detect hemosiderin were used. The origin was presumed by identifying the biggest clot adjacent to one of the two different sites. Lack of GMH clot was confirming CP-IVH in case of clot adjacent to CP.

Results. 159 out of 181 infants bled from a sole origin showing 225 bleedings distributed as follows: 144/225 (64%) from the caudothalamic groove matrix (CTG-GMH) only; 51/225 (22.7%) from the posterior matrix (P-GMH); 30/225 (13.3%) from the choroid plexus (CP-IVH). P-GMH and CP-IVH were distributed, respectively, inversely (11.6%-0.9%) and directly (1.3%-6.2%) proportional to the GA (23-36 weeks). All the diagnosis were based on SWI albeit T2 weighted scans correctly identified the origin of GMH-IVH in 35.4% of the cases.

Conclusions. GMH-IVH is confirmed to be the most frequent form of IVH and is inversely proportional to the GA. CP-IVH is more represented in babies closer to full term.



Neurodevelopmental outcome at 3 years of age in VLBW infants according to brain development and lesions

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DOI: 10.36129/jog.2022.S148

Objective. Over the past decades severe brain lesions affecting very low birth weight (< 1500 g, VLBW) infants have been gradually substituted by milder lesions with debatable prognosis. The goal of our study was to define the type, frequency, and 3 years neurodevelopmental outcome of prematurity-related brain lesions in a modern cohort of VLBW infants.

Materials and Methods. VLBW infants admitted to our NICU in a 5-year period with brain MRI at term-equivalent age were included. MRI scans were reviewed to identify and grade white matter lesions (WML), intraventricular haemorrhage (IVH), and cerebellar haemorrhage (CBH). Linear measurements of brain size, biparietal width (BPW) and trans-cerebellar diameter (TCD), were performed. Total maturation score (TMS) was calculated. Developmental Coefficients (DQ) on Griffiths Scale at 3 years of age were compared between patients with different types and grades of lesions and patients without lesions; possible correlations between linear brain measurements, brain maturation and outcome were explored.

Results. The study included 407 patients. Of these, 187 (46%) had at least one brain lesion on MRI, while 37 (9%) had severe lesions. The most frequent lesion was IVH (28%), followed by WML (21%) and CBH (17%). Mild and severe IVH, moderate and severe WML and all grades of CBH were related to worse outcome at 3 years. In patients without lesions, small BPW and small TCD were associated with worse outcome. No correlations were observed between TMS and outcome.

Conclusions. We have observed that even mild brain lesions have a negative influence on neurological outcome at 3 years of age.

Retrospective analysis of a neonatal population with seizures: new ILAE classification and etiology

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DOI: 10.36129/jog.2022.S149

Objective. Seizures are the most common neurological emergency in the neonatal period, with an incidence of 1-5 per 1000 live births. In 2021 the International League Against Epilepsy (ILAE) presented a new classification of neonatal seizure (NS) type and recent studies suggest that clinical features of NS correlate with etiology. The aim of this study is to demonstrate the correlation between certain NS types and specific etiology.
Materials and Methods. This retrospective cohort study comprised neonates (gestational age 23+0-44+6 weeks at seizures presentation) with NS confirmed by EEG (electroencephalogram) or aEEG (amplitude-integrated electroencephalography), admitted during a 14-year period to our third level neonatal intensive care unit.
Results. A total of 141 patients with confirmed EEG/aEEG NS were included in our study: preterm = 43 (30.5%), term = 98 (69.5%), male = 80 (56.7%), female = 61 (43.3%), mean birthweight 2771 g (SD 917 g). The mean age at seizure onset was 7.6 days (SD 14.1): 3.4 days (SD 5.6) in term infants and 17.1 days (SD 20.7 days) in preterm infants. The incidence of NS in our centre was 1.1 per 1000 live births. The most common etiologies were vascular disorders (26.2%), hypoxic-ischemic encephalopathy (23.4%), genetic (17%) and infection (15%). NS according to ILAE classification was significantly different between vascular disorders (54.1% clonic seizure), hypoxic-ischemic encephalopathy (48.5% electrographic-only seizure) and genetic etiology (62.5% sequential seizure) (Fisher Exact test $p < 0.05$).
Conclusions. Our data confirm the correlation between NS types and specific etiologies. These correlations may help to reach an early etiological diagnosis in patients with NS and to establish an appropriate treatment.

A late preterm pregnancy in a patient with cystic fibrosis (CF): case report

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DOI: 10.36129/jog.2022.S150

Background. Literature suggests that maternal and fetal pregnancy outcomes are satisfactory for cystic fibrosis **(**CF) affected women with well controlled clinical features. We present a case highlighting that even in CF patients in stable conditions the risk of severe clinical deterioration in the course of pregnancy is not to be overlooked.
Case presentation. A 25-year-old woman with CF and a history of a previous pregnancy ended in miscarriage. She presented a pre-pregnancy BMI of 21.1 kg/m^2, FEV1 60%, and was colonized by MSSA, therefore resulting in a low risk profile for pregnancy. The patient's general conditions progressively worsened, with four pulmonary infective exacerbations, a gradual decrease of pulmonary function, need of noninvasive oxygen support, and deterioration of nutritional status despite parenteral nutrition (weight before pregnancy 56 kg, at 36 weeks 54 kg). Anticipation of delivery was decided. A healthy female child was delivered by elective cesarean section at 36+0 weeks, Apgar 1' 9-5' 10, weight at birth 2850 g. She was discharged at 4 days with 12.6% loss of the birth weight and mild jaundice. In the following days feedings were switched to infant formula exclusive nutrition, due to lack of breast milk. The patient was discharged 9 days postpartum, after a 12-day i.v. antibiotic cycle, with improved general conditions and basal pulmonary function comparable to usual, pre-pregnancy, standards.
Conclusions. Even in CF women with a low risk profile before pregnancy, a careful monitoring of pregnancy and active collaboration between the CF center, anesthesiology and the Gynecological/Obstetrical Unit is highly recommendable.

Point-of-care hemoglobin analysis vs laboratory assay in preterm infants in NICU: cost effectiveness and neuroprotective implications

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DOI: 10.36129/jog.2022.S151

Objective. Haemoglobin levels assessment is a crucial part of neonatal intensive care practice, the painful experience of heel prick and venepuncture blood sampling may badly affect neonatal health and future cognitive development. To date the reliability of haemoglobin levels obtained by point-of-care testing (POCT) analysis if compared to standard blood cell count remains controversial.

Materials and Methods. A retrospective study conducted on all inborn premature infants (gestational age < 32 weeks) admitted to NICU at the IRCCS Istituto Giannina Gaslini during the period January 2019-December 2021.

We considered blood samplings taken within the first 28 days of life recording the laboratory haemoglobin levels (Hblab) (reference method), the point-of-care haemoglobin levels (Hb-POCT) (alternative method) and the type of puncture (arterial, venous, and capillary). A Bland-Altman analysis was performed to evaluate the Hb agreement, it determines the bias (mean difference between the reference and alternative materials) and limits of agreement (LOA – lower: l-LOA, upper: u-LOA) of measures. An acceptable limit of agreement was 1 g/dl according to the existing literature.

Results. We considered 845 blood samplings from 189 enrolled patients. The comparison between the reference and the alternative method showed a good agreement for the capillary sampling technique with l-LOA of -0.717 (-0.776, -0.659) and u-LOA of 0.549 (0.490, 0.607), these results were not detectable among the other techniques, with LOAs over ± 1 g/dl threshold (venous < arterial).

Conclusions. The possibility of considering capillary POCT haemoglobin levels as reliable may reduce clinical-related costs and painful experiences in NICU, with positive effects on neonatal quality of life and neurodevelopment.

Invasive non-albicans candidiasis: case report

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DOI: 10.36129/jog.2022.S152

Background. Among extremely-low-birth-weight (ELBW) infants, invasive candidiasis is the second most common cause of infectious disease-related death, despite proper antifungal treatment.
Case presentation. A male born at 25+4 weeks by emergency C-section, BW was 600 g. According to our protocols we started immediate empirical wide spectrum antibiotic therapy and registered a repeated C-reactive protein (CRP) negativity. Moreover, antimycotic prophylaxis with fluconazole was administered.
At the end of the first week of life the patient presented signs of hemodynamical and respiratory instability, the concomitant blood culture resulted positive for Candida glabrata (the same as the maternal vaginal swab) and a therapy based on micafungin was promptly initiated. The echocardiography was negative for fungal valvular vegetations while the abdominal ultrasound revealed liver lesions compatible with possible fungal localizations. The CRP resulted persistently negative. After three days of therapy the patient rapidly deteriorated until death from pulmonary haemorrhage.
Conclusions. We raise interest about the epidemiological changes interesting NICUs, with a non-negligible increase in non-Albicans species of Candida (NAsC) detections; we report 2 maternal swab detections of NAsC in 2022. This species can be resistant to the usual therapies, and it is crucial to recognize and treat blood infections as soon as possible. CRP, one of the most used markers for detecting sepsis, may be unreliable in case of NAsC and a high level of attention should be kept in case of clinical suspect, mostly indistinguishable from a bacterial infection.

Neonatal perforator stroke (PS): a postnatal more than a perinatal origin in preterm

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DOI: 10.36129/jog.2022.S153

Objective. Perforator stroke (PS) is a subtype of perinatal arterial ischaemic stroke (PAIS) that involves small branches of middle cerebral artery and may affect important brain structures and functions. Very few studies of PAIS have focused on characteristics and risk factors of the PS subgroup. We report our single center experience.
Materials and Methods. We retrospectively collected data of patients who underwent cerebral MRI from March 2012 to March 2022. We analyzed perinatal and postnatal features of patients with perforator stroke focusing on timing of diagnosis.
Results. Out of 1705 patients we found PAIS in 41 (13 preterm and 8 with asphyxia). PS was present in 16 cases (39% of PAIS, incidence 0.93%), 8 of them (50%) were VLBW preterm (61% in preterm with PAIS) and 8 were term babies (4 asphyxia, 1 hypoglycemia, 3 seizures). PS was identified in 8 of preterm babies with ultrasound (mean age 32 days, range 7-60 days) and with MRI in 5. Placenta data were available in 7 patients, all abnormal although only 2 "malperfusion". Sepsis was diagnosed prior to PS in 33% patients, all of them preterms.
Conclusions. PS represents the most common form of PAIS in preterm babies and in 50% of babies suffering asphyxia. In all preterm babies, diagnosis followed a previous negative ultrasound, 33% had sepsis prior to PS. Placental malperfusion suggesting a thromboembolic origin of PAIS seems to be pretty rare in our population. These data suggest a postnatal development of PS in premature babies more than a perinatal one.

Transporting placentas together with asphyxiated babies to be cooled: preliminary findings from regional survey

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DOI: 10.36129/jog.2022.S154

Objective. Our objective was to investigate pediatricians' and gynecologists' knowledge regarding the importance of placentas and their inclination to transport placenta with the baby as they call for neonatal emergency transport service.

Materials and Methods. We elaborated a survey which was submitted to neonatologists and obstetricians of 7 hospitals (1 tertiary center and 6 primary centers) from the Liguria region. The questionnaire, which included eight questions, was submitted telephonically.

Results. The response rate was 84%: 94 patients underwent the questionnaire. Only 29.8% had ever participated in a training event focusing on the potential help of the placenta in clarifying the nature of perinatal asphyxia. The most frequent (72.5%) placental alteration reported was fetal vascular malperfusion. Almost all the participants (97.8%) knew placental alterations can be associated with MRI brain lesions. Eighty-nine % of our population judged the placenta helpful in understanding the causes of perinatal asphyxia, 87.2% recognized its medico-legal relevance. The attention to undergo placental transport was inhomogeneous: 61.7% of patients in the spoke centers usually asked for placenta while in Center 6 and 7 only 14.3% offered transport; no pediatrician of Center 4 did so.

Conclusions. The majority of patients had never participated in a training event about "placentas in neonatal asphyxia", the majority of those who had participated were gynecologists. Clinicians demonstrated they were well informed about the importance of placental analysis from a clinical and from a medico-legal point of view although only a minority offered transport of the placenta together with the asphyxiated newborn.

Variant in a very preterm newborn: a case report neonatal onset of inherited myocardial hypertrophy due to rare MYBPC3

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DOI: 10.36129/jog.2022.S155

Background. Hypertrophic cardiomyopathy (HCM) is an inherited myocardial disease present in one in 500 of the general population. It represents the most frequent cause of sudden cardiac death of young people. Inherited HCM in the newborn is rare. Genetic testing is necessary to discriminate transient forms of neonatal HCM, which have been related to gestational diabetes and exposition to prenatal or postnatal corticosteroids in preterm infants.

Case presentation. A male infant was born after 31 weeks of gestation to a 45-year-old primigravida, primipara woman who had a medical history of an inherited HCM caused by MYBPC3 mutation. Pregnancy was obtained through homologous blastocyst transfer. Fetal echocardiography performed at 24 weeks of gestation resulted normal. The infant was delivered via cesarean section for non-reassuring fetal monitoring. Initial neonatal resuscitation in the delivery room included intubation, positive pressure ventilation, and oxygen supplementation. Apgar scores resulted 2, 4, and 6 at 1, 5, and 10 minutes, respectively. Afterwards, a transthoracic echocardiography revealed moderate left-ventricular wall thickness, suggestive of an HCM.

Conclusions. Because of the family history of heart disease and due to the persistency of HCM in the postnatal period, genetic testing by next-generation sequencing with a comprehensive cardiomyopathy panel was performed. A heterozygous single-nucleotide missense familial variant was found in the MYBPC3 gene (c.3713T > C p. Leu1238Pro). This anomaly is likely pathogenetic of inherited HCM and is a rare variant which is not detected in the ExAC population database (> 60,000 samples) according to the Atlas of Cardiac Genetic Variation.

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Gynæcology & Obstetrics

The Official Journal of the
Società Italiana di Ginecologia e Ostetricia
(SIGO)