Abstract
Background: The rates of abnormal placentation have increased to a certain extent in today's era. The major risk factors of abnormal placentation are a placenta previa and previous cesarean section. The recent increased frequency of cesarean section has resulted in a high incidence of abnormal placenta. The options for treating abnormal placentation include both conservative and extirpative approaches. However, the generally accepted treatment for the most severe form of abnormal attachment of the placenta is cesarean hysterectomy. Recently, the role of interventional radiology in the field of obstetrical hemorrhaging has been widely investigated. Preoperative internal iliac artery balloon occlusion has been widely performed to reduce the blood loss during cesarean hysterectomy.

Objective: To evaluate the effectiveness of prophylactic balloon occlusion of internal iliac artery on expected massive obstetric hemorrhage as a consequence of abnormal placentation.

Methods: In this series of 2 cases, both the patients seen at our hospital between July 2016 and September 2018 with the antenatal sonographic diagnosis of abnormal placental invasions including placenta increta and placenta percreta had undergone prophylactic internal iliac artery balloon occlusion.
This approach may alleviate temporary the rate of blood loss, allowing for expeditious dissection of the uterine and cervical pedicles, and ultimately hysterectomy, while avoiding the development of additional collaterals.

Results: Two patients were ultimately diagnosed with placenta percreta, and one with placenta increta. The actual invasive depth of the placenta tended to be deeper than had been diagnosed before surgery. The volume of blood loss in the 2 patients whose balloons were placed in the internal iliac artery from the start ranged from 1361-1800 ml (including amniotic fluid and fewer amounts of bleeding than these), and these patients received only autologous blood transfusion. Both the patients were ultimately discharged from the hospital without any serious complications.

Conclusion: In conclusion preoperative prophylactic balloon occlusion of bilateral internal iliac arteries reduces both blood loss and transfusion requirement in patients with abnormal placentation scheduled to undergo elective caesarean hysterectomy. It is an adjunct to be considered in the management of a modern day obstetric problem.

KEY WORDS: Cesarean hysterectomies; iliac artery balloon occlusion; Placenta increta, Placenta percreta
TOPIC: ANOMALIES OF PLACENTATION: FROM DIAGNOSIS TO MANAGEMENT

ABSTRACT ID: 101

TITLE: USE OF MAGNETIC RESONANCE IMAGING AND ULTRASOUND FUSION IMAGING TO IMPROVE PLACENTA ACCRETA DIAGNOSIS

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CONTENT

Background
Placenta accreta is characterized by an abnormal attachment of the placenta to the uterine wall. This can be complicated by severe post-partum hemorrhages which remain one of the leading causes of maternal death (18,1%). Improving placenta accreta diagnosis may involve a better patient’s management. Ultrasound (US) and Magnetic Resonance Imaging (MRI) are now used separately to assess the pathology. Therefore, using MRI and ultrasound fusion imaging could improve the placenta accreta’s diagnosis.

Objective
To determine the feasibility and reproducibility of MRI fusion in the diagnosis of placenta accreta.

Methods
We prospectively included all patients referred for suspected placenta accreta from two university hospitals from January 2014 to July 2017. 32
pregnant women were investigated by both ultrasonography, MRI separately and MRI and ultrasound fusion imaging. We developed a fusion score to assess the risk of placenta accreta which is positive if superior to 4. This score had four categories: placental abnormalities, bladder-uterus interface abnormalities, abnormal vascularization, overall appearance. Fusion imaging sequences were blindly examined by two experienced sonographers and radiologists to assess the risk of placenta accreta. The final diagnosis was assessed by histological placenta analysis and operative report for each patient. We calculated sensitivity, specificity, positive predictive value and negative predictive value and concordance rate corresponding to each imaging exam.

Results
We included 32 pregnant women and 9 presented a placenta accreta. The specificity (Sp) and sensibility (Se) of MRI fusion was respectively 78.3% (IC95% 56.3% - 92.5%) and 88.9% (IC95% 51.8% - 99.7%). The positive predictive value (PPV) was 61.5% (IC95% 31.6% - 86.1%). The negative predictive value (NPV) was 94.7% (IC95% 74.0% - 99.9%). For US, Sp was 73.9% (IC95% 51.6% - 89.8%); Se was 77.8% (IC95% 40.0% - 97.2%). For MRI, Sp was 81.8% (IC95% 59.7% - 94.8%), Se was 77.8% (IC95% 40.0% - 97.2%). The concordance rate with histopathology of MRI fusion was 0.5915 +/- 0.1701. The concordance rate of US and MRI were respectively 0.45 +/- 0.1701 and 0.56 +/- 0.1777.

Conclusions
Our study is the first to analyze the interest of MRI fusion in the diagnosis of placenta accreta. We found a better concordance rate for the MRI fusion than for MRI even if the concordance rate was still moderate. Moreover, we found comparable results for MRI and US in the diagnosis of placenta accreta in literature. MRI fusion has several advantages. It uses the strength of both imaging exams with a sonographer and a radiologist. The use of doppler during MRI fusion prevents to use gadolinium during the MRI. In utero exposure to gadolinium had been discussed to associate with adverse perinatal events. We find also important to analyze systematically the placenta through a score. It could lead to a better evaluation of the risks. In this study, we demonstrated the feasibility of MRI and ultrasound fusion imaging using a fusion score in placenta accreta diagnosis. However, we
need to conduct further studies to strengthen the MRI fusion imaging as an additional tool in the diagnosis of placenta accreta.
Introduction: Placenta previa is an established cause of massive intrapartum hemorrhage at third-trimester pregnancy period. However, massive hemorrhage can occur even during mid-trimester delivery by labor induction. The aim of this study was to first investigate whether placenta previa could be a risk factor for hemorrhage in women attempting labor induction for mid-trimester delivery due to pregnancy termination or spontaneous abortion and to evaluate whether elective cesarean section can decrease the amount of bleeding.

Material and Methods: Women who were in their 14–24 weeks of pregnancy who attempted induction labor for pregnancy termination or spontaneous abortion and those with placenta previa between January 2011 and November 2018 were enrolled. Women with placenta previa were scheduled to try vaginal delivery by labor induction until June 2014. From July 2014 to November 2018, all women had cesarean sections. All patients without placenta previa tried to deliver vaginally by labor induction. First, we analyzed the maternal risk factor for massive blood loss (>1000 g) during labor induction for mid-trimester termination of pregnancy or spontaneous abortion in all women with or without placenta previa. The
women who had elective cesarean sections were excluded in this analysis. In the second analysis, we evaluated the clinical outcomes of all women with placenta previa, including the women who had elective cesarean sections.

Results: A total of 73 women who had mid-trimester vaginal delivery by labor induction were included in the first analysis. Among the 73 women, 4 and 69 women did and did not have placenta previa, respectively. The multivariate analysis revealed that placenta previa was an independent risk factor for massive hemorrhage (>1000 g) during labor induction (Hazard ratio = 21.2, p=0.048). Ten women with placenta previa were enrolled in the second analysis, 6 of who underwent elective cesarean section. Of the 4 women with placenta previa who attempted vaginal delivery, two women failed and had an emergency cesarean section because of intractable hemorrhage during labor. Once the vaginal delivery failed, the mean blood loss was significantly higher compared to the women who had elective cesarean sections (2338 g vs. 1026 g, p=0.02) (Figure 1). All of the women who failed vaginal delivery required blood transfusions and had disseminated intravascular coagulation, and one of them needed intensive care unit treatment. Although the one case who had an elective cesarean section needed a blood transfusion because of uterine atony, the others did not have any complications.

Conclusions: This study demonstrated that placenta previa is a risk factor for hemorrhage at labor induction for mid-trimester delivery, and elective cesarean section could decrease the hemorrhage and can be acceptable.
TOPIC: ANOMALIES OF PLACENTATION: FROM DIAGNOSIS TO MANAGEMENT

ABSTRACT ID: 202

TITLE: METHOD OF BLADDER FILLING TO PREVENT URINARY SYSTEM SURGICAL TRAUMA IN MANAGEMENT OF PATIENTS WITH PLACENTA PERCRETA

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CONTENT

Relevance. The main cause of massive bleeding in obstetrics is placenta percreta. Cesarean section with placenta percreta is technically difficult, accompanied by a high percentage of urological complications, such as wounding of the ureter and bladder. Risk factors for damage of the bladder during cesarean section with placenta percreta are adhesions between the bladder and the lower uterine segment. Mobilization of the bladder in such conditions can lead to bladder injury. Objective of the study was to evaluate the effectiveness of the technique of bladder filling during cesarean section with metroplasty in placenta percreta to reduce intraoperative complications.

Materials and methods. A total of 42 women with placenta percreta were included in the study, and were delivered in the Rostov Regional Perinatal Center from 2015 to 2018. The method of bladder filling included insertion of 200 ml of saline in urine catheter at the stage of bladder mobilization before conducting metroplasty in order to delineate the contour of the
bladder and clarify the plane of the dissection. The course of operations, measures taken to prevent blood loss, the time of surgical intervention and its volume were analyzed. Statistical analysis was performed using the non-parametric Mann-Whitney U-test, Fisher's exact test.

Results. 42 patients with placenta percreta were divided into 2 groups. Group I included 23 pregnant women who had caesarean section with metroplasty using the technique of intraoperative filling of the bladder with saline. Patients of group II (n = 19) had caesarean section with metroplasty without filling the bladder. Total blood loss in group I (M ± σ) was 2177.8 ± 114.9 ml and was statistically significantly less (p <0.05) compared with blood loss in group II - 2545.7 ± 158.8 ml. The duration of surgery in group I (M ± σ) was 2 hours 45 minutes ± 7.1 minutes; in group II -3 hours 31 minutes ± 4.1 minutes. In group I, one woman had a bladder injury, in group II 5 women had bladder injury, which was significantly more frequent (p <0.05).

Conclusion. Filling the bladder with saline and mobilization of the bladder can reduce the duration of surgery and the frequency of bladder injury during cesarean section with metroplasty associated with placenta percreta.
INTRODUCTION
Abnormal invasion of placenta (AIP) refers to the abnormal invasion of the trophoblastic tissue beyond the decidua basalis into the uterine myometrium, uterine serosa or even beyond, involving adjacent pelvic organs. AIP is associated with significant maternal morbidity secondary to massive obstetric haemorrhage and/or injury to adjacent pelvic organs. The Triple-P procedure is a 3-step conservative surgical alternative for AIP, which was developed to avoid the severe maternal morbidity associated with peripartum hysterectomy and conservative management. It consists of perioperative placental localization by ultrasound scan and delivery of the fetus via transverse uterine incision above the upper border of the placenta; pelvic devascularization; and placental non-separation with myometrial excision and reconstruction of the uterine wall. The aim of this study is to assess if the location of the placenta in patients with AIP who underwent the Triple-P procedure influences the degree of blood loss and the histopathological findings.

MATERIAL AND METHODS
A retrospective study of 48 patients with AIP who underwent the Triple-P Procedure since 2012 to 2017 was performed. Patients were managed at
the regional referral service for abnormal invasion of the placenta at St George’s University Hospitals NHS Foundation Trust, London, UK where placenta accreta/increta/percreta and its location was confirmed by ultrasound scan and/or intra-operatively. The estimated blood loss during the procedure was quantified in all cases and placenta was analysed histopathologically. The difference in the intra-operative blood loss regarding the localization of the placenta was tested by Analysis of variance (ANOVA). Also, the association between the location of the placenta and the histopathology of AIP was tested by Chi-square Test. P < 0.05 was considered to indicate a statistically significant difference.

RESULTS
The mean intra-operative blood loss in women who underwent the Triple-P procedure was 2125ml. AIP was confirmed histopathologically in 58.4% of the cases, finding 29.2% accreta, 18.8% increta, 10.4% percreta, in 22.9% no AIP was found, and 18.8% cases had no report. Anterior placenta was found in 64.6% (31) cases, posterior placenta in 12.5% (6) cases and anterior-posterior placenta in 18.8% (9) cases; with a resulting mean blood loss of 2087, 1831 and 2505 ml, respectively. There was one case of cornual AIP and one of right lateral placenta with a blood loss of 1100 and 2650ml respectively. Histopathology results could not be located for both these cases. Differences in blood loss were not statistically significant. Similarly, there was no correlation between location of the placenta (i.e. anterior, posterior, anterior and posterior, lateral and cornual) and histopathological findings (i.e. the incidence of accreta, increta and percreta).

CONCLUSIONS
Histological confirmation was not possible in all cases of Triple P Procedure because the placental tissue invading the bladder was left in situ to avoid cystotomy, with the application of the local hemostat ‘PerClot’ to control bleeding from placental venous sinuses at the site of bladder invasion. In our study, anterior placenta percreta invading the urinary bladder was associated with excessive bleeding as would be expected, because of excessive bleeding from abnormal cervical invasion, which require a cervical tamponade balloon to control bleeding. Posterior placenta seems to be associated to less blood loss but without reaching statistical significance. In cases of posterior and cornual placental
invasion, due to the lack of invasion into vital organs as well as reduced vascularity from vesical arteries, the entire myometrium with the morbidly adherent placenta can be completely removed. This explains the reduced blood loss observed in these situations.

There was no correlation between the location of the placenta (i.e. anterior, posterior, anterior and posterior, lateral and cornual) and the histopathological findings. This appears to indicate that irrespective of the location of the placenta, the ability of the trophoblasts to invade the myometrium, the serosa and adjacent organs remain the same, if there is pre-existing damage to the decidua basalis.
Background: In the last 30 years, with increasing caesarean section rates, the incidence of morbidly adherent placenta has also increased. It is estimated that by the year 2020 there will be nearly 9000 cases annually in the United States. Currently, no consensus exists regarding optimal management. Conventional treatment by cesarean-hysterectomy is perilous, with maternal mortality rates of 12.5% and urinary tract injury rates of 7.5%, in addition to loss of fertility and its accompanying psychological trauma. Innovative approaches seek to preserve the uterus with the adherent placenta in situ, thus maintaining fertility and potentially reducing hemorrhage and adjacent organ injury.

Case report: The case involves a 34-year-old gravida 3 para 1, known with a history of previous caesarean section and uterine curettage. During her pregnancy, she was diagnosed with a morbidly adherent placenta. Ultrasonography and MRI demonstrated an anterior placenta recovering the cervical os with signs of invasion of the right parametrium, cervix and bladder wall at the vesical dome. After discussion with the patient regarding different treatment modalities, she opted for conservative management. She presented with self-limiting vaginal bleeding at 35 weeks warranting a hospitalization until delivery. Elective caesarean section was planned at 37 weeks after multidisciplinary review of the case. A pre-
operative cystoscopy revealed no bladder infiltration, and ureteral stents were inserted. Radiologically guided balloon catheters were introduced. Under general anesthesia, lower transverse incision according to Mouchel was performed. The upper end of the placenta was sonographically marked on the uterine wall intra-operatively. A healthy fetus of 2130 g was delivered via a vertical fundal uterine incision, with good pH and Apgar score. The umbilical cord was ligated near the placenta. The uterus was closed in three layers followed by abdominal closure. Estimated blood loss was approximately 1500 ml. Following the surgery, prophylactic bilateral uterine artery embolization was performed. Prophylactic antibiotics were introduced during surgery and continued post-partum. The patient made a full recovery, with bi-monthly follow-up. Serum BHCG was undetectable 3 months later, and residual placenta size decreased gradually.

Conclusion: Although conservative management was successful in our case, we note that intrauterine infection, delayed hemorrhage and hysterectomy can arise months after the initial surgery. This approach should only be considered in adequately resourced centers equipped with embolization, blood bank, and a surgical team with appropriate expertise in case of failure, followed by strict surveillance in outpatient clinic.
TOPIC: CRITICALLY ILL OBSTETRIC PATIENTS

ABSTRACT ID: 105

TITLE: ASSOCIATION BETWEEN INTRAHEPATIC CHOLESTASIS OF PREGNANCY AND GESTATIONAL DIABETES MELLITUS

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CONTENT

Introduction: Intrahepatic cholestasis of pregnancy (ICP) is a liver specific disorder associated with elevated serum bile acids, liver function tests and increased rates of adverse fetal outcomes. The incidence of ICP depends on demographic variation affecting 0.08%-27.6% pregnant women. In Poland estimated rate of ICP is 1.5%. It has been showed, that the primary bile acid farnesoid receptor (FXR) has an impact on normal glucose homeostasis and cholesterol metabolism pathway. Based on that it was suggested that the level of bile acids correlates with cholesterol and glucose level. Furthermore, in recent research it was observed that ICP may be associated with an increased incidence of GDM. The aim of the study was to evaluate the association between ICP and GDM.

Materials and Methods: A retrospective study included 3826 pregnant women managed at 1st Department of Obstetrics and Gynecology Medical University of Warsaw between January 2015 and December 2016. ICP was diagnosed based on the serum bile acids level above >10 μmol/l. After 24 weeks, universal screening for GDM was performed using the World Health Organisation (WHO) 75 g oral glucose tolerance test (OGTT) and diagnostic criteria were based on the FIGO guidelines. 71 of them were complicated by ICP (1.86%) and 327 by GDM (8.55%). The group
complicated by ICP was divided into two subgroups: ICP without GDM (Group I, 54 patients) and ICP with GDM (Group II n=17). Demographic and clinical outcome data (including maternal age, BMI, infant weight and gender) and ICP and GDM biochemical markers were collected.

Results: A retrospective study included 3826 pregnant women managed at 1st Department of Obstetrics and Gynecology Medical University of Warsaw between January 2015 and December 2016. ICP was diagnosed based on the serum bile acids level above >10 μmol/l. After 24 weeks, universal screening for GDM was performed using the World Health Organisation (WHO) 75 g oral glucose tolerance test (OGTT) and diagnostic criteria were based on the FIGO guidelines. 71 of them were complicated by ICP (1.86%) and 327 by GDM (8.55%). The group complicated by ICP was divided into two subgroups: ICP without GDM (Group I, 54 patients) and ICP with GDM (Group II n=17). Demographic and clinical outcome data (including maternal age, BMI, infant weight and gender) and ICP and GDM biochemical markers were collected.

Conclusions: These data support the hypothesis that the incidence of ICP is higher in women developing GDM.
TOPIC: INDUCTION OF LABOR

ABSTRACT ID: 261

TITLE: COMPARISON OF SEQUENTIAL USAGE OF MIFEPRISTONE AND DOUBLE-BALLOON CATHETER WITH DOUBLE-BALLOON CATHETER ALONE FOR INDUCTION OF LABOUR IN TERM PREGNANCY

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CONTENT

Background. Labor induction is directed toward the development of effective cervical ripening and succeeding safe delivery. The efficacy of single-agent methods for preinduction cervical ripening and labor induction has been well documented. However, concerns remain about the possible failure of induction and an increase in the caesarean section rate. In an attempt to improve labor induction outcomes combined methods are developing currently.

Objective: The aim of this study was to compare the efficacy of sequential usage of mifepristone and double-balloon catheter with double-balloon catheter alone for induction of labour in term pregnancy.

Methods: Retrospective study. 73 pregnant women with a modified Bishop score of 5 or less admitted for induction of labor at term pregnancy at tertiary care centre. All women were divided into two groups, with the first group including women who were induced without mifepristone
pretreatment (38, 31 of them nulliparous) and the second group, women who were given mifepristone 24-48 hours before double-balloon catheter insertion (35, 27 of them nulliparous).
The cohort who did not receive mifepristone was starting induction procedure with double-balloon catheter for 12 hours. The women who were pre-treated with mifepristone were given 200 mg oral mifepristone 24–48 h prior to double-balloon catheter insertion. After removing the balloon, the women were managed in the same manner: intracervical dinoprostone gel (if Bishop score less than 8) or amniotomy (if Bishop score 8 and more). The primary outcomes were rate of failed induction, gain in Bishop score and cesarean section rate. Second outcomes: balloon insertion to labor start interval, labor duration, requirement of oxytocin augmentation, neonatal outcome.
Results: There were no differences among groups in rate of induction failure (0 vs 2, p=0.132), Bishop score change (3.50±1.26 vs 2.79±1.69, p=0.091) and cesarean section rate (31.0% vs 20.7%, p=0.490). Also were not differences in several second outcomes measures, but Apgar score at 5 min. was significantly higher in mifepristone group (8.58±0.59 vs 8.89±0.32, p=0.032). After stratification of patients into three subgroups according to the Bishop scale (≤2, 3 to 4 and 5 to 6), analysis revealed significantly lower cesarean section rate in mifepristone group with Bishop score ≤2 (p=0.033).
Conclusions: double-balloon catheter is effective for labor induction if Bishop score is 3 and higher. In extremely unripe cervix (Bishop score is 2 or less), mifepristone pretreatment significantly improve induction outcome.
ABSTRACT ID: 75

TITLE: UREAPLASMA SPP. COLONIZATION DOES NOT INCREASE INFLAMMATORY CYTOKINES OF AMNIOTIC FLUID IN WOMEN WITHOUT HISTOLOGIC CHORIOAMNIONITIS

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CONTENT

Background: Ureaplasma spp. are the most common organisms isolated from infected amniotic fluid and placenta, and associated with increased risk for preterm labor and perinatal morbidities. Previous studies also showed that chorioamnionitis was positively related to ureaplasma spp. colonization. We compared the chorioamnionitis-associated cytokines of amniotic fluid with or without ureaplasma spp. colonization in preterm delivery.

Methods: This prospectively designed study was conducted at Keimyung University Dongsan Medical Center, Daegu, South Korea, from January 2017 and March 2018. During caesarian section, amniocentesis was performed by a single obstetrician. The collected amniotic fluid was centrifuged, and the supernatant was aliquoted and stored at 70°C until assayed. Samples were not subjected to freeze-thaw cycles before being assayed. Inflammatory cytokines, such as interleukin (IL)-6, IL-8, IL-10, metalloproteins (MMP)-2, MMP-8, and tumor necrosis factor (TNF)-a were measured with Human Magnetic Luminex screening assay. We tested cervical swab specimens using real-time PCR assays for detection of
ureaplasma spp. colonization. Histological chorioamnionitis was diagnosed when acute inflammation was observed in any placental tissues.

Results: The incidence of ureaplasma spp. colonization was 52.2% (60/115). Mean maternal age in ureaplasma positive group was significantly lower than in ureaplasma negative group (31.6±4.5 vs. 33.9±3.5, p=0.002). However, there were no significant differences in parity, preterm labor, premature rupture of membrane, fetal distress, gestational age, birth weight, Apgar scores (1min, 5min) with or without ureaplasma spp. colonization. On the other hand, the incidence of histologic chorioamnionitis was 21.7% (25/115). There was not a significant correlation between histologic chorioamnionitis and ureaplasma spp. colonization (p=0.073). In terms of cytokine expression, IL-6, IL-10, and MMP-8 levels were significantly different according to ureaplasma spp. colonization. In 25 cases with histologic chorioamnionitis, IL-6 level was significantly different according to ureaplasma spp. colonization (p=0.034). In 90 cases without histologic chorioamnionitis, there were no significant differences in inflammatory cytokines with or without ureaplasma spp. colonization (p>0.05). There were not also significantly different in inflammatory cytokines of amniotic fluid between U. urealyticum and U. parvum.

Conclusions: Ureaplasma spp. colonization augments significantly inflammatory cytokines in the women with histologic chorioamnionitis. In the women without histologic chorioamnionitis, ureaplasma spp. colonization is not significantly associated with increased inflammatory cytokines of amniotic fluid.
TOPIC: INFECTIONS

ABSTRACT ID: 207

TITLE: MATERNAL FETAL INFECTIONS AND LONG TERM NEURODEVELOPMENTAL OUTCOMES IN CHILDREN INFECTED AND UNINFECTED AT BIRTH


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CONTENT

Background. Infections during pregnancy can be transmitted to the fetus and may cause brain injury and delayed psychomotor development.

Aim of the study. To explore the association between presence and time of the onset of symptoms and sequelae in children born from infected pregnant mothers, observed in a "long term follow-up".

Methods. We evaluated 112 children born to women with congenital infections at an age of 24 months by a long term multidisciplinary follow up (Cytomegalovirus, n=72; Toxoplasma gondii, n=35; Syphilis, n=31).

Results. We diagnosed congenital infection in 93 infants (67.9%); 26 out of them (20.3%) were symptomatic at birth. At 12 months of age symptomatic children obtained lower scores in cognitive (p=0.04) and in motor Bayley III scales (p=0.02), compared with asymptomatic and uninfected children, without differences related to the type of infection. Most severe or moderate sequelae rose up within the first year of life. At 24 months, 17 (63%) children, who were symptomatic at birth, showed one or more adverse outcomes. The presence of symptoms at birth was predictive of adverse outcomes after controlling for birth weight, type of infection and time of the
maternal infection (P = 0.01). Five asymptomatic children showed lower scores than uninfected children on scales of language at 24 months.

Conclusion. The multidisciplinary follow-up should be performed in all newborns from pregnant infected women. Minor sequelae may become evident in infected children, who are asymptomatic at birth, up to an age of 2-4 years. Neonates with congenital infection, who are symptomatic at birth, have a worse prognosis than infected asymptomatic neonates.
Abstract:
Background: Extracellular vesicle (EV) mediated communication between the female reproductive tract and the pre-implantation embryo seems to play an essential role for the successful establishment of pregnancy (Ng, 2013). In addition, it is well documented that, Toll-like receptor (TLR) activation will influence trophoblast-endometrial interactions (Sanchez-Lopez, 2014). TLR5 is responsible for the recognition of bacterial flagellin, initiating a signaling cascade that results in the production of proinflammatory cytokines, including IL1-β and IL-6 (Honko, 2005). This study investigated how IL1-β and IL-6 expression in endometrial RL95-2 cells in co-culture with human choriocarcinoma (JAr) spheroids, alters in the presence/absence of flagellin. In addition we also investigated the characteristics of EVs secretion in RL95-JAr spheroid co-cultures.

Methods: A two-dimensional culture system was used to study human trophoblast-endometrial interaction prior to implantation. RL95-2 cells were co-cultured with JAr spheroids, separated by an insert, in DMEM/F12 EV-depleted media for 24 hours. Subsequently, inserts were removed and RL95-2 cells were stimulated with 100ng/ml of the TLR5 specific ligand flagellin,
for 8 hours. RL95-2 RNA was extracted, reverse transcribed, and qPCR was performed. EVs were isolated from conditioned media using size exclusion chromatography and EV size, concentration and zeta potential evaluated by nanoparticle tracking analysis.

Results: When exposed to flagellin, RL95-2 cells in co-culture with JAr spheroids showed significantly higher IL1-β and IL-6 expression compared to RL95-2 cells cultured alone (p < 0.05). The size and concentration of EVs in conditioned media of RL95-JAr spheroid co-cultures were significantly different to EVs secreted by RL95-2 cells alone (p < 0.05).

Conclusion: These findings indicate that in the endometrial epithelium, stimulation of the TLR5-mediated innate immune response by bacterial infection may be more pronounced in the presence of the embryo. In addition, bacterial flagellin may influence EV-mediated endometrial-trophoblast communication, indicating a possible diagnostic tool for infection-induced embryo implantation failure.

References:
INTRODUCTION
Early pregnancy loss, IVF failure, intrauterine fetal death, premature delivery, placental abruption, preeclampsia, IUGR may not only worsen the normal course of pregnancy and birth, but also deteriorate the health of the woman in the immediate future. It happens due to the fact that the pathogenic effects of hereditary thrombophilia and hyperhomocysteinemia become noticeable starting with implantation, trophoblastic invasion and placentation. In recent years, due to the Polymerase Chain Reaction (PCR), it has been possible to diagnose a number of genetic defects that create a predisposition to thrombosis, allowing us to clarify concerning the serious forms of pregnancy complications.

MATERIAL AND METHODS
In order to achieve the aim and objectives of the research, we conducted a cross-sectional study within the Obstetrics and Gynecology Department of the "Nicolae Testemitanu" State University of Medicine and Pharmacy Public Institution and the Municipal Clinical Hospital no. 1 Public Medical Sanitary Institution during 2017-2018.
The study was conducted on a group of 114 women of fertile age with bad obstetric history of unknown etiology, including: preeclampsia, eclampsia,
missed abortion, antenatal death, severe IUGR, severe placental abruption, early pregnancy loss, late pregnancy loss. The study protocol was approved by the Ethics Committee of the “Nicolae Testemițanu” State University of Medicine and Pharmacy Public Institution.

The following polymorphisms have been identified: MTHFR C677T, MTHFR A1298C, MTR A2756G, MTRR A66G, FII G20210A, FVL G1691A, FXIII G103T, PAI-1 4G/5G.

Results. The current study included 114 women aged 21-42 years [mean 31.09±0.5 years] with bad obstetric history of unknown etiology: early pregnancy loss – in 73 (64.0%) women, late pregnancy loss – in 20 (17.5%) women, antenatal death – in 10 (8.8%) women, missed abortion – in 8 (7.0%) women, preeclampsia – in 1 (0.9%) woman, eclampsia – 1 (0.9%) woman, severe IUGR – 1 (0.9%) woman.

The frequency of hereditary thrombophilia types in women with bad obstetric history in descending order. PAI-1 4G/5G – in 86 (75.4%) women (including the heterozygous type in 52 – 45.6% of women and the homozygous type in 34 – 29.8% of women), MTRR A66G – in 84 (73.6%) women (including the heterozygous type in 73 – 64.0% of women and the homozygous type in 11 – 9.6% of women), MTHFR A1298C – in 74 (64.9%) women (including the heterozygous type in 62 – 54.4% of women and the homozygous type in 12 – 10.5% of women), MTHFR C677T – in 56 (49.1%) women (including the heterozygous type in 52 – 45.6% of women and the homozygous type in 4 – 3.5% of women), MTR A2756G – in 53 (46.5%) women (including the heterozygous type in 43 – 37.7% of women and the homozygous type in 10 – 8.8% of women), Factor XIII G103T – in 50 (43.9%) women (including the heterozygous type in 41 – 36.0% of women and the homozygous type in 9 – 7.9% of women), FVL G1691A – in 13 (11.4%) women (heterozygous type) and Factor II G20210A – in 2 (1.8%) women (heterozygous type).

Harmful factors – in 37 (32.5%) women (smoking was reported by 2 women – 1.8%, and noxious working environment – by 35 – 30.7% of women), comorbidities (endocrine, vascular) – in 3 (2.7%) women and large varicose veins – in 5 (4.4%) women.

The obstetrical status revealed from 0 to 10 previous pregnancies [mean 2.4±0.2 pregnancies], live births in 28 (24.6%) women, including 1 living child in 24 (21.1%) cases, 2 living children in 4 (3.5%) cases and 3 living children in
1 (0.9%) case. Births were on term in 26 (22.8%) women and premature in 3 (2.6%) women.

Conclusions.
1. Hereditary thrombophilia in women with bad obstetric history is frequently determined by the following: PAI-1 4G/5G was found in 86 (75.4%) women, MTRR A66G – in 84 (73.6%) women, MTHFR A1298C – in 74 (64.9%) women, MTHFR C677T – in 56 (49.1%) women, MTR A2756G – in 53 (46.5%) women, Factor XII G103T – in 50 (43.9%) women, FVL G1691A – in 13 (11.4%) women and Factor II G20210A – in 2 (1.8%) women.
2. The most common forms of hereditary thrombophilia are the result of transmission of an abnormal gene from one of the parents (heterozygous mutation) and more rarely – from both parents (homozygous mutation).
3. In all the women from our study we found 1 to 6 forms of hereditary thrombophilia: one thrombophilic mutation was determined in 3 (2.6%) women, 2 thrombophilic mutations – in 13 (11.4%) women, 3 and more thrombophilic mutations – in 98 (86.0%) women.
**Content**

Background: Intrahepatic cholestasis of pregnancy (ICP) is characterized by the elevation of total bile acids (TBA). The primary concern in women with ICP is the increased risk of stillbirth. ICP is generally considered as ‘mild’ when TBA levels range from 10 to 39 mmol/L and ‘severe’ with levels greater than 40 mmol/L, although levels of TBA >100 mmol/L have been also
considered as a further threshold of severity. However, it is unclear if there are differences in predicting perinatal death and other outcomes between TBA 40-99 mmol/L cut-off and TBA>100 mmol/L cut-off. Thus, the aim of this meta-analysis is to quantify the association between levels of TBA in ICP (TBA 10-39, 40-99, and >100 mmol/L) and perinatal death.

Material and methods: MEDLINE, EMBASE, Scopus, Web of Sciences, and ClinicalTrial.gov were searched from the inception of each database to December 2018. Randomized, cohort, case-control, or case series studies reporting maternal and perinatal outcomes on women with ICP by the three pre-specified TBA levels (10-39, 40-99, and >100 mmol/L) were included. We excluded cases of twin gestations and studies of women with ICP randomized to an intervention or placebo or randomized to different interventions. The primary outcome was perinatal death, defined as stillbirths and neonatal deaths within 28 days. The analysis was performed with Pearson Chi-Square and Fisher’s exact test as appropriate. Continuous outcomes were compared using meta-regression with inverse variance weighting using reported sample sizes and standard deviations. Pairwise comparisons used a Bonferroni correction to control for multiple testing.

Results: Six articles including 1,280 singleton pregnancies affected by ICP were included in the systematic review. Out of the 1,280 singleton pregnancies affected by ICP included, 118 pregnancies had TBA>100 mmol/L. The risk of perinatal death was significantly higher in ICP with TBA>100 mmol/L, compared with TBA 10-39 mmol/L and 40-99 mmol/L (8/118, 6.8% vs 3/789, 0.4% vs 1/287, 0.3%; p<0.0001). In particular, the risk of stillbirth increased as TBA levels increased (2/789, 0.2% vs 1/287, 0.3% vs 7/118, 5.9%; p<0.0001), while no difference was found in case of neonatal death. There was a significantly higher risk of both spontaneous preterm birth (sPTB) (28/523, 5.4% vs 19/220, 8.6% vs 16/88, 18.2%; p<0.0001) and iatrogenic preterm birth – defined as induction of labor before 37 weeks of gestation - (iPTB) (45/415, 10.8% vs 29/134, 21.6% vs 24/67, 35.8%; p<0.0001) as TBA levels increased. The risk of meconium-stained amniotic fluid significantly increased when stratified according to TBA levels (76/840, 9% vs 57/310, 18.4 vs 37/117, 31.6; p100 mmol/L (3155±35.5 vs 2746±108.5; p=0.035). Apgar score < 7 at 5 minutes was significantly more frequent as TBA levels increased (5/762, 0.7% vs 2/310, 0.6% vs 6/116, 5.2%; p=0.001). However, a significant difference between TBA 10-39 mmol/L and 40-99
mmol/L was found only in case of iPTB and meconium-stained amniotic fluid. Conversely, no significant difference was found in neonatal deaths, GA at delivery, CD, PPH, SGA and admission to NICU when stratifying the analysis according to ICP severity.

Conclusions: This systematic review demonstrates that TBA >100 mmol/L was associated with a significantly higher incidence of perinatal death and adverse perinatal outcomes, including sPTB, iPTB, meconium-stained amniotic fluid, Apgar score < 7 at 5 minutes compared with TBA < 100 mmol/L, and the strength of this association persisted when comparing TBA >100 mmol/L both with TBA 40-99 mmol/L and TBA 10-39 mmol/L. These findings suggest that delivery in the late preterm period, between 34/0 and 36/6 weeks of gestation, may be reasonable for TBA >100 mol/L.
ABSTRACT ID: 4

TITLE: THE ASSOCIATION BETWEEN EXPOSURE TO NON-STERoidal ANTI-INFLAMMATORY DRUGS DURING PREGNANCY AND RISK OF SUBSEQUENT MISCARRIAGE: A SYSTEMATIC REVIEW

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CONTENT

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most common type of medication used by women during pregnancy. Despite this, concrete data on the risks associated with foetal NSAID exposure are limited. Recent concerns have been raised regarding NSAID use in pregnancy and a potential increased risk of miscarriage (spontaneous abortion); however, no definitive conclusion on the topic has been reached.

Objectives: The principal objective of this research is a reliable assessment of the relationship between foetal intrauterine exposure to NSAIDs and risk of subsequent miscarriage by synthesising the relevant evidence. Specifically, the following research question was proposed: Does the use of NSAIDs by women during pregnancy, compared with nil-use, increase the subsequent risk of miscarriage during that pregnancy?

Methodology: An extensive electronic database search was conducted using the terms ‘NSAIDs’, ‘miscarriage’, ‘pregnancy complications’ and ‘pregnancy outcome’. Multiple sources of grey literature were also searched. Returned records were screened for applicability through a three-stage process: title-screen, abstract-screen and, finally, full-text
At each stage, records were excluded if they did not meet pre-defined eligibility criteria. Comprehensive data extraction was completed for all included studies.

Results: The search returned 8,066 records of potential relevance, from which seven were ultimately included in this review, all of observational design. Significant heterogeneity was present across the included studies, and their results were largely inconsistent. However, on balance, an increased risk of miscarriage associated with prescription non-aspirin NSAID use during pregnancy was suggested, especially when exposure was near conception and for longer than one week. There was also evidence to support a potential class-effect (specifically of the propionic acid NSAIDs), but not a dose-response relationship.

Conclusions: The limited evidence available is suggestive of an increased risk of miscarriage following use of prescription non-aspirin NSAIDs during pregnancy. However, due to the small number of included studies, the results must be interpreted cautiously. There is significant need for further research targeting NSAID exposure during pregnancy, with risk of miscarriage particularised as the primary outcome.
TOPIC: MISCELLANEA

ABSTRACT ID: 96

TITLE: MATERNAL SMOKING IN PREGNANCY, FETAL BEHAVIOR & NEWBORN STATE: AN OBSERVATIONAL ULTRASOUND STUDY

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CONTENT

Background: Maternal smoking during pregnancy (MSDP) is associated with medical risk for the fetus and altered behavior in newborns. We hypothesize that MSDP will be associated with altered fetal behavior measured by observational ultrasound and altered newborn behavioral state.

Methods: Participants were 74 healthy mother-fetus/newborn pairs (36% smokers). MSDP was measured by maternal interview and verified by saliva cotinine. Mothers completed a 2nd or 3rd trimester fetal ultrasound including baseline, vibro-acoustic stimulus and recovery periods. Total activity, coordinated body movements, and isolated movements were coded using a modified Fetal Neurobehavioral Coding System (FENS). After delivery, newborn post-handling behavioral state was assessed by detailed observational coding.

Results: During 2nd trimester, MSDP-exposed fetuses showed greater activity and complex body movements in response to a vibro-acoustic stimulus. Exposed newborns showed increased arousal and spent more time crying. Fetal activity was significantly associated with newborn state.
Conclusions: MSDP is associated with alterations in fetal behavior detectable by ultrasound observation and increased newborn arousal and crying. Monitoring of fetal behavior via ultrasound offers a unique opportunity to identify at-risk infants. Associations between MSDP and increased newborn fussiness highlight opportunities for education and anticipatory guidance in the postpartum period.
TOPIC: MISCELLANEA

ABSTRACT ID: 201

TITLE: FEATURES OF THE NEONATAL PERIOD OF CHILDREN WITH BRONCHIAL ASTHMA

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CONTENT

Introduction. Bronchial asthma (BA) is one of the most common chronic respiratory diseases of childhood. The early administration of adequate basic therapy of the disease is the basis for achieving the effectiveness of its treatment. Due to the impossibility of performing a standard functional study of the lungs, the diagnosis of asthma in children younger 5 years causes some difficulties and is based predominantly on clinical and anamnestic data. Thus, an analysis of the neonatal period features in patients and increased alertness regarding the possible development of asthma in children will improve the effectiveness of its basic therapy and improve the outlook for the disease.

Objective of the research. To analyze the features of the neonatal period in children with asthma in order to improve the results of its treatment and prognosis.

Materials and methods. In the conditions of the pulmonologic department of the Regional Children's Clinical Hospital in Chernivtsi, 98 children with asthma were examined. The group included 63 boys (64.3%) and 35 girls (35.7%).

According to the classification of bronchial asthma in children, given in GINA-2015 and its subsequent versions, controlled asthma was observed in 14 (14.28 ± 3.4)%; partly controlled asthma - in 56 children (57.15 ± 4.3) and uncontrolled asthma was recorded in 28 (28.57 ± 4.5)%.

All children were analyzed for anamnestic data, in particular, the middle body weight at
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birth and the period of breast-feeding. The results obtained were analyzed by means of variational statistics methods using statistical program StatSoft Statistica v5.0. From the position of clinical epidemiology sensitivity (Se) and specificity (Sp) tests, and also absolute (AR), relative (RR) risk and odds ratio (OR) were evaluated with calculation of confidence intervals (95% CI).

Results and discussion. In the cohort of patients, the first children in the family were dominated (86.8%) and only 11.4% of the patients were born with a third or fourth child in the family (P<0.01). Probably such a distribution of school-age children is due to the fact that, according to the "hygienic" theory of the occurrence of asthma, children from the first childbirth had less contact with infectious agents, just because they did not switch T-helper II of the order of T-helper I.

The middle-weight of children at birth was 3495 ± 45.9 g, which corresponds to body mass index of infant newborns. However, patients whose body weight at birth was higher than 3500 g (58.2 ± 4.8%) dominated, at the same time, children with weight at birth was less than 2500 g noted only in (2.8 ± 1.6%) cases (P<0.01). The overweight at birth was associated with the risk of developing asthma as follows: AR – 0.65, RR – 3.17 (95% CI 0.98-10.1). The obtained results coincide with the literature data, which indicate that overweight at birth associated with a high risk of developing bronchial asthma.

Among the examined children, 87 patients (88.8 ± 3.4%) received breastfeeding up to 6 months, while only 11 patients (11.2 ± 3.1%, P<0.01) were on artificial feeding. Indicators of the diagnostic value of the presence of breastfeeding for the development of asthma in school-age children comparatively to the artificial one were marked by high sensitivity and specificity: 84.9% (95% CI 76.3-91.3) and 88.8% (95% CI 80.8-94.2). These data can be explained by the protective role of breast milk in relation to infectious factors, which contributes to a shift in domination of T-helper type II. Thus, in patients who were born the first in the family with overweight and who had breastfeeding more than 6 months, the risk of developing bronchial asthma was three times higher in future life.

Conclusions. 1. Overweight at birth is associated with a high risk of developing bronchial asthma in children (RR – 3.17 (95% CI 0.98-10.1)).
2. The presence of breast-feeding up to 6 months and longer was associated with the risk of developing bronchial asthma in children with a sensitivity of 84.9% and a specificity of 88.8%.

3. Children who were born the first in a family with overweight and had breastfeeding more than 6 months is determined by the high risk of implementing bronchial asthma, which should cause particular disturbance to district pediatricians for the timely detection and initiation of treatment of the disease.
TOC: MISCELLANEA

ABSTRACT ID: 251

TITLE: INTERACTIVE MEDICAL INTELLIGENCE UTILIZATION TO ACHIEVE OPTIMAL OUTCOME FOR NEONATE AND MOTHER

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CONTENT

Background
The landmark report in the United States by the Institute of Medicine in 2000, "To Err is Human, building a safer Health System" indicated that up to 90,000 Americans die from medical errors largely attributed to illegibility of medical orders and directives.
Current electronic medical record systems used worldwide solve the illegibility concerns. But the question remains, what about true quality of care?
The vast majority of systems today are used for tracking billing and inventory issues. No system has a checking system to assist the clinician in determining if a medical mistake has occurred or to identify medical risks for the fetus or mother.
An interactive medical intelligence (IMI) has the ability to assist the clinician to accurately, efficiently and rapidly deliver obstetrical care and dramatically reduce, if not eliminate, medical errors by using evidenced based algorithms in real time during the pregnancy. Risks are identified and reminders issued. An Interactive Medical Intelligence system was able to identify and prevent 388 errors out of 1,000 pregnancies.
Material and Methods
Seven busy obstetrical practices were selected to transfer the patient clinical information from their system, both paper and electronic based, into the Interactive Medical Intelligence system. Over a 1,000 pregnancies were followed until delivery. The number of omissions or inactions identified by the Interactive Medical Intelligence system were determined and tabulated. These were compared to the risks identified by the traditional methods and some of the standard commercial Electronic Medical Record vendors.

Clinical Cases & Summary Results
Seven obstetrical practices and 1,000 patients were enrolled in this study. 388 errors or omissions were detected when patient records were transferred to an Interactive Medical Intelligence system. This would extrapolate to 1,668,400 obstetrical errors annually in the USA. One can only imagine what this number might be if extrapolated globally.

Conclusions
As the Institute of Medicine has indicated, humans are human and are prone to making mistakes. When mistakes occur in obstetrics, the resultant problems can be lifelong for the neonate. Extrapolated over the 4.3 million births every year in the United States, approximately 1,668,000 omissions or inactions occur in the care of the pregnant patient. Some of these errors have the potential to lead to catastrophic outcomes for the child and family. This would include a financial burden and a medical legal impact affecting the family, clinician and hospital.

The dream has been to utilize computer technology to help humans reliably recognize risk factors, identify mistakes and take corrective actions. This has not been realized until now with the development of Interactive Medical Intelligence. This system follow the mother from conception through the postpartum period an is simple to use. Verify-IMI will be launching a free app. for the expectant mother to use word wide. We strongly believe together we can dramatically reduce maternal and neonatal morbidity/mortality globally.

An Interactive Medical Intelligence system collects data during the history and physical exam. Risks are identified and diagnostics are suggested. The results of these diagnostics may further identify additional or refine the
noted risks. The system never forgets, and continues to remind the clinician of outstanding results or if another test needs to be ordered. All abnormalities are noted on the front page so the clinician does not need to search the chart, especially in an emergency situation.

The Interactive Medical Intelligence system integrates with the commercial labs and interprets the data and does not depend on the commercial lab to identify abnormal labs. We have identified at least 7 situations when the commercial lab reported an abnormal result but did not flag the result and the result was not in red print. Unfortunately, in three situations, permanent harm occurred to the baby.

We believe all clinicians should use an Interactive Medical Intelligence system to act as a “check and balance” system to help protect the baby, mother and clinician.

The Interactive Medical Intelligence system also enable the patient to be more involved in her care and will improve communication with her providers.

End result: optimal outcome.
TOPIC: NEONATAL HAEMODYNAMICS

ABSTRACT ID: 237

TITLE: THE RELATION BETWEEN CAPILLARY REFILLING TIME AND KIDNEY INJURY IN ASPHYXIATED PRETERM INFANTS

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CONTENT

Introduction: Fetal and neonatal “asphyxia” are the main causes of transient renal impairment or acute kidney injury (AKI) in neonates. The mechanism of renal impairment in perinatal asphyxia includes diminished renal blood flow due to hypovolemia and hypotension, which can lead to impaired GFR and tubular function. One of the specific sign of circulatory status is a capillary refilling time (CRT). The goal of this study is to assess the relationship between CRT and clinical and biochemical markers of AKI.

Material and methods: Premature infants with gestational age of 31-36 weeks with perinatal asphyxia admitted to the NICU were divided into three groups: 8 infants with CRT 0-3 seconds, 43 infants with CRT 4-7 seconds and 9 infants with CRT 7-10 seconds. Renal function was evaluated by detecting urinary output (UO) and kidney injury molecule (KIM-1) level in urine. CRT was measured with a manual stopwatch. Statistical comparisons between groups were performed using the Mann-Whitney test.

Results: The mean level of KIM-1 and UO were 0.21±0.038 ng/ml and 1.8±0.6 ml/kg/h in the first group of newborns, 0.31±0.045 ng/ml and 1.6±0.2 ml/kg/h in the second group and 0.7±0.152 ng/ml(p<0.05) and 1.0±0.3 ml/kg/h respectively in the third group.

Conclusion: High level of KIM-1 in infants with prolonged CRT has indicated that CRT may serve as a useful clinical sign of renal injury in asphyxiated
newborns facilitating the early diagnosis of the disease. The absence of reliable dependence between UO and CRT could be explained by the greater content of total body water percentage and immature tubular development in premature babies.
TOPIC: NEONATAL HAEMODYNAMICS

ABSTRACT ID: 304

TITLE: A UK NATIONAL SURVEY ON THE CURRENT PRACTICE OF USING PARACETAMOL TO TREAT PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS

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CONTENT

INTRODUCTION
Haemodynamically significant patent ductus arteriosus (hsPDA) can be treated surgically or medically with one of two prostaglandin inhibitors, indomethacin or ibuprofen. Evidence is emerging that paracetamol is a safe and effective alternative therapy for hsPDA. Although there is no consensus opinion on its routine use for PDA in preterm infants, paracetamol is being used increasingly in many centres to treat hsPDA.

OBJECTIVE
We conducted a national survey across the United Kingdom (UK) to look at the current national practice of PDA treatment using paracetamol in preterm infants.

METHODS
All the local and tertiary neonatal units across the UK were contacted between May and August 2018 through a web-based and telephone survey. They were asked 10 questions on the use of paracetamol for hsPDA in preterm infants, including choice of medication for hsPDA, dosage and duration of paracetamol if used.

RESULTS
Out of 146 units, 143 (98%) responded; 46% were tertiary and 54% were local units. Survey responders included consultants (17%), registrars (29%), SHOs
(8%), ANNPs (8%), senior nurses (36%) as well as associate specialists and pharmacists (1%).

First line medication for hsPDA treatment was ibuprofen in 92% (131/143), indomethacin in 3% (4/143) and paracetamol in 2% (3/143) of units. 3%(5/143) of the units did not provide medical treatment for PDA. 33%(47/143) of the units use paracetamol; 3 out of whom use it as a first line and 44 use it as a second line. Indications of its use as a second line are contraindications for the first line in 55%(24/44), failure of the first line in 18%(8/44), complications of the first line 14%(6/44) and consultant preference in 14%(6/44) of the units. 62% of the units use a dose of 15mg/kg QDS. Duration of paracetamol varies with 3 and 5 days are the most common in 33% and 31% of the units respectively. 60% of the units give 1 course of paracetamol, while 40% give 2 courses. Table 1 44% of the units do routine blood investigations for monitoring patients, 23% use liver function tests (LFTs) only, paracetamol level and routine blood investigations are used in 19%. 90% of the units require verbal consent while written consent is required by 11%. Table 1

CONCLUSION

Our survey revealed that although there is no strong evidence to support its routine use, 33% of neonatal units across the UK offer paracetamol to treat hsPDA in preterm infants. Currently, there is wide variation in practice regarding the dose, duration of paracetamol and monitoring of infants during treatment. One strategy would be to develop national guidance once we get strong evidence to support its routine use for hsPDA.
TOPIC: NEONATAL INTENSIVE CARE

ABSTRACT ID: 7

TITLE: EFFECT OF ORAL ZINC SULFATE ON HYPERBILIRUBINEMIA OF LOW BIRTH WEIGHT NEONATES

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CONTENT

Introduction: Jaundice is considered as a common clinical condition during infancy. In preterm newborn hyperbilirubinemia is higher, persistent, longer, and more likely to be associated with neurological injury than term neonates. In some animal studies, zinc elements were found effective in reducing jaundice. The aim of study was to determine the effect of oral zinc sulfate on hyperbilirubinemia in low birth weight (LBW) infants.

Materials & Methods: This randomized, double-blind clinical trial was performed on 61 icteric LBW neonates (IRCT201401041162N22). Included neonates were randomly placed in two groups (case and placebo) and their total serum bilirubin (TSB) was measured at 0, 24, 48, 72, 96, 120 hours after start of treatment. The participant received either 10 mg of zinc sulfate or placebo twice daily till day five or end of treatment. The termination point of phototherapy was defined as a bilirubin level less than 50 percent of exchange point. Data were analyzed using SPSS software version 16 and T-test, Chi-square and repeated measurement ANOVA.

Results: According to age, sex, birth weight, gestational age, hemoglobin, reticulocyte count, blood group, kind of feeding and level of G6PD, two groups were comparable. Mean Baseline total serum bilirubin levels were 14.87±2.65 and 14.73 ±3.22 mg/dL in zinc and placebo groups. Mean (SD)
Duration of treatment were 58.84±14.97 and 65.60±16.59 hours in zinc and placebo groups (P=0.0). Mean reduction of TSB after 24 hours 2.71 mg/dl and 2.13 mg/dl (p=0.04) and after 48 hours 5.59 mg/dl and 4.94 mg/dl (p=0.19) and after 72 hours 6.65 mg/dl and 6.70 mg/dl (p=0.95) in zinc and placebo groups respectively. Mean reduction of TSB in 69 and 120 hours after treatment were also not significant in two groups. Duration of treatment and phototherapy and hospitalization were the same in two groups.

Conclusion: Overall current study showed that the administration of oral zinc sulfate for icteric LBW infants reduces TSB significantly only at first 24 hours of treatment.
TOPIC: NEONATAL INTENSIVE CARE

ABSTRACT ID: 47

TITLE: EARLY RESPIRATORY SUPPORT FOR MECONIUM ASPIRATION SYNDROME- IS HIGH FLOW NASAL CANNULA (HFNC) AN ANSWER?

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CONTENT

Introduction:
Meconium aspiration syndrome (MAS) occurs in around 5% of pregnancies with meconium stained amniotic fluid. Supplemental oxygen administration is the mainstay of treatment for MAS infants. If infants require escalation of respiratory support, mechanical ventilation remains the only option of treatment, which has multiple associated complications.

Objectives:
In this trial we wanted to study if the use of high flow nasal cannula (HFNC) as primary respiratory support reduces the need for mechanical ventilation in moderate MAS.

Material and Methods:
It was a randomized controlled trial in Infants with gestation > 35 weeks and birth weight >2 kg who had moderate MAS (Downe score>2 and x-ray features suggestive of MAS). Infants were randomized within 24 hours to either standard therapy with oxygen by hood or HFNC groups. Primary outcome was need for mechanical ventilation within 7 days.

Results:
After excluding 20 infants, 60 infants were randomized into standard and intervention group. Baseline characteristics were similar between the two groups. The need for mechanical ventilation was similar between the two
groups. It was 7 (24.1%) in the control group versus 6 (19.35%) in the HFNC group. (p = 0.70).
However, the onset of mechanical ventilation (hours) was significantly delayed in the HFNC group [median (IQR):10(8.24) vs 67(47.25,101.5) p <0.001] and the duration of mechanical ventilation also was significantly lesser in the HFNC group [Median:5(4,7) vs 3.25(2.25,3.875) p= 0.004].

Conclusion:
Though the need for mechanical ventilation was similar in the two groups, the onset of mechanical ventilation was significantly delayed in the HFNC group and the duration of mechanical ventilation was significantly shorter.
TITLE: THE EFFECTIVENESS OF SURFACTANT REPLACEMENT THERAPY IN LATE PRETERM NEONATES WITH SEVERE RESPIRATORY DISORDERS. A RETROSPECTIVE COHORT COMPARATIVE STUDY

AUTHORS: O Ionov 1,2; E Kim 1; T Kosinova 1; A Kirtbaya 1,2; E Balashova 1; A Ryndin 1,2; V Zubkov 1; D Degtyarev 1,2

AFFILIATIONS: 1 National Medical Research Center of Obstetrics, Gynecology and Perinatology named by V.I. Kulakov, Moscow, Russia
2 Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University of the Ministry of Healthcare of the Russian Federation (Sechenovsky University)

CONTENT

Introduction. Surfactant replacement therapy in early preterm infants significantly improves outcomes and reduces mortality. However, the advisability of surfactant therapy for late premature newborns (gestational age 34-36 weeks) is not clearly defined. There are no available data about the effect of surfactant replacement on the total duration of respiratory therapy, the use of mechanical ventilation, length of stay in neonatal intensive care unit (NICU) for this population.

Material and Methods. We have analyzed the hospital neonatal records of 71 newborns with gestational age of 34 and 35 weeks, who were admitted to NICU of National Medical Research Center of Obstetrics, Gynecology and Perinatology named by V.I. Kulakov (NMRCOGP n. by V.I. Kulakov) for the period from January 2013 to December 2015. The study included late preterm infants, who needed respiratory support from the first day of life and were stabilized on non-invasive respiratory support when being admitted to NICU and then had a progression of respiratory disorders in the first day of life and met the criteria of failure of initial non-invasive respiratory therapy as follows: FiO2 > 0.4 and / or Silverman score ≥ 4. All patients were
divided into 2 groups. In the first group of newborns (n=32), INSURE with poractant alfa with initial dose of 200mg/kg was performed when we saw the criteria of initial non-invasive respiratory therapy failure. Newborns of the second group (n=39) were switched to the next step of respiratory therapy without using surfactant. Indication for high frequency oscillatory ventilation (HFOV) was: conventional ventilation failure (ventilation settings required for SpO2 91-95% and PaCO2 35-55 mmHg with pH > 7.22) were: Mean airway pressure (MAP) ≥ 12 cm H2O and FiO2> 0.5. These indications for HFOV were identical for both groups. The analyzed groups were comparable (p>0.05). The length of stay in NICU, the duration of respiratory therapy, significant outcomes, including the need for conventional mechanical ventilation and HFOV were assessed in both groups.

Results. Our study showed that the need for conventional mechanical ventilation in group 1 and group 2 did not differ significantly: 47% vs 59%, OR 0.652 [0.238; 1.692]. In the meantime, newborns from the second group (treatment without surfactant) significantly more often were in need of "hard" parameters (Mean airway pressure ≥ 12 cm H2O and FiO2 > 0.5) of conventional ventilation (6% vs 28%, p=0.0286) and therefore significantly more often required HFOV OR 0.17 [0.034; 0.85] without significant increasing the duration of respiratory therapy (Me: 88 vs 114 hours) and the length of stay in NICU (Me: 6 days in both groups). There was no incidence of intraventricular hemorrhage grade II-III in group 1 but one case in group 2 (not significant). There was no significant differ between group1 and 2 in nosocomial pneumonia (9% vs 8%), pulmonary bleeding (0 vs 2 cases). There was an absence of NEC, ROP, PDA and BPD in both groups. In group 2 the requirement of inotropes and/or vasopressors therapy was higher than in group 1 (31% vs 13%), although there were no statistically significant differences: OR0.322 [0.091; 1.137].

Conclusions. In our study surfactant therapy did not affect the need for conventional mechanical ventilation, the length of stay of newborns in NICU and main outcomes. Therefore the internal guide-line NICU of NMRCOGP n. by V.I. Kulakov does not provide the surfactant replacement in late preterm infants for routine use. Well-timed and correct HFOV in late preterm infants is a qualitative and cheaper alternative to surfactant therapy.
TOPIC: NEONATAL INTENSIVE CARE

ABSTRACT ID: 311

TITLE: USING UMBILICAL CORD BLOOD FOR NICU ADMISSION LABORATORY TESTS: CURRENT PRACTICE AND LITERATURE REVIEW

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CONTENT

Background:
Infants at the Neonatal Intensive Care Unit (NICU) usually experience the largest blood loss on the admission day due to laboratory testing. It is well known that phlebotomy loss is one of the major factors associated with increased red cell transfusions in premature and critically ill neonates. Opportunity to obtain admission laboratory tests from the otherwise discarded cord blood may be one of the ways to prevent the development of early anemia and avoid blood transfusion. Common samples that collected from cord blood immediately after delivery are cord blood gases. By drawing initial laboratory blood tests (CBC, diff, blood type, and antibodies screen, Direct Antibody Test, bilirubin level, blood culture, and metabolic screening) from Umbilical Cord Blood (UBC) health practitioners can minimize blood testing on the neonates, that is especially important for very low birth weight (VLBW) infants.

Objective:
The purpose of this literature review was to determine the current situation with the laboratory use of UBC for NICU admission tests.

Methods:
Medical electronic databases such as Google Scholar, Ovid Medline, PubMed, CINAHL, EMBASE, the Cochrane Library, Science Citation Index and Evidence-Based Emergency Medicine were used.
Search terms included: newborn, prematurity, VLBW, umbilical cord blood, laboratory testing, admission tests, transfusion tests, placental blood tests, cord blood sampling.

Results: 618 records were identified through database searching; 79 full-text articles were assessed for eligibility. Inclusion criteria: all RCTs, cohort and case-control studies relevant to the subject of UCB laboratory testing. 48 studies were included in the final review. Reviewed studies were highly heterogeneous in design, approach, laboratory tests used and recommendations. The majority (47 studies) of researchers are in support of using UBC for blood type and antibiosis screen testing. 75% of studies showed high correlation CBC, diff on UBC with neonatal samples. 66.75% of reviewed sources showed high reliability of blood microbiology performed on the UBC for negative cultures, and heterogeneous results for the true positive reports. Very few sources reported the significance of contamination for UBC (0.4%). There are three ongoing clinical trials on the UBC use for metabolic screening.

Conclusion
We anticipated that the studies included in this literature review might be heterogeneous and planned to use Q and I² statistics to assess heterogeneity between studies and determine if meta-analysis was appropriate. Unfortunately, due to limited literature sources, we were unable to come to a clear conclusion with respect to our research question.
TOPIC: NEONATAL RESUSCITATION

ABSTRACT ID: 39

TITLE: A CLINICAL SCORING SYSTEM TO PREDICT THE NEED FOR EXTENSIVE RESUSCITATION AT BIRTH IN VERY LOW BIRTH WEIGHT INFANTS

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CONTENT

Objectives: To analyze the risk factors for extensive cardiopulmonary resuscitation in the delivery room and develop a prediction model for outcomes in very low birth weight (VLBW) infants.

Methods: The sample was 5298 VLBW infants registered in the Korean neonatal network (KNN) database from 2013 to 2015. Univariate and multivariate analyses were used to analyze the risk factors for extensive resuscitation. In addition, a multivariable model predicting extensive resuscitation in VLBW infants was developed.

Results: Lower gestational age and birth weight, and male sex were associated with extensive resuscitation. Maternal characteristics predicting extensive infant resuscitation were hypertension, abnormal amniotic fluid volume, histologic chorioamnionitis, and less use of antenatal steroid. The final prediction model for extensive resuscitation included gestational age, amniotic fluid, and antenatal steroid use.

Conclusions: Lower gestational age, abnormal amniotic fluid volume, and less use of antenatal steroid in VLBW infants are important predictors of extensive resuscitation in the delivery room.
TOPIC: NEONATAL RESUSCITATION

ABSTRACT ID: 91

TITLE: THE EARLY IMMUNOLOGICAL DIAGNOSTICS OF NEONATAL SEPSIS WITH RESPIRATORY PATHOLOGY

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CONTENT

Introduction: the sepsis diagnostics during the pre-clinical stage remains a most complex issue in neonatology.

Purpose: increasing the efficiency of sepsis diagnostics.

Materials and Methods: the randomized controlled clinical testing was performed on 200 full-term newborns with respiratory pathology admitted to the Intensive Therapy department for artificial pulmonary ventilation during the first 24-hour period of their lives; no clinical signs of bacterial infection were diagnosed. On the 5th and 20th days after admission, the plasmic concentration of IL-1ß, IL-6, IL-8, TNF-a, G-CSF, s-Fas, FGF, NO was determined by capture ELISA; CD3+CD19-, CD3-CD19+, CD3+CD4+, CD3+CD8+, CD69+, CD71+, CD95+, HLA-DR+, CD34+, CD14+, CD3-CD56+, lymphocytes with expression AnnexinV-FITC+PI-, AnnexinV-FITC+PI+ were determined by means of immunophenotypical analysis.

By applying the statistical cluster population analysis of the immunological criteria under study we have evaluated the feasibility of sepsis diagnostics at the admission to the intensive therapy unit. The diagnostic rule for sepsis has been formulated by applying the "decision tree" approach to the "R" statistic medium.

Results: The cluster analysis confirms the presence of two clusters (presence of absence of sepsis: these two components explain the 60.81% of the point variability).
The diagnostic rule for the early diagnostics of sepsis is as follows: disease develops providing during the first 24 hours CD95≥16.8% and NO≤9.6 mkmol/l or CD95≤16.8% and CD34≤0.2% and CD69≥4.12% or CD95≤16.8% and CD34≤0.2% and CD69≤4.12% and lymphocytes with expression AnnexinV-FITC+PI-≥12.3%.

The accuracy of this diagnostics amounts to 95.41%; sensitivity to 97.06%; specificity to 94.67%; diagnostic false positive share to 5.33%; diagnostic false positive share to 2.94%; positive result accuracy to 89.19%; negative result accuracy to 98.61%.

Of the 200 patients accepted, 45 newborns featured the confirmed sepsis development.

Conclusions: A substantial part in developing sepsis is due to the prevailing of the alteration of immunocompetent cells over the proliferation and endogenic synthesis of NO.

The aggregate determination of CD95+, CD69+, AnnexinV-FITC+PI-, CD34+ and the plasmic concentration of NO enables the pre-clinical diagnostics of sepsis development.
TOPIC: NEW TRENDS IN NEONATOLOGY

ABSTRACT ID: 97

TITLE: IDENTIFICATION OF PARENTAL NEEDS IN A NEONATAL INTENSIVE CARE UNIT: A FIRST STEP IN THE DEVELOPMENT OF THE NEOPARENT MOBILE APPLICATION

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CONTENT

Background
The admission of a baby on a neonatal intensive care unit (NICU) is often acute and unexpected, announcing the beginning of an emotional, difficult period for parents. Such an admission can be very stressful, because parents are overwhelmed by a high amount of information, medical jargon and the critical care environment. Therefore, parents need personalised information and individual support. Also interaction and communication with caregivers and parent participation are important. Currently, there is no adequate solution to answer all questions of parents on the right moment, in a well-balanced manner, taking pathology, reason for admission and personal information needs into account. A digital solution, in particular a mobile application could be one of the solutions.
Objective
As a first phase of the development of a NeoParent© mobile application, parental needs and experiences in a NICU were identified. In addition, we explored to what extent a mobile application could be of added value to address these needs.

Methods
A descriptive qualitative approach was used consisting of semi-structured interviews. Parents were recruited between January –May 2018 at two university hospitals with a NICU and through social media. Inclusion criteria were (1) a NICU-admission less than 1 year ago, 18 year and Dutch-speaking. In total 11 semi-structured interviews, individual (n=5) or with both parents (n=6), were conducted. The interviews were audiotaped and transcribed verbatim. All data were coded using NVivo. Thematic analysis was performed to identify themes and patterns that emerged in the narrative content. Ethical approval was obtained from the ethical committees of the two university hospitals. All participant gave written informed consent. Anonymity and confidentiality were assured.

Results
Every far-reaching event seemed to be important for parents, in particular every progress or milestone however small, or any relapse in the situation of the baby. Parents identified four major key moments: (1) Initial admission as overwhelming moment, (2) medical events such as respiration support, nutrition, weight, operations, treatments, etc., (3) moments of intimacy in physical and figurative sense and (4) discharge to a local neonatal unit or at home (preparation, difference in caring).

Parents addressed the following themes: communication and information needs, role of caregivers, importance of a supportive environment, lived experience and emotions, influence of the infrastructure and facilities. Parents attached great importance to an open and honest communication as well as personalized, comprehensible information. They actively searched for information (books, Internet) and indicated the need of repetition, thereby using different information sources (visual, written, oral). Parents showed confidence in the knowledge, expertise and competences of caregivers. They expressed a need of continuity of care as well as psychosocial support. Parents perceived interaction and communication with caregivers as important and appreciated their
accessibility and humane touches. Nurses were considered as a central point of contact for parents. They were important to stimulate parent participation gradually and promote intimacy between parents and their baby, often realised by initiating small things, such as a personalised environment. Parents fell into a kind of survival mode and emotional rollercoaster, characterized by anxiety, uncertainty, stress, feelings of guilt, etc. Support was experienced mainly by caregivers, peers and to a lesser extent family and friends who had often difficulties to understand their situation. The (high-tech) infrastructure and facilities of the neonatal unit were insufficient to meet privacy and intimacy needs of parents. They mentioned lack of an individual room and distraction during their stay at the unit.

Conclusions
This study highlights the needs of parents on NICU including personalised information, communication, interaction with caregivers, need of intimacy, involvement and supportive environment from admission until hospital discharge. These parental needs should be addressed by health care providers on NICU. The results of this study can guide the development of a personalised mobile application to support parents with an admitted baby on NICU and to promote information, communication and parent participation.
ABSTRACT ID: 180

TITLE: HOW IS ARGinine INTAKE FROM PARENTERAL NUTRITION REFLECTED IN PLASMA ARGinine LEVELS OF THE PRETERM NEONATAL POPULATION? – A SYSTEMATIC REVIEW

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CONTENT

Background
Very preterm neonates (VPN) are defined as babies ≤28 days’ old following birth at ≤32 weeks for the purpose of this review. VPN are unable to digest breast milk and therefore rely on parenteral nutrition (PN) formulations. Arginine is an amino acid (AA) that is part of the protein supplied from PN. It is a conditionally essential AA in the VPN population and accounts for more than 12% of protein AA content. Arginine has four nitrogen atoms per molecule, making it the most abundant nitrogen carrier AA. This is reflected in the important role arginine plays in neonatal nutrition, metabolism, inflammation and infection function as well as synthesis of nitric oxide, creatine and polyamines. Term babies obtain arginine from human milk (4% arginine). Despite the low arginine content, intestinal metabolism of enteral arginine results in endogenous synthesis of arginine to ensure sufficient supply. Since enteral and parenteral arginine metabolism differs significantly, human milk is not a good model to design PN formulations. Although all current UK licensed AA formulations have arginine content more than 4%, studies have shown that these formulations commonly cause hypoargininaemia in VPN. In order to determine optimal arginine content
in PN for VPN, the first step would be to study the existing evidence in the literature to understand the relationship between PN arginine intake and plasma levels in this population.

Aims

The review research question was ‘In VPN, are high amounts of arginine in PN compared to low amounts of arginine, associated with appropriate circulating concentrations of arginine?’ The review aimed to (i) quantify the relationship between parenteral arginine intakes with plasma arginine levels in PN dependant VPN; (ii) identify any features of study design that affect this relationship and (iii) estimate the target parenteral arginine dose to achieve desirable preterm plasma arginine levels. This systematic review was prepared following PRISMA-P 2015 guidelines.

Methods

PubMed, Scopus, Web of Science and Cochrane were searched regardless of study design except that review articles were not included. The PICOS formula was used. Only articles that met the inclusion criteria were included. Data was obtained using a data extraction form devised for the purpose of this review. Arginine intake data were collected both as percentage content (% arginine) as well as absolute intake (mg/kg/day) to ensure AA composition as well as protein intake effects were taken into consideration. The main outcome was the plasma arginine levels of VPN. Secondary outcomes included type of study design, type of AA intake reported and also type of AA analysis technique used. These were used in studying possible bias factors that affected primary outcome of the study. Quality assessments of the articles included as well as the data extracted were done.

Results

12 articles met the inclusion criteria. The dose concentration relationship of arginine content (%) and absolute arginine intake (mg/kg/day) with plasma arginine levels showed a significant positive correlation and regression equations (p<0.05). Arginine, limiting the ability to interpret the relationship between parenteral arginine and plasma arginine levels at high dose. It is of note that this group of infants were in the intervention arm of a RCT (19% arginine) that showed key clinical benefits for arginine supplementation (reduced NEC incidence). This may indicate that the plasma levels of arginine required for optimal clinical care in PN-dependent
infants are higher than the reference ranges quoted for healthy enterally fed infants.

Conclusions
This systematic review revealed a linear relationship between plasma arginine levels and both PN arginine content (% arginine) and arginine intake (mg/kg/day) in VPN. Further clinical studies using neonatal PN AA solutions with arginine content of >12% are required to investigate the optimal arginine intake and plasma arginine levels for this population.

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Mr Jamie Kirkham provided statistical support/advice.

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Introduction
Arginine (Arg) plays a vital and versatile role in nutrition and metabolism. Low plasma Arg levels have been reported in children with severe sepsis and Arg depletion has been shown to have effects on T-cell function with reduced T-cell proliferation. Preterm infants have underdeveloped Arg-synthetic pathways and a reduced intestinal mass for Arg production. As a result, Arg is an essential AA for the PN-dependent preterm infant. Our neonatal unit delivers standardised, concentrated, added macronutrient PN by a regimen of incrementally increasing protein, fat and energy intake over the first 7 days of life. We have previously shown there is both overprovision of essential amino acids (AA) and underprovision of some conditionally essential AA, including Arg, in current neonatal parenteral nutrition (PN) formulations. We conducted a physiological study assessing a range of doses of arginine (6-15%) alongside routine PN to address arginine deficiency and investigate its role in immune function. We hypothesised that arginine supplementation would affect gene expression that is consistent with changes in immune function.

Materials and Methods
Very preterm infants born <29 weeks’ gestation and/or <1200g were eligible for PN. Infants were assigned to receive standard PN only or standard PN
alongside a range of doses of arginine supplementation until day 10 of life. Blood samples were taken on day 3 and day 10 of life. Plasma AA levels were measured using ion exchange chromatography and RNA was extracted and used for microarray and qPCR. The study received the appropriate ethical and regulatory approval.

Results
The study included 26 infants with a mean gestational age at birth of 26+4 weeks and a mean birth weight of 855g. 8 infants received standard PN only (6% arginine), 12 received 12% arginine and 6 received 15% arginine. Plasma arginine levels were significantly higher on day 10 of life in the supplemented infants (mean 72.8 v 45.5 mol/L, p=0.03). Microarray and qPCR validation experiments showed significant changes in gene expression associated with immune system development between day 3 and day 10 of life (Image 1). Significantly differentially expressed genes were defined as those with a False Discovery Rate (FDR)-adjusted p-value of <5%. There were 215 differentially expressed genes identified on the microarray analysis with 115 being upregulated and 100 downregulated. KEGG and Ingenuity pathway analysis (IPA) of these differentially expressed genes link these changes to pathways involved in immune function, including B cell differentiation and activation, phagocytosis and pathogen recognition. qPCR validation experiments confirm significant up regulation in expression of mRNA of: B cell differentiation factors APRIL (p<0.01) and BAFF (p<0.05) and pathogen recognition receptors TLR2 (p<0.01) and TLR4 (p<0.05) between day 3 and day 10 of life.

Image 1 – Heatmap Day10/Day3 and HighArg/LowArg (Uploaded file)

Conclusions
Arginine supplementation can reduce arginine deficiency in PN dependent very preterm infants. Infants with normal (versus low) plasma arginine levels exhibit changes in immune pathways similar to the temporal changes seen from day 3 to day 10 of life. These gene expression changes are consistent with the development of a functional immune system.

References

TOPIC: PREDICTION OF DISEASE IN FIRST TRIMESTER

ABSTRACT ID: 5

TITLE: FIRST TRIMESTER ULTRASOUND FEATURES ASSOCIATED WITH SUBSEQUENT MISCARRIAGE: A PROSPECTIVE STUDY

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CONTENT

Background
First trimester miscarriage is common, affecting one in five pregnancies. Women symptomatic of miscarriage are offered an ultrasound scan to assess location, plurality, gestational age and pregnancy viability.

Objective
This study aimed to determine whether there were any differences in the early (<9 weeks gestation) ultrasound appearances of pregnancies that continued to be viable or resulted in subsequent miscarriage before 12 weeks gestation.

Methods
This was a prospective cohort study collecting clinical and obstetric history, ultrasound measurements and pregnancy outcome information from women who presented for ultrasound assessment prior to 9 weeks gestation. Standardised ultrasound measurements included mean sac diameter (MSD), yolk sac diameter (YSD), crown-rump length (CRL), fetal
heart rate (FHR), trophoblast thickness, trophoblast volume and mean uterine artery pulsatility index (meanUAPI). Regression models were fitted for each parameter and Z-scores compared between cohorts that progressed or miscarried after the scan but before 12 weeks gestation. Logistic regression analysis was used to create a prediction model for miscarriage prior to 12 weeks gestation based on the standardised ultrasound measurements recorded during the early first trimester scan.

Results
913 women were enrolled in the study including 863 (94.3%) that progressed and 50 (5.7%) that miscarried before 12 weeks gestation. The mean (range) gestational age of these groups were significantly different; 7+2 weeks (5+1 – 8+5 weeks) and 7+0 weeks (5+3 – 8+5 weeks) respectively (p<0.001). Comparison of Z-Scores for meanUAPI (0.00 (-0.07-0.07) vs. -0.48 (-0.82 -0.14); p=0.001), trophoblast volume (0.00 (-0.07-0.07) vs. -0.50 (-1.10-0.10); p=0.002), fetal heart rate (0.00 (-0.07-0.07) vs. -0.55 (-1.04 -0.06); p=0.031), MSD (0.00 (-0.07-0.07) vs. -0.52 (-1.05-0.00); p=0.05) demonstrated significant variation between the two groups. The proposed logistic regression model using a combination of MSD, YSD, FHR, trophoblast volume and meanUAPI resulted in an area under the receiver operator curve of 0.81. At a false positive rate of 30% the model resulted in sensitivity of 76% (95%CI 64-89%).

Conclusion
Fetal heart rate, meanUAPI, trophoblast volume and MSD measured prior to 9 weeks gestation are significantly reduced in pregnancies that subsequently miscarry prior to 12 weeks gestation. Combining these measurements into a prediction model for miscarriage may prove to be of value for ongoing pregnancy management in the first trimester.
TOPIC: PREDICTION OF DISEASE IN FIRST TRIMESTER

ABSTRACT ID: 230

TITLE: PLASMA LIPIDS IDENTIFY GESTATIONAL DIABETES MELLITUS IN EARLY PREGNANT STAGE

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CONTENT

Background
Gestational diabetes mellitus (GDM) is one of the major pregnant complications. Early prediction of GDM is important to minimize the risk of adverse outcomes to mother and fetus. However, current prediction of GDM typically relies on oral glucose tolerance test (OGTT) in the mid-trimester. Alternative prediction methods at early pregnancy have always been a research hotspot, and metabolomics is a promising approach to identify GDM biomarkers in the first trimester.

Objectives
We intended to determine the dynamic change of the circulating lipids throughout pregnancy in the plasma of GDM women using the liquid chromatography–mass spectrometry (LC-MS). We compared this lipid profiling in GDM pregnancies with the pregnancies of healthy controls, aiming to identify lipid markers associating with the onset of GDM.

Methods
Plasma samples of the first trimester (12th to 13th week), second trimester (20th to 22nd week), and third trimester (30th to 32nd week) from 100 GDM women and 100 normal pregnant women were retrospectively obtained
from the collaborative hospital. Lipid extraction of each plasma sample was performed following the standards protocols. Chromatographic analysis was performed with an Acquity UPLC system (Waters Ltd., Elstree, UK). Mass spectrometry was performed on a quadrupole time-of-flight (Q-TOF-MS) instrument (Xevo G2-XS QTOF, Waters Corporation, USA) operating in either negative (ESI−) or positive (ESI+) electrospray ionization mode. Identification of lipids was performed by Progenesis QI software and metaX software through searching the HMDB and Lipidmaps database.

Results
In ESI+ mode, 217 features were solely associated with GDM, and 456 features were uniquely associated with pregnancy duration. Specifically, DG lipids (61.73%) were associated with GDM, while CE (66.67%), Ceramides (70.73%), Lyso (78.57%), PS (66.99%), and SM (76.60%) were associated with pregnancy duration. In ESI− mode, most features were significantly associated with pregnancy duration yet independent to GDM. Using Random Forest (RF) analysis, 12 types of lipids, mostly DGs and TGs lipids, showed distinctive features between normal pregnant women and GDM women at each trimester. A receiver operating characteristic (ROC) analysis using these 12 features showed the area under the curve (AUC) of 0.813, 0.844, and 0.815 at the first, second, and third trimester, respectively. In particular, the alteration of DGs was strongly connected to the onset of GDM with a significantly higher level in GDM women comparing with normal pregnant women, especially at early pregnancy. Ethnicity may also contribute to the metabolite differences observed between GDM and normal pregnancy.

Conclusions
We found that in both health and GDM women, Ceramides, SM, PA, PC, PE, PG, and PS continued to rise in all three trimesters, while Lyso continued to decrease during the whole pregnant duration. Importantly, we observed that DGs and TGs were significantly up-regulated in the GDM women in the first trimester of pregnancy. The 12 lipid biomarkers had good ability to predict GDM with AUC=0.813 in early pregnancy and reached 0.844 in second-trimester. The prediction on second-trimester had been improved compared to the other early researches.
TOPIC: PREGNATAL DIAGNOSIS

ABSTRACT ID: 98

TITLE: PREDICTIVE ABILITY OF UTERINE DOPPLER VELOCIMETRY IN 1ST TRIMESTER TO DETECT GROWTH RESTRICTION

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CONTENT

Background: Restricted intrauterine growth (CIR) is an estimated fetal weight below the 3rd percentile or percentile between 3 and 10. These fetuses have an increase in morbidity and mortality, which seems to be reduced with the use of acetylsalicylic acid as prevention. If we identify these fetuses prenatally, the resulting complications are minor. For this reason, screening methods such as the measurement of Doppler indices of the uterine arteries have been developed. Persistent increases in IPmAUt have a higher risk of adverse perinatal outcomes. The measurement of the uterine arteries in 2nd trimester has better predictive capacity than in the 1st trimester. Some authors consider uterine Doppler in 1st trimester a useful tool for the prediction of early preeclampsia and other adverse outcomes and justify the use of prophylactic acetylsalicylic acid.

Objective: evaluate the predictive capacity of the IPmAUt 1st trimester in relation to the Restricted Intrauterine Growth.

Methods: A retrospective cohort study was conducted in patients assessed in the 1st trimester at the University Hospital of Fuenlabrada, from January 2017 to December 2017, with single pregnancies, CRL between 45-84 mm in 1st trimester ultrasound, maternal age > or equal at 16 years, absence of major fetal malformations in which the measurement of IPmAUt was made. In the case group, patients were selected with IPmAUt 1st > 2.30 (prophylaxis with acetylsalicylic acid 100 mg daily was started before week
16) while for controls those with an index ≤2.30 were selected and paired 1-to-1 with cases by age, tobacco and ethnicity. The clinical histories were reviewed and the outcome variables were collected. The qualitative variables were expressed with n° of cases and%. Quantitative variables with their mean and standard deviation or with median and interquartile range. The cohorts were compared with the chi-squared test, for qualitative variables and with Student’s t test for independent data or the median test for quantitative variables. The results have been adjusted with univariate logistic regression models. Relative effects are presented as odds ratios (OR) with 95% CI. Discrimination was calculated with the ROC curves and their area under the curve and with 95% CI. In all contrasts, the null hypothesis was rejected with an alpha error of less than 0.05. The packages used were SPSS see 20 and STATA see 15.

Results: The group of cases consisted of 95 patients who met the inclusion criteria, compared to 91 patients who formed the control group. In the group of abnormal uterines, there was a higher frequency of CIR before week 34 (8.5% vs. 4.4%, p = 0.256), of caesarean or instrumental delivery indicated by risk (16% vs 12.1%, p = 0.449). Statistically significant differences were found between both groups in the frequency of termination of pregnancy by PE or CIR (18.1% vs 8.8%, p = 0.045) with a tendency to statistical significance in the frequency of abnormal uterines in the 2nd trimester (19.1% vs. 6.4%, p = 0.009). A relation was observed between IPmAUt in 1º> 2.30, and a higher frequency of completion by PE or CIR (OR 2.29, 95% CI 1.00-5.73) and higher frequency of uterine in 2nd trimester with IPmAUt> 1.50 in the case group, both with statistical significance (OR 3.24, 95% CI 1.23-8.53). The relative effect of IPmAUt in 1st trimester> 2.30 was evaluated and it was represented as an area under the curve (AUC), both univariably (IPmAUt 2ºt> 1.50 AUC ROC 0.64 IC 95% 0.55-0.74) and adjusted for parity, antecedent of placental disease in previous pregnancy, ADT, PAPP-A and BMI levels (IPmAUt 2ºt> 1.50 AUC ROC 0.71 IC 95% 0.61-0.80).

Conclusions: Pregnant women with abnormal uterine result in the 1st trimester have more frequent CIR of onset before week 34 and higher rates of cesarean or instrumental delivery indicated by risk.
The presence of abnormal uterine in 1st trimester is related to the persistence of abnormal uterine during 2nd, although in those patients who normalize the uterine in the 2nd trimester, the risk of CIR decreases until it is practically the same as that of the population without alterations. It is also related to a higher frequency of completion by PE or CIR.

The predictive capacity of the IPmAUt $1^\circ t > 2.30$ in our study for CIR was low, but we consider that with abnormal $1^\circ$ IPmAUt ultrasound control of fetal growth in week 28-30 is recommended and to maintain a more strict control.
TITLE: THE INTRODUCTION OF 3D/4D BASED SPATIO – TEMPORAL IMAGE CORRELATION (STIC) DURING ROUTINE FETAL ANOMALY SCAN IMPROVES RATE OF COMPLETION OF FETAL CARDIAC EXAMINATION AND DECREASES REFERRAL FOR FETAL ECHOCARDIOGRAM.

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CONTENT

Objective:
To evaluate the role of STIC in completing fetal cardiac evaluation, during routine anomaly scan

Methods:
This is a longitudinal observational study at a single center. All the scans were performed by a single experienced feto - maternal specialist. 8750 patients had Routine anomaly scan including fetal heart examination according to ISUOG practice guidelines. Scan time was kept to the time frame allotted to routine anomaly scan. STIC technique both conventional and Electronic probes were used only when the examiner could not complete all the list recommend by ISUOG (ISUOG practice guidelines) which include demonstration of Situs and general aspect, atrial chambers, ventricular chambers and atrioventricular junction and valves. For the conventional STIC we employed a multiplanar approach, tomographic ultrasound imaging (TUI) and rendering approach. For electronic STIC, in addition to rapid acquisition of the volume we have used Biplane and sonoVCAD.
Results:
During the study time, 8750 patients were seen for routine anomaly scan. During study time, 52 patients were diagnosed with congenital cardiac defects. The total number of fetal malformations diagnosed during the time of the study was 350 which mean cardiac anomalies constituted (4%) of all fetal malformation in this study.
In 1312 patient (15%) of the total number of patients the examiner could not obtain the full images required as per ISUOG protocol. Accordingly both conventional and electronic STIC was used in this group, depending on the condition. In all these patients the obstetrician was able to complete the examination.
STIC was also applied to patients where a cardiac anomaly was suspected. More information with regards to these abnormal cases was found in 10% of the cases.

Conclusion:
In this study we have shown that using STIC technique we can obtain a volume of adequate quality which will allow us to complete the cardiac examination and reduce the number of cases referred to fetal cardiologists and hence decrease patient anxiety. STIC did not influence our detection rate of cardiac anomaly, however, when the diagnosis is made STIC added more information which helped us with our initial counseling.
TOPIC: PRETERM BIRTH AND PREMATURITY

ABSTRACT ID: 24

TITLE: LONGITUDINAL CHANGES OF URINARY BIOMARKERS IN LATE PRETERM INFANTS DURING EARLY NEONATAL PERIOD

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CONTENT

Background: Urinary biomarkers may be indicators of acute kidney injury (AKI), although little affecting serum creatinine. We aimed to find out the extent of kidney injury and longitudinal changes of urinary biomarkers during early neonatal period.

Methods: Thirty late-preterm infants were measured urine biomarkers and serum creatinine on postnatal days 1, 2, 5, and 7. Urine biomarkers included urine creatinine (uCr), osteopontin (OPN), epidermal growth factor (EGF), monocyte chemotactic protein-1 (MCP-1), neutrophil gelatinase-associated lipocalin (NGAL), T-H glycoprotein (THP), and liver fatty-acid-binding protein (L-FABP). Demographic and maternal data were recorded, including gestational age, nephrotoxic drug exposure, and maternal disease such as hypertension and diabetes during pregnancy.

Results: Mean gestational age, and birth weight was 34.4 ± 1.1 weeks, and 2153.4 ± 269.5 g, respectively. Eighteen infants (60.0%) were diagnosed as stage I AKI, and 20 infants (66.7%) treated with aminoglycosides. At the seventh day, the serum creatinine levels of all participants were with normal range. Serum creatinine levels at birth were correlated with maternal serum creatinine levels (r=0.627, P=0.001) and gestational age (r=0.392, P=0.035), but not with urine biomarkers. Serum creatinine was increased at the second day of life, and then decreased. Inversely to serum creatinine, the
ratio of urinary biomarkers to uCr were decreased at the second day of life, and then increased. There were no significant differences in urine biomarkers and serum creatinine during early neonatal period between infants treated with and without aminoglycosides. Gestational age (odds ratio [OR], 0.383; 95% Confidence interval [CI] 0.143-0.922, P=0.033) and serum creatinine levels at the first day (OR, 0.000; 95% CI, 0.000-0.1012, P=0.012) were associated with AKI in preterm infants. The ratio of urinary biomarkers and uCr at the first day were not associated with AKI. The longitudinal change of urinary biomarkers were not different between infants with and without AKI during early neonatal period.

Conclusions: In our study, there was no significant differences in longitudinal changes of urinary biomarkers in infants with AKI compared to infants without AKI. And serum creatinine levels in AKI infants were normalized at the seventh day. The therapeutic dose of aminoglycosides did not affect the serum creatinine levels and the ratio of urinary biomarkers to uCr.
Background: Children born extremely preterm have higher blood pressure (BP) than term-born children. This might be attributed to adverse developmental programming by altered early-life exposures. We assessed associations between nutrition, growth and hyperglycemia early in infancy, and BP at 6.5 years of age in children born extremely preterm.

Methods: Nutrition, growth and glycemia status data were collected from the Extremely Preterm Infants in Sweden Study (EXPRESS), a population-based cohort including infants born <27 gestational weeks during 2004-2007. At follow-up at 6.5 years of age, three BP measurements were performed at resting conditions and height and weight measured in a sub-
cohort of 171 children. Z-scores for systolic (SBP) and diastolic (DBP) blood pressures were calculated as outcomes.

Results: An increase of 1 g/kg/d in daily protein intake during postnatal weeks 1 to 8 was associated with 0.4 SD higher DBP at follow-up. An increase of 1 g/kg/d in daily carbohydrate intake during the same period was associated with 0.18 SD higher SBP and 0.14 SD higher DBP. Increase in weight and length was not associated with higher BP. Occurrence of neonatal hyperglycemia was associated with higher DBP.

Conclusions: Modifiable early-life factors, such as perinatal nutrition and neonatal hyperglycemia, have a role in the development of later cardiovascular outcomes in children born extremely preterm.
TOPIC: PRETERM BIRTH AND PREMATURITY

ABSTRACT ID: 161

TITLE: NOVEL PANEL OF MIDTRIMESTER PROTEIN BIOMARKERS PREDICT PRETERM BIRTH

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CONTENT

Introduction
The accurate prediction of spontaneous preterm birth (PTB) remains one of the greatest unmet needs in maternal-fetal-medicine. Although advances in perinatology and neonatology have seen increased survival rates for the extremely premature infant, the morbidity rate remains high. Healthcare costs for the short and long-term care of the premature infant are considerable. In recent decades, the incidence of PTB has continued to increase in most countries. The best-known predictors of preterm birth are short cervical length and a history of spontaneous preterm birth. However, over 60% of women will have no risk factors for preterm birth. Universal cervical length screening has been proposed but has not been widely accepted. Present methods of preterm birth prediction in conjunction with existing biomarkers fail to identify the majority of asymptomatic women who will deliver prematurely, thereby limiting the potential implementation of preventative and therapeutic treatments. We propose that our newly
identified suite of protein biomarkers (patent pending) detected in the cervicovaginal fluid (CVF) are predictive of spontaneous preterm birth. Our aim in this study was to validate an immunoassay-based multi-marker test that would, independently of other clinical risk factors, predict the potential for preterm birth (<35 weeks) based on samples obtained in the mid-trimester.

Materials and Methods

Patient recruitment – A sample of CVF from each asymptomatic pregnant woman was collected during their routine antenatal care from various clinics, located at two major hospitals in Melbourne, Australia, including one high risk clinic. Signed consent was obtained from all women and CVF sample collection was performed between 15 and 26 weeks’ gestation. CVF samples from 139 women were collected, 5 of whom experienced spontaneous preterm labour <35 weeks’ gestation.

CVF collection - A posterior vaginal fornix sample was obtained by insertion of a sterile bivalve speculum into the vagina and a sterile 15 cm double-tipped swab was placed into the posterior vaginal fornix for 30 seconds. The swab was removed and placed directly into a polypropylene tube containing 1 mL of sample collection buffer.

Protein analysis - Samples were assessed for protein concentration and each individual biomarker independently, utilizing an ELISA Immunoassay method. The assays were conducted with internally developed protocols optimized for the use of CVF samples. The raw concentration values were then used in statistical analysis and algorithms.

Data collection - Data collection was initially conducted in Case Report Form (CRF) format followed by entry into a central database. This allowed the anonymization of patients and collection of further data from hospital records to enable a comprehensive understanding of the patient’s outcomes and birth related features.

Statistical analysis - Results were divided into two groups on the basis of gestational age at birth < 35 weeks’ gestation or greater than or equal to 35 weeks’ gestation. The groups were compared using a 2-tailed, non-paired t-test.

Results

This study validates a retrospective study conducted by the same research group. The multivariate biomarker models based on specific biological
pathways produced mini panels that indicated sub-groups of preterm birth. These mini-panels identified a significant difference between the two groups (P<0.0091 for all panels). By combining the mini-panels, a ROC curve was obtained with AUC of 0.814. Finally, the mini-panel models were combined into a singular binary result with a sensitivity of 80% and specificity of 93% to detect the outcome of preterm birth less than or equal to 35 weeks’ gestation.

Conclusion
Whilst these results require revalidation in a larger cohort, this has the potential to generate a novel test that would predict preterm birth, weeks or even months prior to any clinical presentation, thereby addressing this important unmet need in asymptomatic women. Accurate prediction of spontaneous preterm labour would allow triage of pregnant women into appropriate models of care with the aim of preventing or delaying the onset of labour and to improve preterm survival with the fewest complications.
Background: Evidence for stem cells as a potential intervention for neurological diseases is emerging. Existing trials working with autologous umbilical cord blood (UCB) cells mostly involve mature neonates with hypoxic brain damage or metabolic/immunological diseases affecting the brain (e.g. autism, Krabbe’s disease). It is unclear whether UCB collection is feasible for other neonatal populations at high risk of brain damage, such as very early preterm gestations. Collection of UCB in this critical risk group is organisationally and technically challenging, late cord clamping and anatomic conditions may reduce the availability of UCB.

Study design: Candidates for UCB collection were infants born between 12/2017-12/2018 from 4 high-risk groups: Perinatal symptomatic hypoxemia, gestational age ≤30+0 weeks of gestation, intrauterine growth restriction (IUGR) and monochorionic twins with twin-to-twin transfusion syndrome (TTTS). Feasibility of the collection (successful patient enrolment, technical realization, puncture number and localisation) and quality of obtained blood (volume, sterility, cell-viability etc.) were assessed.

Aim of the study: To assess feasibility of UCB collection in high risk pregnancies and newborn infants at increased risk of brain damage.
Preliminary Results: Of 175 neonates enrolled, UCB collection was successful in 140 patients (hypoxemia n=10; gestational age ≤ 30 weeks n=54; IUGR n=70; TTTS n=6). 26 cases were missed due to organisational difficulties. In 9 cases the collection failed due to acute life-threatening conditions or anatomical limitations (3 placental abruption n=3, uterine rupture n=2, transplacental delivery n=2, gestational age < 24+0 weeks n=2). Additional UCB was collected from 19 neonates in initially critical clinical condition (shoulder dystocia n=2, placental abruption n=3, terminal bradycardia n=14) and later discarded for not meeting the inclusion criteria of symptomatic hypoxemia defined as metabolic or mixed acidosis (cord pH≤ 7.0 or base deficit of ≥ 12), Apgar score at 10 minutes of age less than or equal to 5, needing mechanical ventilation and/or ongoing resuscitation at 10 minutes.

The median gestational age of included neonates was 32 weeks (range 24-40 weeks) and median birthweight 1550g (range 477-3155g) depending on the group as expected. Eight UCB units were microbiologically contaminated and median total nucleated cell viability was 86% (range 32-96.3%).

Conclusions: Collection and preparation of UCB in neonates at high risk of brain damage is challenging but possible with a multidisciplinary approach that includes extensive preparations, and detailed team-briefings.
TOPIC: THE BRAIN OF THE FETUS AND THE NEWBORN

ABSTRACT ID: 257

TITLE: NEONATAL NEUROPROTECTIVE EFFECT OF LACTOFERRIN IN A RAT MODEL OF PRENATAL HYPOXIA

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CONTENT

INTRODUCTION

Lactoferrin (LF) is a cationic transferrin found in mammalian milk, other body fluids and leukocytes. About 90% of LF in human milk is iron-free (apo-LF) and shows extreme affinity towards Fe(III) [1]. LF as an iron chelator is often compared with desferoxamine (DFO), which stabilizes hypoxia-inducible factor-1 alpha (HIF-1 α) and is regarded as a pharmacological mimic of hypoxia. At normoxia HIF-1α is modified by iron-sensitive hydroxylases, then undergoes ubiquitination and proteasomal degradation. Under hypoxia or iron deficiency HIF-1α enters the nucleus and binds to HIF-1β stimulating expression of ca. 200 genes, many of which secure the survival of cells under stress, regulating iron metabolism and erythropoiesis e.g. ceruloplasmin (CP), erythropoietin (EPO) etc. We showed recently that human apo-LF is a physiological mimetic of hypoxia stabilizing HIF-1α and HIF-2 α, which is followed by expression of their target CP and EPO genes.
[2,3]. Effect of harmful factors during pregnancy, including hypoxia, result in postnatal motor and cognitive dysfunctions, as shown in our previous studies [4,5]. In this study we analyzed the effects of LF on cognitive function in the offspring of pregnant rats subjected to hypoxia.

**MATERIALS AND METHODS**

Recombinant human LF purified from the milk of transgenic goats was obtained from the Belorussian State University and Scientific Practical Centre of Animal Breeding of the Belorussian National Academy of Sciences and branded “CAPRABEL”. About 90% of such LF was iron-free (apo-LF). Pregnant Wistar rats (200g) were subjected to hypoxia (7% O2, 3h) on the 14th gestation day in an altitude chamber as described in [4]. Half the pregnant rats were injected i.p. with CAPRABEL (10 mg per rat) on the 9, 12, 13 and 15th day of gestation or during nurturing (every day starting from P0 after delivery up to P15). According to our data after i.p. injection of CAPRABEL to lactating dams human apo-LF could be detected in their milk within 4-24 h [6]. Organ homogenates of some females and suckling pups were analyzed by Western blotting or ELISA with anti-HIFs or anti-EPO. Another group of pups was allowed to grow and their short-term working memory was tested in a two-level radial maze. The “Novel Object Recognition” (NOR) test was also used to assay both short-term and long-term memory.

**RESULTS**

In hypoxia-treated pregnant rats, which received i.p. injections of CAPRABEL and were sacrificed 3 h after the last injection Western blotting revealed HIF-1α, HIF-2α and EPO in the brain, liver, heart, spleen and placenta, but not in the embryos. HIFs or EPO were not detected in the organs of control pregnant rats. In young (P22) or adult (P40) rats born from the apo-LF-treated mothers subjected to hypoxia significant memory improvement was registered compared with the offspring of untreated rats, as judged by the radial maze and NOR tests.

Injection of CAPRABEL to hypoxia-treated lactating dams caused persistence of human apo-LF in their milk for 4-24 hrs and resulted in detectable levels of HIF-1α, HIF-2α and EPO in the pup brain, liver and spleen. CAPRABEL injections during lactation also resulted in significant improvement of short- and long-term memory of their offspring in NOR test on P22 and P40.
CONCLUSION: Apo-LF protects developing brain against harmful effect of prenatal hypoxia when applied both during prenatal and postnatal ontogenesis most likely due to its ability to induce EPO biosynthesis in brain and other tissues via HIF-signaling mechanism. As such both endogenous LF or pharmaceutical in the breast milk or substitute formulas can have therapeutic value providing a neuroprotective effect.

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ABSTRACT ID: N/A

TITLE: LABOUR PROBABILITY ESTIMATION USING A WEARABLE PREGNANCY MONITOR: PRELIMINARY VALIDATION

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CONTENT:
INTRODUCTION
Preterm birth (PTB), or birth before the completion of 37 weeks of pregnancy, is the leading cause of neonatal morbidity and mortality and the second-leading cause of death in children under the age of five [1]. The importance of early intervention to prevent and reduce the impact of PTB is clear [2]. However, no solution is currently available to easily allow for early detection of labour. The Bloomlife WISH system is a small wearable pregnancy monitor, worn on a pregnant woman’s abdomen, that measures uterine electromyogram (EMG), maternal heart rate and movement, and uses that information to compute a probability of a woman being in labour. Here we report the preliminary validation of the labour probability estimated using this wearable pregnancy monitor.

MATERIAL AND METHODS
A two-center, national, prospective, interventional study (N=150) was designed to evaluate the accuracy of the Bloomlife WISH system in detecting labour. The study was approved by the ethics committees of Ziekenhuis
Oost-Limburg (Genk, Belgium) and CHR Citadelle Hospital (Liège, Belgium), and by the Belgian Federal Agency for Medicines and Health Products. After consenting to participate, all study participants received a Bloomlife WISH system, and were asked to use it at least 3 nights per week until they deliver. Follow-up visits were organized regularly to check compliance with the protocol, and to collect clinical information. Data from the Bloomlife WISH system were collected during the study visits, for later analysis. All recordings performed by the study participants were analyzed using our labour detection model [3]. The uterine EMG, maternal heart rate and movement data are processed to filter artifacts and extract relevant features for labour detection. One feature set is extracted for every segment covering 20-min of non-artifacted data. These features are fed into a linear regression model that computes a probability of the user being in labour (labour probability). The labour probability is a number between 0 (very unlikely to be in labour) and 1 (very likely to be in labour). The 20-min data segments are labelled in two groups: labour and non-labour, depending on whether they were recorded within 24 hour of birth (labour) or not (non-labour). Labour probabilities for labour and non-labour segments are compared using a Welch Two Sample t-test to for the alternative hypothesis that there is a true difference in means not equal to 0.

RESULTS

145 pregnant women were enrolled in the study; 19 participants dropped out. Gestational age at inclusion was 27.6 ± 2.2 weeks. 67 (53%) participants were nulliparous and 11 (9%) participants had a history of preterm birth. Gestational age at delivery was 39.3 ± 1.7 weeks. 11 (9%) participants delivered preterm (<37 weeks), 35 (28%) delivered early term (37-38 weeks), and 78 (63%) delivered at term (39+ weeks). 103 (83%) participants had a vaginal birth, 40 (32%) were induced, 10 (8%) had a planned C-section, and 11 (9%) had an emergency C-section. The results are reported for the first 50 participants who delivered. These participants recorded a total of 7,714 20-min non-artifacted data segments, including 214 labour segments and 7,500 non-labour segments. Probabilities for all segments are visualized in a box plot that shows the labour probability for every segment, grouped per gestational week. The figure shows that labour probabilities for the labour group are consistently higher than the ones for the non-labour group, regardless of gestational age. Applying a
Welch Two Sample t-test to the distributions of labour and non-labour recordings shows a statistically significant difference (p-value < 0.001) between labour probabilities of these two groups.

CONCLUSIONS
The Bloomlife WISH system is a small wearable pregnancy monitor worn on a pregnant woman’s abdomen that measures uterine EMG, maternal heart rate and movement, and uses that information to compute a probability of a woman being in labour. This preliminary analysis on the first 50 participants recruited in the study shows that the labour probability computed on labour data segments is statistically higher than the labour probability computed on non-labour segments. Future work shall focus on extending the validation to preterm births prior to 35 weeks.

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REFERENCES
CONTENT:
INTRODUCTION
Currently major commercialized non-invasive prenatal test (NIPT) products are based on massive parallel sequencing or microarray hybridization. These methods usually take place in centralized laboratories, are time consuming, and are expensive. Therefore, there is a need to develop a low cost and fast method. Atila Biosystems has invented a novel PCR technology that enables highly multiplexed PCR. Based on the technology, we have developed a droplet digital PCR (ddPCR) based NIPT, that utilizes minimal amount of cfDNA from maternal blood and simultaneously detects aneuploidy of chromosome 21, 18, and 13. The ddPCR method is fast, cost efficient, and doesn’t require centralized laboratory or complicated bioinformatics. Therefore, ddPCR potentially can overcome the difficulties in the NGS NIPT tests. In addition to the NIPT assay, based on the same technology, we have developed multiple cancer mutation detection assays for liquid biopsy. For example, the EGFR assay detects 63 EGFR mutations in a single reaction and the KRAS assay detects 62 KRAS mutations in a single reaction.

OBJECTIVE
To evaluate the droplet digital PCR based NIPT assay for aneuploidy detection (T21, T18 and T13) performance.
METHODS
Two sets of samples were tested in the current study, a set of 78 samples (76 euploid, 2 trisomy 21, collected by University Hospital of Perugia) and a set of 193 samples (175 euploid, 15 trisomy 21, 2 trisomy 18, and 1 trisomy 13, collected by various sources in China). cfDNA were purified from 4-5mL of maternal plasma and were directly used as templates in the Atila NIPT ddPCR assay. PCR took 2 hours and ddPCR droplets were read in the Bio-Rad QX200 droplet reader for 12-15 minutes per sample.

RESULTS
High multiplex droplet digital PCR technology can detect aneuploidy (T21, T18 and T13) in single reaction and showed 100% sensitivity and 100% specificity for trisomy 21, 18, and 13 detection. The results were confirmed by NGS results, clinical outcome and also amniocentesis.

CONCLUSIONS
The study demonstrates the Atila NIPT ddPCR assay as a new approach for chromosome aneuploidy detection. The assay performed equally well as NGS methods. It only required a standard cfDNA purification and did not require further sample processing. It is extremely simple and fast suitable for decentralize NIPT detection.