Oral presentations

O1 – PREDICTION OF CERVICAL SHORTENING AND PRETERM DELIVERY USING SPECIFIC CELL FREE PLASMA MICRORNAS.

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Background
MicroRNAs are small, single-stranded molecules that control gene expression by regulating mRNA stability and transcription. Upon excretion into plasma, they remain in a stable, cell-free state where they can be assayed and used as bio-markers. We aimed to identify maternal plasma microRNAs in healthy pregnancy and evaluate if specific circulating microRNAs were altered in women who experienced subsequent cervical shortening and preterm delivery.

Methods
Longitudinal maternal plasma samples and cervical length measurements were collected from women at 12-14+6, 15-17+6 and 18-21+6 weeks gestation. nCounter microRNA plasma profiling was used to compare expression levels between women who went on to experience cervical shortening (n=55 samples) with normal controls (n=48 samples). Candidate miRNAs were validated using real-time polymerase chain reaction in the original and a second, independent cohort at 12-14+6 weeks gestation (n=87 samples).

Results
Fifty-six microRNAs were stably expressed across gestation in uncomplicated pregnancies. A panel of nine plasma microRNAs predictive of subsequent cervical shortening from 12 weeks gestation was identified: hsa-let-7a-5p, hsa-miR-374a-5p, hsa-miR-93-5p, hsa-miR-150-5p, hsa-miR-15b-5p, hsa-miR-185-5p, hsa-miR-191-5p, hsa-miR-19b-3p and hsa-miR-23a-3p. Our findings were replicated in an independent cohort of women at 12-14+6 weeks gestation (ROC curve analysis AUC 0.90).

Conclusion
We have identified a panel of circulating microRNAs predictive of cervical shortening and preterm birth secondary to cervical weakness. The second trimester is a key period in pregnancy when pathological changes can be identified, but time remains to deliver outcome-modifying interventions (ie progesterone or cervical cerclage) in those known to be at risk.

O2 – AN EARLY, CUSTOMIZED, LOW-GLYCAEMIC INDEX (GI) DIET PREVENTS ADVERSE PREGNANCY OUTCOMES IN OVERWEIGHT/OBESE WOMEN.

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Background
A high pre-pregnancy BMI is associated with many unfavorable pregnancy outcomes such as gestational diabetes mellitus (GDM), pregnancy induced hypertension (PIH), Preterm Birth (PTB).

Materials and methods
A case-control study (1:3) included single pregnant women with BMI≥25, enrolled at 1st trimester. Cases (95) were prescribed a low-GI diet of 1700/1800 Kcal/day (for obese/overweight) plus 30 minutes walking at least 3 times/week after a counselling by both the dietitian and gynecologist from enrollment until delivery (with four follow-up visits). Controls (275) received a nutritional booklet about a healthy lifestyle, than attended their scheduled visits until delivery by the obstetricians in charge.

Results
Gestational weight gain was similar between groups, despite obese women were higher in Cases (67.4%) than in Controls (54.5%, p=0.029). The occurrence of GDM was lower in Cases (21.5%) than in Controls (32.7%; p=0.041). Such reduction remained related with the group of intervention (p=0.005) after correcting for confounders (BMI≥ 30, a family history of diabetes, age ≥ 35 and ethnicity). A higher number of Controls developed PIH (11.6% vs 1.1% in cases, p=0.0007). PTB occurred in one Case (medically indicated for severe PIH) and in 28 Controls (10.2%; p=0.004). In the half of them, PTB was spontaneous while medically indicated for Intrauterine Growth Restriction, haemorrhage, PIH, GDM/macrosomia, Rh isoimmunisation in the remnant.

Conclusion

An early behavioral intervention among overweight/obese pregnant women (individualized counselling by a dietician, a physical activity program and a close follow-up) reduces unfavorable pregnancy outcomes, namely both spontaneous and medically indicated PTB.

O3 – USE OF CERVICAL PESSARY TO PREVENT PRETERM BIRTH IN SINGLETON PREGNANCIES WITH MATERNAL SHORT CERVIX AFTER THREATENED PRETERM LABOUR: A RANDOMISED CONTROLLED TRIAL.

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Background

As cervical pessary is known to be effective in preventing spontaneous preterm birth (SPB) in asymptomatic singleton pregnancies with short maternal cervical length (CL), we propose its use for preventing SPB in pregnant women with short CL after a threatened of preterm labour (TPL).

Methods

The PECEP-RETARD Trial, an open randomised controlled trial, was conducted at the Hospital Universitari Vall d'Hebron, Barcelona. This trial was undertaken to ascertain whether the insertion of a cervical pessary reduces the SPB rate in pregnant women with singleton pregnancies and a remaining short CL (≤25 mm or ≤15 mm depending on GA at randomisation) after an arrested TPL episode (if after 48 hours of tocolysis no contractions are detected). Three hundred and fifty-two pregnant women with short CL after an episode of TPL were randomly assigned to receive a cervical pessary or routine management without a cervical pessary (1:1 ratio). The primary objective was to ascertain the SPB rate before 34 weeks of gestation between groups; the SPB rate before 28 and 37 weeks and neonatal morbidity and mortality were also evaluated. This study is registered as clinicaltrials.gov NCT01242384.

Findings

No inter-group differences were observed in the SPB rate before 34 weeks of gestation. However, SPB before 37 weeks was significantly less frequent in the pessary group than in the routine management group (25% vs 14%, relative risk [RR]: 0•38; 95% confidence interval [CI]: 0•58 to 0•90; p=0•0016); a significant reduction in TPL recurrence was observed (women in the expectant management group required readmission for a new TPL episode more frequently than those in the pessary group: one or more episodes (4•5% vs. 20%; RR: 0•23; 95% CI: 0•11 to 0•47; p<0•0001). No serious adverse events associated with cervical pessary use occurred, and neonatal morbidity and mortality were similar in both groups.

Interpretation

Cervical pessary reduces both the SPB rate before 37 weeks of gestation and TPL recurrence in women with remaining short CL after a TPL episode.

O4 – LONG-TERM EFFECTS OF CERVICAL PESSARY FOR PRETERM BIRTH PREVENTION IN TWIN PREGNANCY WITH SHORT CERVIX: A 3 YEARS FOLLOW-UP TO THE PROTWIN TRIAL.

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Objective

To report the long-term outcome of the children included in the ProTWIN trial.

Methods

In the ProTWIN trial, women with a multiple pregnancy had been randomised to pessary or no pessary. As positive effects of pessary on prolongation and improvement of neonatal outcome had only been seen in women with a CL <38mm, we limited follow-up to that group (78 versus 55 mothers, 157 versus 111 children in pessary and control group respectively). At 3 years corrected age, the children were invited to undergo a Bayley Scales of Infant and Toddler Development-third edition (Bayley-III) assessment. We compared mean cognitive, language and motor function scores between the pessary and control group (Table).

Results

Of 268 children born to 133 women in our study group, 241 surviving children were eligible for follow-up of whom 171 children (71%, 111 pessary vs 60 control group) underwent a Bayley-III assessment. In total 27 children died (7 in pessary vs 20 control group). Analysis including deceased and disabled children showed a higher survival without disability in the pessary group when compared to controls (92.4 vs 73.8%, RR 1.25; 95% CI 1.24-3.78). When analysis was limited to survivors, we found neither statistical nor clinically relevant differences in Bayley-III scores between both groups (Table). Analysis using multiple imputation showed comparable results.

Conclusion

In women with a twin pregnancy and a CL < 38 mm, cervical pessary increases survival without neurodevelopmental disability at three years corrected age. As among survivors Bayley-III scores were similar between pessary and non-pessary users, use of a pessary seems to be without adverse long-term neurodevelopmental effects for children.

Table 1. Results of linear mixed effects model (adjusted for possible confounders) on Bayley Scales of Infant and Toddler Development-third edition (Bayley-III) test results amongst survivors and survivors+deceased children.

Analysis	Bayley-III cognitive composite score		Mean difference (95% CI) adjusted*	Bayley-III language composite score		Mean difference (95% CI) adjusted*	Bayley-III motor composite score		Mean difference (95% CI) adjusted*
	Pessary	Control		Pessary	Control		Pessary	Control	
Survivors only	N=111	N=60		N=107	N=56		N=109	N=58	
mean score (+/-SD)	101.3 (14.1)	103.9 (8.2)	-2.3 (-5.1 to 0.5)	104.4 (14.6)	104.7 (8.3)	-0.1 (-3.1 to 2.8)	106.2 (15.4)	105.9 (8.9)	0.7 (-2.4 to 3.8)
Survivors + deceased children	N=118	N=80	Relative Risk (95% CI)	N=114	N=76	Relative Risk (95% CI)	N=116	N=78	Relative Risk (95% CI)
Survival without disability n(%)†	109 (92.4)	59 (73.8)	1.25 (1.24 to 3.78)**	98 (86.0)	53 (69.7)	1.23 (1.04 to 1.45) **	110 (94.8)	57 (73.1)	1.30 (1.13 to 1.49)**

Bayley-III: Bayley III Scales of Infant and Toddler Development

*multilevel analysis adjusting for dependence of twin or triplets and potential baseline confounding known to have influence on child development: parental education, smoking, ethnic origin, children being the eldest in the family, use of daycare, bilingual and received breastfeeding>6 months.

** P-value: <0.006

†Survival without disability: all surviving children with a Bayley score >85points (less than -1SD below the mean).

O5 – WHY PROGESTERONE SHOULD NOT BE USED IN WOMEN WITH THREATENED PRETERM LABOR? RESULTS OF THE 4P TRIAL.

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Objective
Recent meta-analysis recommends vaginal progesterone (P) as maintenance tocolysis in women with preterm labor (PTL). The objective of this study is to summarize the results of the 4p trial.

Study design
The 4P trial was an international (Switzerland & Argentina), multicenter, double-blind randomized placebo-controlled (RCT) trial comparing vaginal P to placebo in women treated with acute tocolysis for PTL (24 0/7 to 33 6/7 wk). The study included 385 women (P: 193, Placebo: 188 and excluded 6). We also performed 2 secondary analysis: 2a) including women not having delivered after 48h of acute tocolysis, to assess the efficacy of P as maintenance tocolysis; and 2b) comparing differences in treatment effects between countries.

Results
In the 1ary study, preterm birth (PTB) occurred in 42.5% of women in the P group versus 35.5% in the placebo group, (RR 1.2; 95% CI 0.93-1.5). Delivery at <32 and <34 weeks did not differ between groups. Rate of spontaneous PTB was higher, 74/185 (40.0%) in the P group than in placebo group, 48/168 (28.6%);P=0.03. In the study 2a, 370 women (P: 187 & placebo: 183), there were no differences in the rates of PTB at <37 wk, <34 wk and < 32 wk or neonatal morbidity between groups. In the study 2b, P increased the risk for delivery <14 days [HR 4.4 (95%CI 1.3 to 15.7)] and PTB <37 weeks, [HR 2.5 (95% CI 1.4 to 4.8)] in the Swiss population.

O6 – MATERNAL GLUCOCORTICOID TREATMENT AND THE DOSE-DEPENDENT EFFECTS ON FETAL AND NEONATAL OUTCOMES IN TERM AND PRETERM GESTATIONS.

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Background
Antenatal betamethasone (BET) treatment given to women at risk of preterm delivery might result in a dose dependent growth restriction. We aimed to compare the effects of different BET dosage regimes (≤16mg, =24mg and >24mg) on fetal growth and neonatal outcome parameters in exposed vs. age-matched controls.

Methods
Retrospective case-control study. Data from BET-treated (n=1799) and non-treated pregnancies (n=42,240) including fetal growth measures, neonatal anthropometrics, placental weight, cord blood gases and Apgar scores were analyzed. Growth curves were constructed from the control population.

Results
In all BET dosage regimes analyzed, birth weight was significantly reduced. Fetuses exposed to BET between 23+5-34+0 wks and born from 34+0 wks onwards were lighter at birth (on average -154g) compared to age-matched controls, even after adjusting for confounders (e.g. hypertension, smoking, maternal weight and BMI gain during pregnancy etc.), sex or gestational age at treatment (P<0.05). Higher BET dosages resulted in a greater birth weight reduction without further improvement of neonatal morbidity and mortality. There was a significant and dose-dependent decline in expected fetal weight gain as estimated on serial ultrasound examinations up to 6-8 weeks after BMS exposure.

Conclusions
BET treatment was associated with a reduction in fetal growth. Higher BET dosages resulted in a greater growth reduction, without further improvement of neonatal mortality, morbidity and "maturity" at birth. These effects may have impacts later in life.

O7 – IMPACT OF MICROBIAL-ASSOCIATED INTRA-AMNIOTIC INFLAMMATION AND "STERILE" INTRA-AMNIOTIC INFLAMMATION ON SHORT-TERM NEONATAL OUTCOME IN WOMEN WITH PRETERM LABOR AND INTACT MEMBRANES

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Introduction
Microbial-associated intra-amniotic inflammation (IAI) and "sterile" IAI have been related with an earlier gestational age (GA) at delivery and a shorter latency to delivery. The aim of this study was to evaluate the impact of microbial-associated IAI and "sterile" IAI on short-term neonatal outcome in women with preterm labor when GA was taken into consideration.

Material/methods
Prospective cohort study including women (20.0-34.6 weeks) with an amniocentesis to rule out microbial invasion of the amniotic cavity (MIAC). Four subgroups were identified according to the presence of MIAC or IAI. MIAC was defined based on amniotic fluid aerobic/anaerobic/genital Mycoplasma cultures and IAI based on interleukin-6 levels (> 13.4 ng/mL). Short-term neonatal outcomes were recorded above 24.0 weeks in women delivered < or ≥ 34.0 weeks, respectively.

Results
One hundred fifty-seven women were included. Below 34.0 weeks, microbial-associated IAI and "sterile" IAI were found in 26% and in 14% of women, respectively. We did not found MIAC in women delivered ≥ 34.0 being "sterile" IAI present in 3%. Below 34.0 weeks, significantly earlier GA at delivery and shorter latency to delivery were observed in women with Microbial-associated IAI or "sterile" IAI when were compared with the "No-MIAC/No-IAI" group. However, no differences in short-term neonatal outcome were found between groups after adjustment for GA at delivery. Above 34.0 weeks, we did not found neonatal differences between groups.

Conclusions
A similar short-term neonatal outcome was observed between women with microbial-associated IAI or "sterile" IAI and the "No-MIAC/No-IAI" group when GA was taken into consideration.

Table 1

	Gestational age at delivery < 34.0 w(n 69)							Gestational age at delivery ≥ 34.0 w (n 88)		
	Group A Microbial-associated IAI n=18	**Group B "Sterile" IAI n=10**	**Group C MIAC alone n=6**	**Group D "No-MIAC/ No-IAI" n= 35**	***p*[1] *A vs. D***	***p*[2] *B vs. D***	***p*[3] *A vs. B***	**Group B "Sterile" IAI n= 3**	**Group D "No-MIAC/ No-IAI" n= 85**	***p*[2] *B vs. D***
Maternal age	32.5 (11)	32 (9)	33 (14)	33 (8)	0.903	0.732	0.847	35 (24-37)*	30 (9)	0.534
GA at admission	26.7 (6.2)	25.4 (2.5)	30.1 (6.7)	29.5 (4.2)	0.104	0.003	0.171	32.4 (19.6-34.5)*	30.0 (5.4)	0.520
GA at sampling	26.8 (6.2)	25.2 (4.1)	30.1 (6.7)	29.5 (5.6)	0.106	0.002	0.125	32.4 (19.6-34.5)*	30.0 (5.4)	0.520
AF IL-6 (ng/mL)	46.7 (88.9)	31.5 (55.8)	2.8 (1.7)	2.7 (3.7)	0.002+	0.006+	0.180+	54.1 (15.6-57.7)*	1.1 (1.1)	<0.001+
CRP (mg/dl)	5.0 (5.6)	1.5 (2.6)	3.6 (6.4)	0.4 (0.5)	<0.001	0.038	0.037	3.1 (1.0-3.4)*	0.5 (0.7)	0.023
GA at delivery	27.7 (6.3)	27.9 (2.5)	30.7 (7.0)	31.0 (3.3)	0.008	0.004	1.000	34.6 (34.0-39.0)*	38.1 (2.9)	0.132
Latency to delivery (days)	193.5 (4.5)	193.0 (20)	214.0 (47)	214.0 (22)	0.011	0.002	0.796	239.0 (234-267)	264.5 (20)	0.089
Birthweight (g)	1090 (1076)	1127.5 (503)	1357.5 (945)	1590 (520)	0.368	0.649	0.372	2800 (2592-3134)*	2934.1 (608)	0.291
Days in the NICU (days)	15 (30)	7 (8)	4.5 (19)	5 (9)	0.064	0.631	0.111	0 (0-5)*	0 (0)	0.106
Apgar score < 7 at 5 min	6 (33)	1 (10)	1 (17)	4 (11)	0.686	0.073	0.120	0	1 (1)	1.000
IVH grade III-IV	3 (17)	1 (10)	1 (17)	2 (6)	0.648	0.453	0.568	0	0	–
RDS	10 (55)	4 (40)	2 (33)	11 (31)	0.726	0.422	0.375	0	1 (1)	1.000
EONS	3 (17)	1 (10)	1 (17)	2 (6)	0.590	0.966	0.612	0	1 (1)	1.000
PVL	0	0	0	2 (6)	0.999	1.000	1.000	0	0	–
NEC	0	1 (10)	0	0	-	1.000	1.000	0	0	–
ROP	3 (17)	0	0	2 (6)	0.797	0.999	0.999	0	0	–
Fetal and neonatal death	1 (5)	3 (30)	0	2 (6)	0.177	0.823	0.103	0	0	–
HCA	16/17 (94)	6/9 (67)	5/5 (100)	9/28 (32)	<0.001	0.118	0.104	–	1/22 (4)	–
Funisitis	13/17 (76)	1/9 (11)	3/5 (60)	2/28 (7)	<0.001	1.000	0.003	–	1/22 (4)	–

GA: Gestational age; AF: Amniotic fluid; IL-6: Interleukin-6; CRP: C-reactive protein; NICU: Neonatal Intensive Care Unit; IVH: Intraventricular haemorrhage; RDS: Respiratory distress syndrome; EONS: Early-onset neonatal sepsis; PVL: Periventricular leukomalacia; NEC: Necrotizing enterocolitis; ROP: Retinopathy of prematurity; HCA: Histological chorioamnionitis; MIAC: Microbial invasion of the amniotic cavity. IAI: Intra-amniotic inflammation. Continuous variables were compared using a nonparametric Mann-Whitney U test presented as medians (interquartile range or max-min*). Categorical variables were compared using Chi-square or Fisher exact tests and presented as number (%). p^1 compares women with microbial-associated IAI and the" No-MIAC/No-IAI"group. p^2 compares women with "sterile" IAI and the"No-MIAC/No-IAI"group . p^3 compares women with microbial-associated IAI and "sterile" IAI. + variables adjusted for gestational age at sampling. Neonatal outcomes adjusted for gestational age at delivery

O8 – LINKING THE P2X7 PATHWAY WITH THE NLRP3 INFLAMMASOME OF PREGNANCY

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Background

The purinergic P2X7 receptor generates an electric current that mediates potassium efflux. Through this pathway and gated by the DAMP, extracellular ATP, the P2X7 receptor mediates the efficient maturation and release of the proinflammatory cytokine interleukin (IL)-1b via inflammasome activation and has been linked with spontaneous preterm birth.

We have previously reported functional P2X7 receptors in cord blood (CBMCs) and placental mononuclear cells.1 The aim of this study was to determine P2X7 pharmacology in CMBCs as well as to measure mRNA for the receptor and NLRP inflammasome components in CBMCs and villous tissue.

Methods

CBMCs, purifed from human term placentae were stimulated with the P2X7 agonist benzoylbenzoyl ATP (BzATP) in the presence and absence of various inhibitors of the P2X7 pathway and the effects on pore formation and expression measured fluorometrically by ethidium bromide transport, caspase-1 enzyme activity and qPCR.

Results and Conclusion

Caspase-1 activity was inhibited by the selective P2X7 antagonist, A740003, YVAD-CHO (a caspase-1 inhibitor), the antioxidant N-acetyl cysteine, an NfkB inhibitor, BAY11-7085 and a KATP channel blocker, glibenclamide ($N = 6\text{-}8$; $p < 0.05$). These inhibitors also blocked P2X7 pore formation ($N = 6$; $p < 0.05$. With the exception of NLRP3 which was increased 2-3 fold compared with controls, mRNA expression ($N = 6\text{-}8$ in all cases) of inflammasome components (P2X7, ASC, pro-caspase) preincubated with BzATP and LPS was unchanged in villous tissue and CBMCs. These data indicate that the P2X7 pathway engaging the NLRP3 inflammasome is a potential target through which spontaneous preterm birth may be inhibited.

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[1] Maneta et al., Front Physiol. 2015 Jun 23;6:186. doi: 10.3389/fphys.2015.00186. eCollection 2015.

Oral poster presentations

PO1 – ASSOCIATON BETWEEN FIRST TRIMESTER CERVICAL CONSISTENCY INDEX (CCI) AND PRETERM BIRTH IN LOW RISK POPULATION

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Objective

To establish the association between cervical consistency index (CCI) in the 11 to 13.6 weeks ultrasound screening and spontaneous preterm delivery before 35 weeks.

Methods

Prospectively, CCI and cervical length were measured in a cohort of pregnant women who had been evaluated at routine first trimester scan for aneuploidy screening (11-13.6 weeks). The association between CCI, cervical length and subsequent preterm delivery before 35 weeks was evaluated. In addition we recorded maternal age, parity, weight, height and body mass index (BMI). Women who had spontaneous preterm delivery before 35 weeks were selected as cases. Pregnancies with fetal malformations were excluded.

Results

We evaluated 843 pregnant women and identified 23 cases (2.73%) with spontaneous preterm delivery below 35 weeks. No statistically significant differences were found in the variables: maternal age, parity, maternal weight, height, BMI between cases and controls. The CCI was lower in cases than in controls: mean 71.2% [range 67.3-77.6%] vs. 78.6% [range 72.4-84.5%](p <0.001), respectively. Cervical length did not differ between cases and controls: mean 37.2 mm [range 34-40 mm] vs 39.1mm [range 35-42 mm] (p = 0.14), respectively.

Conclusions

Women who presented with preterm birth before 35 weeks had significantly lower values of CCI at first trimester than women who delivered at term. The measurement of CCI in ultrasound screening at 11-13.6 weeks may have clinical value for the early identification of women at risk of preterm birth before 35 weeks.

PO2 – COMPARISON OF VAGINAL PROGESTERONE AND ARABIN PESSARY FOR TREATMENT OF SHORT CERVIX IN ASYMPTOMATIC WOMEN WITH HIGH RISK PREGNANCIES.

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Background

Previous spontaneous preterm birth (sPTB) or excisional cervical surgery are risk factors for sPTB. On finding a short cervix in a subsequent asymptomatic pregnancy, uncertainty remains regarding best preventative therapy. At Liverpool Women's Hospital vaginal progesterone (VP) 200mg was used as first-line therapy between 2008-2012 whilst Arabin pessary (AP) has been first-line between 2012-2015. Our aim was to assess the difference in outcomes between these 2 treatment cohorts.

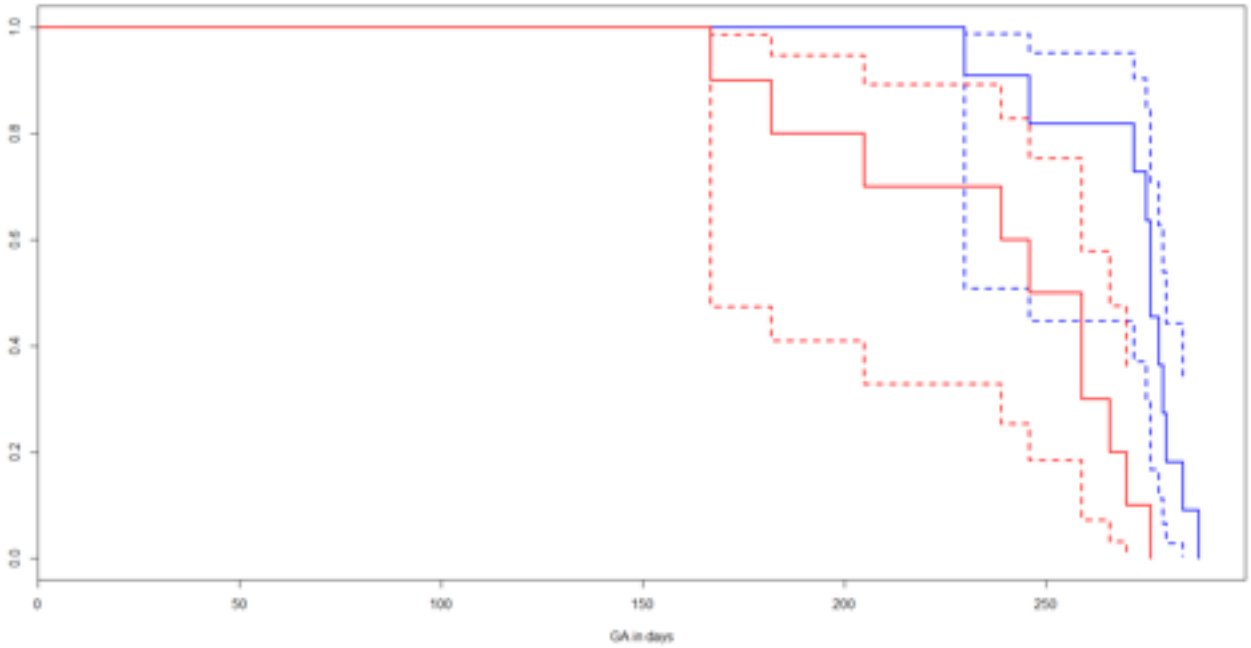
Material/Methods

Women treated with progesterone or pessary were matched for cervical length and gestation when first treated, and high risk status (previous cervical surgery, prelabour ruptured membranes (PPROM), sPTB). The groups were compared using McNamer test and (non-conditional) logistic regression analysis.

Results
From a prospectively collected database, 81 women with VP and 63 with AP were identified with 40 pairs matched for all 3 characteristics. sPTB were more common with VP compared with AP group, but the difference was not significant (42.5% vs 37.5%; OR 1.2 (CI 0.5-3.0) p=0.815) Women with a history of PPROM appeared to respond better to VP than AP (p = 0.00219). In women with history of sPTB and cervical surgery there was no significant difference between two groups.

Conclusion
The rate of sPTB between high risk women receiving vaginal progesterone or Arabin pessary was similar. Vaginal progesterone may be more advantageous than pessary for a subgroup of women with a history of PPROM, but this must be tested in different, ideally randomized, cohorts.

Figure 1. Kaplan Meier plot – indication 2 – blue Progesterone – red Arabin pessary - p = 0.00219



* Indication 2 = history of PPROM (Confidence Intervals shown as dotted lines)

PO3 – LONG TERM FOLLOW-UP AFTER ABDOMINAL CERCLAGE. A POPULATION-BASED COHORT STUDY.

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Objective

To examine perioperative complications, gestational length of pregnancies, long-term complications and the presence of pain following abdominal cerclage placement.

Methods

Retrospective cohort study of all procedures of abdominal cerclage in Denmark in 1999-2012 using a combination of data from the National Patient Register, medical records and a questionnaire. Women were categorized by indication of cerclage into groups of extensive cervical surgery and classic cervical insufficiency. The questionnaire recorded details of the caesarean sections in subsequent deliveries, indications for the reapplication and removal of cerclage, and a description of pain, if present.

Results

A total of 255 procedures were performed. Of these, 195 were indicated by classic cervical insufficiency and 60 by extensive cervical surgery. The median number of deliveries following abdominal cerclage was 1 (range, 0 -5). Among a total of 321 deliveries, 298 proceeded at ≥ 34 weeks of gestation (92.8%), 14 (5.5%) proceeded at 28-34 weeks and nine patients (2.8%) experienced a second-trimester delivery (16-28 weeks). Perioperative complications were unusual. Of the 242 women who received the questionnaire, 192 (79%) responded. Fourteen patients (7.3%) had a re-cerclage, and 12 (6.3%) a permanent removal of the cerclage. In 23 women, mild pain/discomfort during intercourse or menstrual periods were reported, but no patients reported persistent pain.

Conclusion

Abdominal cerclage is associated with favorable neonatal outcomes in up to 5 subsequent deliveries. The prevalence of self-reported pain and discomfort in women with abdominal cerclage is low.

PO4 – A TWO-HIT HYPOTHESIS: PRENATAL EXTERNAL AND IMMUNE STRESS INFLUENCE EXPRESSION OF STRESS AND INFLAMMATION RELATED GENES IN UTERUS AND HIPPOCAMPUS OF RAT OFFSPRING.

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Background

We showed that a single ancestral stressor in F0 generation dams augments preterm birth (PTB) risk and associates with changes in the miR-200 family and targets Stat5b and Zeb1/2, regulators of uterine contractility, in subsequent generations, and that two distinct prenatal stressors or "hits" combined affected pregnancy outcomes in F0 dams. We hypothesize that two hits differentially alter epigenetic effectors involved in the stress response, IL-1 signaling, and miR-200 family when combined compared to either hit alone.

Methods

Pregnant F0 rats were exposed to psychological (forced swimming/restraint) and/or immune stress (interleukin(IL)-1β, 5μg/kg/day, i.p.) on gestational days (GD) 12-18 and from GD17 to delivery, respectively, resulting in four groups: no stress/saline (NS/S), stress/saline (S/S), no stress/IL-1β (NS/IL-1β) and stress/IL-1β (S/IL-1β), n=3-6/group. mRNA abundance in uterus and hippocampus of adult virgin F1 females was evaluated by qRT-PCR for genes of interest and normalized to Cyclophilin. One-way ANOVA or Kruskal-Wallis test with post-hoc testing, $p<0.05$.

Results

Administration of S/IL-1β to F0 dams decreased the F1 uterine Stat5b mRNA expression versus NS/S ($p<0.05$). Hsd11b1 was downregulated in S/IL-1β versus NS/IL-1β ($p<0.05$). In hippocampus Nr3c1 mRNA expression was reduced in NS/IL-1β and S/IL-1β ($p<0.05$) vs. control. Hsd11b2

expression was lower in all treatment groups than NS/S (p<0.01).

Conclusion

Multiple prenatal stressors affect the F1 uterine and hippocampal mRNA levels of mediators of stress, inflammation and uterine contractility. This suggests multiple hit ancestral stress may be transferred to offspring, increasing their "stress state," possibly through epigenetic changes, thereby programming physiological responses and pregnancy outcomes.

PO5 – PRETERM RUPTURE OF THE FETAL MEMBRANES INDUCES VAGINAL MICROBIAL DYSBIOSIS, WHICH IS EXACERBATED BY ERYTHROMYCIN TREATMENT.

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Background

Infection is a major cause of preterm prelabour rupture of the membranes (PPROM), which precedes 30% of preterm births. Detailed understanding of the qualitative and quantitative composition of the vaginal microbiome before and after PPROM is pivotal for the development of predictive, preventive and personalized therapeutic strategies.

Methods

Vaginal swabs were taken from pregnant women with PPROM before (n=40) and after (n=42) treatment with Erythromycin and from low risk women (n=39) at four antenatal time points. Bacterial species composition was examined by sequencing of 16S rRNA gene amplicons (V1-V2) and quantitative RT-PCR to calculate total bacterial load/sample.

Results

Prior to membrane rupture, women experiencing PPROM harbour significantly lower levels of L.crispatus compared to gestational-age matched controls delivering at term (z-score2.2,p=0.02). L.iners is the dominant Lactobacillus spp. observed in PPROM. After rupture the proportion of women with a highly diverse, Lactobacillus spp. deplete community structure increases 2.5-fold (17% v 40%) and is further exacerbated by Erythromycin treatment (74%). Analysis of paired samples (n=16) demonstrates Erythromycin is associated with increased dysbiosis (40% v 56%). Bacterial load is significantly reduced following membrane rupture (p<0.001, Mann Whitney) but remains stable despite antibiotic treatment.

Conclusion

A vaginal microbiome dominated by L.crispatus may be protective against PPROM. Preterm membrane rupture and Erythromycin treatment are associated with dysbiosis and the emergence of organisms implicated in neonatal and maternal sepsis. Conservation of bacterial load indicates re-modelling of existing microbial community structure rather than depletion of dominant Lactobacillus spp. post treatment.

PO6 – CESAREAN SECTION AT 22-27 GESTATIONAL WEEKS IN SWEDEN, INDICATIONS, PROCEDURES AND MATERNAL COMPLICATIONS

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Background

Maternal complications associated with cesarean section (CS) in the extremely preterm period need to be investigated.

Material and methods

Review of medical records of women, who delivered at 22-27 weeks of gestation (n=647), 2001-2012 at two level III units in Sweden. CS was stratified into 22-24 (n=105) and 25-27 (n=301) gestational weeks. For comparison, women who underwent a CS at term were identified in a register-based database. Blood loss ≥ 2000 ml, sepsis, hematoma, re-operation, or thromboembolisms were considered as major maternal complications.

Results

The rate of CS in extremely preterm births was 62.8 %. Major maternal complications occurred in 6.6 % compared with 2.1 % in the extremely preterm and term CS, respectively (p< 0.01); a maternal indication of extremely preterm cesarean delivery increased the risk. A corporal incision was required in 12.6 % of all the women, and in 19.6 % at 22-24 compared to 10.2 % at 25-27 gestational weeks (p 0.02). There was no difference in the complication rates in 22-24 versus 25-27 gestational weeks.

Conclusion

Extremely preterm compared to term cesarean delivery is associated with an increased risk of major maternal complications. The risk is related to the underlying maternal condition and the indication for delivery and may therefore not be avoidable.

Posters

P1 – CERVICAL LENGTH ASSESSMENT AT 15+0+16+6 WEEKS GESTATION IS USEFUL TO GUIDE PRETERM BIRTH PREVENTION TREATMENT.

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Background
Most prediction models to guide preterm birth prevention treatment that are based on cervical length scanning start after 18 weeks gestation. We commence cervical measurement in high risk women at 15-16+6 weeks gestation to avoid delaying treatment for women with early cervical shortening. We analysed our rate of treatment prior to 20 weeks, to determine whether early scanning is clinically useful.

Methods
We performed a retrospective analysis of our Preterm Birth Prevention Clinic database. Women with singleton pregnancies and spontaneous previous preterm birth (sPTB) or preterm premature rupture of membranes (PPROM) before 34+0 weeks or significant cervical surgery (multiple LLETZ or knife cone biopsy) were included if their first scan was between 15+0 and 16+6 weeks gestation. Cervical length and gestation of commencing preterm birth prevention treatment were analysed.

Results
Cervical length was significantly shorter compared with published low risk populations (n=79; 43.3mm, SD 6.7mm); sPTB (n=160; 36.4mm, SD 9.6mm, p= <0.0001); PPROM (n=73; 35.8mm, SD 10.8, p=<0.0001); cervical surgery (n= 64; 33.0mm, SD 10.0mm, p=<0.0001).

25.8% of our high risk women with previous sPTB or PPROM required preterm birth prevention treatment because of significant cervical shortening, as did 15.6% of those scanned due to previous cervical surgery. 27.1% of all treatments were started at the initial scan before 17+0 weeks, and in total 44.3% were started before 20 weeks gestation.

Conclusion
Clinically important cervical shortening can be present prior to 20+0 weeks gestation and so prediction models are needed to guide treatment at these early gestations.

P2 – PROSPECTIVE OBSERVATIONAL STUDY ON SONOGRAPHIC CERVICAL LENGTH MEASUREMENTS IN MIDGESTATION.

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Background
The prevalence of preterm birth (PTB) and of sonographically short cervix (<25mm) in mid-pregnancy seems to be lower in northern Europe than in published studies performed mainly outside Europe.

Objective
To estimate the prevalence of and the sensitivity and specificity with regard to PTB < 33 completed gestational weeks (gws) of a sonographically short cervix at mid-gestation in an unselected Swedish population of singleton pregnancies.

Sample size: 11000 women with cervical length measurement (the rate of PTB < 33 gws is estimated to be 0.9%, i.e. 11000 women will generate 100 PTBs < 33 weeks)

Recruitment period: May 2014 to May 2017.

Setting
Four university hospitals, one regional hospital

Outcome measures: Prevalence of short cervix, receiver operating characteristic (ROC) curves, area under ROC curve, sensitivity, specificity of sonographic cervical length with regard to predicting PTB < 33 gws.

Volunteers

Asymptomatic women with singleton pregnancy, no ultrasound signs of fetal malformations

Ultrasound examination: Cervical length is measured with transvaginal ultrasound by specially trained midwives once at 18+0 - 19+6 gws and once at 22+0 - 23+6 gws. A system with four annual checks of the quality of the measurements is in place. Medical staff is blinded to the results of the cervical length measurements. A "short cervix" is not acted upon.

Results

Preliminary results expected 2018.

P3 – CEPEIC: CERCLAGE VS CERVICAL PESSARY IN WOMEN WITH CERVICAL INCOMPETENCE.

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Background

Cervical insufficiency (CI) is a complex disease in terms of its diagnosis and treatment. It is thought to be responsible of the 8% of preterm deliveries and has a high morbidity and mortality. Cervical cerclage has demonstrated its effectiveness in the CI treatment. The cervical pessary is a treatment with a high potential considering its promising results for the prematurity prevention.

We would like to demonstrate that the cervical pessary could reduce the rate of preterm delivery under 37 weeks of gestation (WG) in women with cervical incompetence, at least from 33,5% to 26,6%, as the cerclage does.

Material and methods

This is a pilot, multicentre, prospective and longitudinal, cohorts randomized study. It will enrol pregnant women with a history of 3 or more second trimester losses or preterm deliveries, or one or more second trimester losses or preterm deliveries and cervical length <25mm before 24 WG. Only singleton pregnancies between 12+0 – 25+6 WG will be included. They will be randomized either to cervical cerclage or pessary treatment. The aleatorization will be done with an electronic programme, in a proportion of 1:1. As it is a pilot study, the sample size should be of 60 women, 30 included in the cervical cerclage group and 30 in the pessary group.

Results

We estimate a period of two years to include all women the study needs.

Conclusions

The cervical pessary could ease and improve the cervical insufficiency treatment, either for patients and professionals by reducing the learning curve, the associated morbidity and improving its cost-effectiveness.

P4 – IMPACT OF LATENCY DURATION ON PRETERM INFANT PROGNOSIS AFTER PRETERM PREMATURE RUPTURE OF MEMBRANES: THE EPIPAGE 2 NATIONAL POPULATION-BASED STUDY.

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Background

Whether the duration of the latency period after preterm premature rupture of membranes (PPROM) affects perinatal prognosis remains unclear. We aimed to assess the impact of latency duration on survival and survival without severe mor-

bidity of premature infants born at 24 to 34 weeks' gestation (WG) after PPROM.

Methods

This study was based on the French prospective nationwide population-based EPIPAGE 2 cohort conducted in 2011. Latency duration was defined as the time from spontaneous rupture of membranes to delivery. Multivariable logistic regression was used to assess the relationship between latency duration and survival or survival without severe morbidity at discharge.

Results

For 702 singleton infants delivered at 24 to 34 WG after PPROM occurring ≥ 12 hr before birth, the median PPROM age was 29 WG (interquartile range [IQR] 27-31), median latency 6.1 days (IQR 3-12.1), and median delivery age 31 WG (IQR 28-33). Rates of survival and survival without severe morbidity were 93.5% (95% CI 91.8-94.8) and 85.4% (82.4-87.9), respectively. On adjusting for gestational age at birth, latency duration was not associated with survival (adjusted odds ratio [aOR] 1.0 [reference], 1.6 [95% CI 0.7-3.7], 1.1 [0.5-2.4], and 0.9 [0.3-2.7], for latency durations from 12 hr to 3 days, 4 to 7 days, 8 to 14 days and > 14 days respectively). Accordingly, on adjusting for gestational age at PPROM, prolonged latency was associated with improved survival.

Conclusion

Long latency had no independent effect on neonatal outcome when considering gestational age at birth.

P5 – EVALUATION OF PERINATAL FACTORS ASSOCIATED WITH POOR NEURODEVELOPMENTAL OUTCOME IN INFANTS WITH SPONTANEOUS PRETERM BIRTH.

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Background

Antenatal exposure to an inflammatory environment has been associated with a poor neurodevelopmental outcome. The objective was to evaluate perinatal factors including microbial invasion of the amniotic cavity (MIAC), intra-amniotic inflammation (IAI) and placental findings to predict a poor neurodevelopmental outcome in infants with spontaneous preterm birth (sPTB).

Material/Methods

Prospective cohort study performed in infants up to 5 years old with sPTB <34.0 weeks. MIAC was defined based on amniotic fluid aerobic/anaerobic/Mycoplasma cultures and IAI based on amniotic fluid interleukin-6 levels. Histological chorioamnionitis and funisitis were defined as neutrophil infiltration of the chorion/amnion/umbilical vessel walls. Neurodevelopment was evaluated by Ages & Stages Questionnaires® mailed-out at 23.5 corrected months. We defined poor neurodevelopmental outcome when at least one of the areas evaluated (communication, fine and gross motor, problem solving and personal social) scored below expected for age. Logistic regression analysis evaluated the independence of antenatal, intra-partum and neonatal outcomes to predict a poor neurodevelopmental outcome.

Results

Among 97 infants evaluated, 43% were born from women with preterm prelabor rupture of membranes and 57% with preterm labor. MIAC and IAI occurred in 54% and 70% of cases, respectively, and funisitis in 34%. Twenty-one infants (22%) scored below expected for age. Among all variables evaluated, only funisitis showed to be an independent factor of poor neurodevelopmental outcome (Odds Ratio 3.0; 95% Confidential Interval (1.06-8.51)). No association was found with MIAC or IAI.

Conclusions

In infants with sPTB, funisitis was a predictive factor of poor neurodevelopment outcome, while MIAC or IAI were not.

Table 1. Poor neurodevelopmental outcome (n 21)

	Odds Ratio	95% Confidential Intervals
Smoking	1.25	0.36-4.38
Low educational status	4.13	0.51-33.5
IAI	1.08	0.37-3.15
MIAC	1.01	0.38-2.65
"Sterile" IAI	1.25	0.36-4.38
Breastfeeding < 6 months	0.73	0.27-1.96
Antenatal corticosteroids	0.16	0.02-1.04
PPROM > 18 hours	1.12	0.41-3.02
Intra-partum fever	1.36	0.43-4.34
GA at delivery	0.88	0.73-1.06
Emergency cesarean section	0.94	0.35-2.54
Male gender	1.88	0.69-4.87
Birthweight	0.99	0.99-1.0
Apgar at five minutes < 7	3.00	0.68-14.6
Umbilical artery pH < 7.10	0.34	0.002-68.5
Days of admission to NICU	1.02	0.99-1.03
Intra-ventricular hemorrage grade IIII/IV	2.06	0.62-6.88
Periventricular leukomalacia	3.89	0.51-29.5
Histological chorioamnionitis	1.74	0.58-5.16
Funisitis	**3.01**	**1.06-8.51**

MIAC: Microbial invasion of amniotic cavity
IAI: Intra-amniotic inflammation
PPROM: Preterm prelabor rupture of membranes
GA: Gestational age
NICU: Neonatal intensive care unit

P6 – EARLY PREDICTION OF SPONTANEOUS VERY PRETERM DELIVERY IN TWINS: A POPULATION BASED STUDY 2002-2012.

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Background
The aim of this study was to establish early pregnancy risk indicators for spontaneous very preterm birth in twins.

Methods
We conducted a retrospective observational population-based study in Slovenia, 2002 - 2012. Twenty-one potential early pregnancy risk factors gathered from National Perinatal Database were analysed using multivariable logistic regression to determine which of them was independently associated with spontaneous twin very preterm birth. The unit of analysis was twin pregnancy. Pregnancies in which both fetuses died before the onset of labor were excluded from analysis.

Results
In the cohort of f 1815 spontaneous twin births, 15.3% (277) occurred between 22 weeks 0 days and 31 weeks 6 days. Among several potential risk factors, previous preterm birth (aOR 3.73; 95% CI, 2.52-5.52), nulliparity (aOR 2.94; 95% CI, 2.09-4.14), body mass index <18.5 kg/m2 (aOR 1.86; 95% CI, 1.12-3.10), body mass index ≥30 kg/m2 (aOR 1.87; 95% CI, 1.21-2.89), monochorionicity (aOR 1.83; 95% CI, 1.28-2.63), history of hysteroscopic metroplasty (aOR 1.63; 1.07-2.49) and history of conization (aOR 2.05; 95% CI, 1.07-3.94) were independently associated with spontaneous very preterm birth in twins in Slovenia.

Conclusion
Pending verification in other populations, twin pregnancies at significant risk for spontaneous very preterm birth can be identified in early pregnancy using several risk indicators. Since a high rate of twins is conceived after in vitro fertilisation techniques, awareness of the risk indicators of very preterm birth in twins before embryo transfer might support single embryo transfer.

P7 – A CORE OUTCOME SET FOR EVALUATION OF INTERVENTIONS TO PREVENT PRETERM BIRTH

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Objective
To develop consensus on a set of key clinical outcomes for the evaluation of preventive interventions for preterm birth in asymptomatic pregnant women.

Methods
A two-stage web-based Delphi survey and a face-to-face meeting of key stakeholders were employed to develop consensus on a set of critical and important outcomes. We approached five stakeholder groups (parents, midwives, obstetricians, neonatologists and researchers) from middle and high-income countries. Outcomes subjected to the Delphi survey were identified by systematic literature review and stakeholder input. Survey participants, identified utilising a comprehensive strategy, scored each outcome on a nine point Likert scale anchored between 1 (limited importance) and 9 (critical importance). For consensus, defined a priori, outcomes required at least 70% of participants of each stakeholder group scoring them as 'critical' and less than 15% as 'limited'.

Results
A total of 174 participants from five stakeholder groups 10 middle-income and 17 high-income countries completed the two survey rounds. Consensus was reached on 13 core outcome: Four related to pregnant women: maternal mortality, maternal infection or inflammation, prelabor rupture of membranes, and harm to mother from intervention; Nine related to offspring: gestation age at birth, offspring mortality, birth weight, early neurodevelopmental morbidity, late neurodevelopmental morbidity, gastro-intestinal morbidity, infection, respiratory morbidity, and harm to offspring from intervention.

Conclusions
This core outcome set for studies that evaluate prevention of preterm birth developed with an international multidisciplinary perspective will ensure that data from trials that assess primary prevention of preterm birth can be compared and combined.

P8 – LIPOTEICHOIC ACID STIMULATES THE PRODUCTION OF NEUTROPHIL EXTRACELLULAR TRAPS IN CORD BLOOD LEUKOCYTES.

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Neutrophil extracellular traps (NETs), discovered in 20041, are triggered by various stimuli, including infection. The formation of NETs is characterised by the release of DNA associated with histones and granule proteins. In pregnancy, bacterial infection originating in the mother is a leading cause of spontaneous preterm birth (<37 weeks gestation) and whether NETs play a role in this syndrome remains unknown. The aim of our study therefore was to characterise the NET response in cord blood leukocytes.

A mixed population of leukocytes was purified following Dextran sedimentation of umbilical cord blood collected from term, healthy placentae. NET production was induced by stimulation with lipoteichoic acid (LTA), a polymer contained within the cell wall of gram positive bacteria, and phorbol 12-myristate-13-acetate (PMA), a widely studied inducer of NET formation. A cell impermeable Sytox green-based fluorescence assay was used to measure extracellular DNA while the presence and localisation of neutrophil elastase (NE) and myeloperoxidase (MPO) was determined by immunofluorescence.

LTA and PMA both stimulated the externalisation of DNA from leukocytes in a concentration dependent manner (n = 8, $p < 0.01$, Bonferroni). NET production was confirmed by visualisation of DNA, NE and MPO in extracellular structures emitting from the leukocytes.

Our observations demonstrate that NET formation occurs in cord blood leukocytes in response to LTA and PMA. During pregnancy, NETs form part of the host-defence mechanism, dysregulation of which may be a novel component of spontaneous preterm birth. Further studies are underway to compare NET production in preterm and term deliveries.

[1] Brinkmann, V. et al. Neutrophil extracellular traps kill bacteria. Science 303, 1532-1535 (2004).

P9 – NEUTROPHIL LYMPHOCYTE RATIO (NLR) AS A MARKER OF DELIVERY AND THE AETIOLOGY UNDERLYING PRETERM BIRTH.

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Background
Placental inflammatory response (PIR) is associated with adverse neonatal outcomes. Neutrophil lymphocyte ratio (NLR) is a recognized marker of subclinical infection.

Methods
The relationship between NLR and placental inflammation was evaluated in 156 women with preterm birth (<37 weeks) managed through a high-risk Prematurity Surveillance Clinic 2002 - 2015. NLR was measured at booking and at presentation in threatened preterm labour. Data from all women who went on to deliver within 48hours, with available placental histopathology, was analysed.

Results
Inflammatory histology was found in 70% of women (109/156). NLR was significantly raised at delivery compared to booking: 8.8 (SD6.4) vs 3.69 (SD2.3), $p<0.0001$. Mean NLR at delivery in women with inflammatory placental histology (n=109) was significantly higher than non-inflammatory placental histology (n=47): 9.8 (SD 6.54) vs 6.55 (SD 4.31): $p=0.002$.

Using a threshold of 6.48, previously suggested in the literature as a predictor for placental inflammatory response, NLR was "positive" in 65% of women with inflammatory placental histology at delivery as compared to 34% of women with non-inflammatory histology (odds ratio 3.62, 95% CI 1.76 - 7.44, $p=0.0005$) and a positive predictive value of 82%.

Conclusion
Raised NLR has shown a strong correlation to PIR, known to be associated with adverse neonatal outcome. As NLR is routinely obtained in all pregnant women, even in a low-income setting, this highlights a potential role for NLR as a cost-effective biomarker of both delivery and placental inflammation. Future research should establish optimal rule-out and rule-in thresholds, and clinical pathways following these findings.

P10 – TREATMENT OF BACTERIAL VAGINOSIS IN PREGNANCY IN ORDER TO REDUCE THE RISK OF SPONTANEOUS PRETERM DELIVERY – A CLINICAL GUIDELINE.

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Introduction

Bacterial vaginosis (BV) is characterized by a dysbiosis of the vaginal microbiota with a depletion of vaginal Lactobacillus spp. During pregnancy, the prevalence varies between 7-30% depending on the study population and BV definition. BV may be associated with an increased risk of spontaneous preterm delivery (sPTD). However, it is controversial whether or not BV positive pregnant women will benefit from antibiotic treatment in order to reduce the risk of sPTD. We could not identify any good quality national or international guideline addressing this issue. Consequently we aimed to produce this clinical guideline based on the GRADE principles.

Material and methods

Systematic literature searches were conducted in the following databases: Guidelines International Network: G-I-N, Medline, Embase, The Cochrane Database of Systematic Reviews, Web of Science and www.clinicaltrials.gov from 1999 to 3 October 2014. Thus, nine guidelines, 34 reviews, 18 randomized controlled trials (RCT), and 12 observational studies were included.

Results

Treatment with metronidazole increased sPTD<37 weeks in low risk pregnancies, RR 1.11 (95% CI 0.92-1.34) whereas it decreased the risk in high risk pregnancies, RR 0.92 (0.75-1.14). Treatment with clindamycin at any GA was associated with a lower risk of sPTD<37 weeks, RR 0.87 (0.73-1.05). Including studies with treatment before gestational week 20, a RR of 0.95 (0.71-1.26) was found. However, the quality of evidence was consistently rated low or very low.

Conclusion

This guideline recommends against treatment of BV in both high and low risk pregnancies due to a questionable effect on the sPTD rate.

P11 – IMPACT OF "STERILE" INTRA-AMNIOTIC INFLAMMATION ON SHORT-TERM NEONATAL OUTCOME IN WOMEN WITH PRETERM PRELABOUR RUPTURE OF MEMBRANES.

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Introduction

There has been reported that intra-amniotic inflammation (IAI) without microbial invasion of the amniotic cavity (MIAC) ("sterile" IAI) has a perinatal outcome similar to MIAC. The aim of the study was to evaluate the impact of "sterile" IAI on short-term neonatal outcome in women with preterm prelabour rupture of membranes (PPROM) when gestational age (GA) was taken into account.

Material and methods

Prospective cohort study including singleton pregnancies with PPROM <34.0 weeks. MIAC was defined as positive amniotic fluid aerobic/anaerobic/genital Mycoplasma culture and IAI based on interleukin (IL)-6 levels (≥1.43 ng/mL). Four phenotypes were identified according to the presence of MIAC and/or IAI. Short-term neonatal outcome was adjusted for GA at delivery.

Results

Among 102 women evaluated, microbial-associated IAI and "sterile" IAI were present in 26% and 40%, respectively. Only two women had MIAC with low levels of IL-6. No differences were observed in any of maternal or short-term neonatal outcomes evaluated between women with "sterile" IAI and the "No-MIAC/

No-IAI" group. Significantly earlier GA at PPROM, at delivery and a higher rate of preterm delivery before 28.0 and 32.0 weeks was found in women with microbial-associated IAI when were compared with those with "sterile" IAI. No other differences in short-term neonatal outcome were observed after adjustment for GA at delivery.

Conclusions

A similar maternal and neonatal outcome was observed in women with "Sterile" IAI and in the "No-MIAC/No-IAI" group. GA at delivery seems to be more important for short-term neonatal outcome than the presence of "sterile" IAI in PPROM.

Table 1

	Group A Microbial-associated IAI n= 27	Group B "Sterile" IAI n= 41	Group C No-MIAC/No-IAI n= 32	p^1 (B vs. C)	p^2 (A vs. B)
Maternal age	31 (10)	32 (6)	34 (10)	0.260	0.619
GA at PPROM (weeks)	28.5 (4.6)	30.8 (3.8)	31.6 (3.3)	0.322	0.011
GA at sampling (weeks)	28.2 (4.2)	30.4 (5.6)	31.4 (4.1)	0.311	0.082
CRP at admission (mg/L)	1.6 (2.4)	0.6 (0.7)	0.4 (0.9)	0.191	0.001
WBC count at admission (x109/L)	12960 (4880)	11920 (5045)	11290 (4850)	0.824	0.051
AF IL-6 (ng/mL)	44.1 (119.3)	4.6 (13.6)	0.5 (0.7)	<0.001+	<0.001+
Preterm induction of labor	6 (22)	21 (51)	10 (31)	0.130	0.057
GA at delivery (weeks)	30.2 (4.5)	32.6 (3.5)	32.8 (1.4)	0.689	<0.001
Latency from PPROM-delivery (days)	6 (13)	10 (14)	5 (11.5)	0.287	0.187
Delivery < 28.0 (weeks)	8 (30)	2 (5)	0	0.501	0.011
Delivery < 32.0 (weeks)	22 (81)	16 (39)	6 (19)	0.075	0.001
Clinical chorioamnionitis	5 (18)	5 (12)	6 (19)	0.518	0.502
Birthweight (g)	1440 (770)	1800 (720)	1895 (394)	0.848	0.426
Apgar score < 7 at 5 minutes	5 (18)	3 (7)	1 (3)	0.437	0.885
Days in NICU	7 (7)	1 (4)	2.5 (4)	0.959	0.547
Intraventricular hemorrhage III-IV	4 (15)	3/40 (7)	0	0.999	0.546
Respiratory distress syndrome	8 (30)	9/40 (22)	9/31 (29)	0.355	0.083
Neonatal transient tachypnea	9 (33)	8/40 (20)	7/31 (22)	0.767	0.092
Early-onset neonatal sepsis	2 (7)	3/40 (7)	5/31 (16)	0.194	0.467
Periventricular leukomalacia	1 (4)	0	1/31 (3)	1.000	1.000
Necrotizing enterocolitis	1 (4)	0	1/31 (3)	1.000	1.000
Retinopathy of prematurity	4 (15)	1/40 (2)	0	1.000	0.991
Fetal and neonatal death	0	3 (7)	2 (6)	0.971	0.999

MIAC: Microbial invasion of the amniotic cavity.
IAI: Intra-amniotic inflammation.
GA: Gestational age;
PPROM: Preterm prelabor rupture of membranes;
CRP: C-reactive protein;
WBC: White blood cell count Amniotic fluid. Continuous variables were compared using a nonparametric Mann-Whitney U test presented as median (interquartile range or min-max*). Categorical variables were compared using Chi-square or Fisher exact tests and presented as number (%). p1 compares women with "Sterile" IAI and the "No-MIAC/No-IAI"group. p2 compares women with Microbial-associated IAI and the "Sterile" IAI group (all neonatal variables were adjusted for gestational age at delivery; amniotic fluid IL6 variables was adjusted for gestational age at sampling+).

P12 – CONTRIBUTION OF THE AMNIOTIC FLUID ALONG GESTATION TO THE PREDICTION OF PERINATAL MORTALITY IN WOMEN WITH EARLY PRETERM PREMATURE RUPTURE OF MEMBRANES.

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Objective

To evaluate contribution of largest vertical pocket (LVP) of amniotic fluid as a time-dependent factor for the prediction of perinatal mortality in women with early preterm premature rupture of membranes (EPPROM).

Methods

Observational cohort study of women with EPPROM < 24 weeks admitted to the Department of Maternal and Fetal Medicine at Hospital Clinic of Barcelona from December 2000 to December 2013. After excluding microbial invasion of amniotic cavity and under antibiotic prophylaxis, women were followed including clinical and ultrasound surveillance. Termination of pregnancy (TOP) was considered upon request if LVP was < 2 cm at 7 days. The maternal and neonatal characteristics of on-going pregnancies were recorded. Prediction of perinatal mortality was estimated based on influence of LVP as a time-dependent factor after adjustment for gestational age at EPPROM, the presence of an invasive procedure and maternal age.

Results

Of 104 women, 39 requested TOP. Perinatal survival was 40%, increasing to 74% if pregnancies achieved 24 weeks of gestation. LVP at admission, latency to delivery and gestational age at delivery were independent predictors of mortality. When evaluating LVP at different time-points of gestation, highest mortality risk was established at two weeks (OR 14.67 (p<0.001) after membrane rupture, being of 5.75 (p=0.05) the week after and of 10.93 (p=0.037) beyond 2 weeks of EPPROM.

Conclusions

Perinatal mortality prediction based on measurement of LVP as a time-dependent factor found that worst prognosis related to perinatal mortality was at 2 weeks after EPPROM.

Table 1. Association between the LVP at weekly US and the perinatal mortality

				Follow-up (weeks)		
			Admission	At 1 week	At 2 weeks	+2 weeks
Perinatal mortality	LVP (cm)	< 1	16 (41)	12 (36.4)	5 (27.8)	2 (66.7)
		1–2	14 (35.9)	7 (21.2)	8 (44.4)	0
		> 2	9 (23.1)	14 (42.4)	5 (27.8)	1 (33.3)
Neonatal survival to discharge	LVP (cm)	< 1	4 (15.4)	2 (7.7)	5 (19.2)	3 (15.8)
		1–2	10 (38.5)	12 (46.2)	6 (23.1)	8 (42.1)
		> 2	12 (46.2)	12 (46.2)	15 (57.7)	8 (42.1)
OR (95% CI)(*)			1	5.75 (1.68, 19.74)	14.67 (3.54, 60.82)	10.93 (1.16, 103.08)
p-value				0.005	<0.001	0.037

Data presented as number (percentage, %)

(*) OR Adjusted by prior invasive procedure, gestational age at PPROM and maternal age.

P13 – USE OF MAGNESIUM SULPHATE IN WOMEN DELIVERING BEFORE 32 WEEKS OF GESTATION; A EUROPEAN COHORT STUDY.

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Background

The use of magnesium sulphate (MgSO4) in European obstetric units is unknown. The aim was to describe reported polices and actual use of MgSO4 in women delivering before 32 weeks of gestation by indication.

Material/methods

We used data from the EPICE (European Perinatal Intensive Care in Europe) cohort study. This is a population-based cohort of infants born before 32 weeks of gestation in 18 regions in 11 European countries. Data were collected from April 2011-September 2012 through medical records and questionnaires. The study population comprised 694 women with severe pre-eclampsia and 3,840 without preeclampsia delivering from 24+0 weeks to 31+6 weeks of gestation in 119 maternity units with 20 or more very preterm deliveries per year.

Results

Among women with severe preeclampsia, 240 (36.0%) received MgSO4. In the 47 units stating use of MgSO4 whenever possible, only 23 units (49%) used MgSO4 in ≥40% of women with severe preeclampsia. In women without pre-eclampsia, 95 (2.6%) received MgSO4. Only nine units reported using MgSO4 for neuroprotection whenever possible and of these only three units actually used it in more than 20% of the non-preeclamptic deliveries. One unit reported using MgSO4 as a first-line tocolytic. Among women without preeclampsia, use of MgSO4 was not higher for women with preterm labor (2.6%).

Conclusion

Severe preeclampsia is not treated with MgSO4 as often as evidence-based medicine prescribes. MgSO4 is very seldom used for neuroprotection, and is no longer used for tocolysis. To continuously lower morbidity, greater attention to usage of MgSO4 is needed.

P14 – CAN WE REDUCE NON-SPONTANEOUS LATE PRETERM BIRTHS? 10 YEARS TRENDS IN GENEVA, SWITZERLAND

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Background

Late preterm deliveries (LPT, [34 0/7 -36 6/7 wks]), have higher short and long-term morbid-mortality than term infants (≥37 wks). Recently, a set of indications for delivery have been considered to constitute evidence-based (EB) criteria to justify a non-spontaneous LPT (NSLPT). Our objectives were A) To assess the numbers, rates and temporal trends of NSLPT and EB-NSLPT between 2002 and 2012; B) To evaluate the number of avoidable LPT; C) To evaluate neonatal morbidity.

Study design

Retrospective cohort study including LPT in the Maternity Unit of the University Hospitals of Geneva, Switzerland. NSLPT were considered as EB if indications were those accepted (severe preeclampsia, IUGR with abnormal doppler, acute abruption, abnormal NST, cholestasis, and uterine rupture).

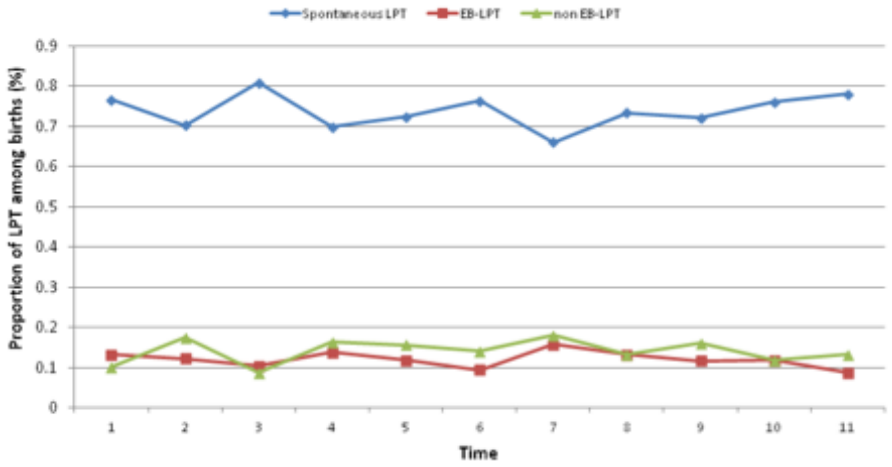
Results

In 10 years, there were 40,609 alive-singleton deliveries, 4,223 (10.48.7%) preterm births and 2,017 (4.9%) LPT. There were 26.3% NSLPT (EB: 12.0% and NEB: 14.3%) The most frequent indications for EB-NSLPT were severe preeclampsia (51.8%) and abnormal NST (24.7%). The most frequent indications for non-EB-NSLPT cases were haemorrhage (36.2%) and preeclampsia (15.7%). Rates of different LPT remained stable over time (Figure 1). In 10 years, a maximum of 287 cases of preterm birth could have been avoided if an EB-protocol for indicating delivery had been used. The rate of neonatal complications diminished over time (37.7% in 2002 and 33.3 in 2012: p<0.001) but remained high.

Conclusions

Over 10 years, the rates of LPT remained stable and neonatal complications diminished but remained high. Efforts should be made to avoid LPT without formal indications.

Figure 1. Proportion of each type of LPT across time



P15 – VALIDATION OF THE WELLBEING AND PREGNANCY QUESTIONNAIRE IN CHONGQING, CHINA.

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Background

Maternal stress is increasingly recognized as a contributor to preterm birth (PTB), leading cause of perinatal mortality/morbidity. Our group conducted a retrospective case-control study in Edmonton evaluating the chronic stress – PTB association using our "Wellbeing and Pregnancy Questionnaire," demonstrating adverse childhood experiences (ACEs) and abuse associated with PTB risk. We aimed to validate the questionnaire for use in a culturally, ethnically different population in Chongqing, China.

Methods

Validation included translating the questionnaire to Mandarin and back, establishing a protocol and applying it to a sample population. Participants were recruited as postpartum in-patients. Cases (20) had spontaneous singleton PTBs (38 weeks), without PTB history. Sociodemographic/medical data were collected. A combined childhood and adult abuse score was calculated from the ACE score and Abuse Assessment Screen (AAS). Logistic regression, $p<0.05$, reporting odds ratios for sPTB and 95% CIs.

Results

Cases were 3 years younger (OR 0.874; CI 0.78-0.99), less educated ($p<0.001$) and had lower annual income ($p<0.001$). The ACE, AAS and childhood and adult abuse score associated with sPTB in univariate analyses (OR 2.00, CI 1.08-3.71; OR 13.06, CI 1.28-133.38; OR 5.89, CI 1.92-18.01).

Conclusion

These results validate the Mandarin translation of the Wellbeing and Pregnancy Questionnaire and protocol used. Results were similar to our Edmonton study with small sociodemographic differences. The ACE score, AAS and childhood and adult abuse score associated with sPTB, suggesting a universal association between ACEs, abuse and sPTB.

P16 – PERFORMANCE OF CERVICAL LENGTH AND CERVICAL CONSISTENCY INDEX TO PREDICT SPONTANEOUS PRETERM BIRTH IN GENERAL POPULATION.

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Background

Women with a cervical length (CL) ≤ 20 mm, which was estimated to correspond to the 5th centile, are at increased risk for spontaneous preterm birth (SPTB). However, due to its low prevalence and sensitivity in the general population, other methods aiming to detect early stages of cervical remodelling would be advisable. We described and evaluated the performance of CL and the CCI, a biomechanical cervical measurement assessing the maximum tissue deformability, in the mid-trimester of pregnancy in the general population.

Material/Methods

The study population included 464 singleton pregnancies between 19-24.6 weeks. CL was measured from the internal to the external os. To measure the CCI, we followed the method described by Parra-Saavedra et al. The ratio between the anteroposterior diameter at maximum compression and at rest was calculated. To obtain the measure under compression, pressure is applied on the cervix until no further shortening of the anteroposterior diameter is observed.

Results

Characteristics of the population and outcomes are shown in the Table. The prevalence of a CL ≤ 20 mm was 0.6%. Performance of the 5th centile of CL and CCI to predict SPTB was Se 22.7%, Sp 95.9%, PPV 21.7%, NPV 96.1% and Se 45.5%, Sp 97.1%, PPV 43.4%, NPV 97.3%, respectively.

Conclusion

Due to the low prevalence and sensitivity of short cervix in the low risk population, only a small proportion of the screened women would be identified as being at risk. CCI, which assess the cervical softness, performed better than CL to identify the women who will present a SPTB.

		General population (n=464)
Maternal age		32,3 (0,3)
Weight		63,6 (0,9)
Height		1,62 (0)
BMI		24,4 (0,4)
Caucasian		320 (68,9)
GA at scan		21 (0,1)
Nulliparity		249 (53,6)
Previous SPTB		27 (5,8)
GA at delivery		39,2 (0,1)
PTB		33 (7,1)
SPTB		22 (4,7)
Birth weight		3206,3 (25,3)
Cervical Length	P1	23,5 (11,7--26,2)
	P5	29,9 (28,8--31,2)
	P50	39,7 (39,2--40,3)
CCI	P1	44,2 (37,1--46,7)
	P5	54,9 (50,8--57,1)
	P50	71,9 (71,2--73,4)

Data given as mean (SD or CI 95%) or n (%),
GA= Gestational age; PTB= preterm birth;
SPTB= Spontaneous preterm birth,
CCI= Cervical Consistency Index,

P17 – QUANTITATIVE ULTRASOUND ANALYSIS OF CERVICAL TEXTURE AND CORRELATION WITH GESTATIONAL AGE.

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Background

Structural cervical changes throughout pregnancy are subtle and difficult to detect with a clinical or a routine sonographic examination. In this study, we explored the ability of a texture-based method to provide robust textural features related to gestational age as a surrogate of cervical remodeling during normal pregnancy.

Material/methods

The study population included ultrasound images of the cervix from singleton pregnancies between 20-41 weeks. Images from multiple pregnancies, patients treated to prevent spontaneous preterm birth (SPTB) and women who delivered <37 weeks were excluded. Cervical length was measured and a selected region of interest (ROI) in the cervix was manually delineated off-line. A quantitative ultrasound analysis was performed to extract textural features from the ROI of the cervix. A model of gestational age based on textural features from cervical images was developed following three steps: data splitting, feature transformation and regression model computation.

Results

From 903 cervical images, 49 from women who delivered preterm and 153 which did not pass the image quality control were excluded. 701 images (≥30 images by each gestational week) were finally included for analysis. Demographic characteristics of the study population and perinatal outcomes were recorded (Table 1). There was a strong correlation between the real gestational age and the estimated gestational age by quantitative analysis of the cervical texture (R=0.88) (Figure 1).

Conclusion

This study provides preliminary evidence that quantitative analysis of cervical texture can extract features from cervical ultrasound images which are correlated to gestational age.

Further research is needed to evaluate its applicability as SPTB risk image biomarker, as well as its role in cervical assessment in other clinical situations in which cervical evaluation might be relevant.

Figure 1

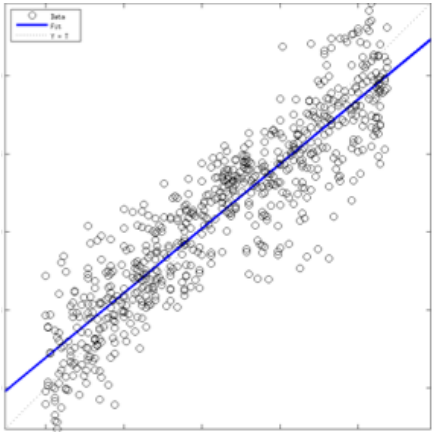

Table 1

		Total (n=701)
Maternal age		33 (0,2)
Weight		61,6 (0,5)
Height		1,62 (0)
BMI		23,44 (0,2)
Caucasian		471 (67,2)
GA at scan		31,1 (0,3)
Nulliparity		412 (58,8)
Previous SPTB		53 (7,6)
GA at delivery		39,37 (0,8)
Onset of labor	Spontaneous	356 (50,8)
	Induction	249 (38,4)
	Elective CS	76 (10,8)
Mode delivery	Vaginal	484 (69)
	Non-elective CS	130 (20,2)
	Elective CS	76 (10,8)
Birth weight		3220 (23,7)
Cercvical Length		35,79 (0,4)

Data given as mean ± (SD) or n (%.)
GA= Gestational age
SPTB= Spontaneous preterm birth
CS= Cesarean section

P18 – SEVERE CERVICAL RUPTURE AFTER PESSARY INSERTION FOR PREVENTION OF PRETERM DELIVERY

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Background

Here we present a case of cervical rupture during pregnancy after pessary insertion for prevention of preterm delivery. This is the first report of this kind in literature. Cervical pessaries are widely use in obstetrics practice for preventing preterm deliveries, although the results of the randomized controlled trials published so far are inconsistent in terms of their effectiveness. Basing on literature review it seems reasonable to insert pessaries in women with cervical length less than 25 mm, before 24th week of pregnancy.

Case presentation

A 31 years old woman, of white race, in the 35th week of gestation was admitted to the Department of Perinatology due to preterm labour. The patient history revealed cervical pessary insertion in the 29th week of pregnancy due to a cervix of 18 mm length. Because of threatened preterm labour the pessary was removed. After pessary removal a 4 cm longitudinal rupture of the cervix was diagnosed. Because of lasting labour and severe cervical rupture a Caesarean section was performed. After Caesarean section the

cervical rupture was sutured. Five days after the first operation the patient was operated again because of necrotically changed distal part of cervix which was removed. Two months after Caesarean section the cervix healed.

Conclusion

Insertion of cervical pessaries in some cases might cause serious injuries to women and thus pessaries should not be placed in medically unjustified cases.

P19 – NEONATAL BENEFIT AS A COMPOSITE ENDPOINT FOR SPONTANEOUS PRETERM LABOUR CLINICAL TRIALS: COMPARISON OF REAL-WORLD RATES OF NEONATAL OUTCOMES BETWEEN UNITED STATES AND EUROPEAN SETTINGS.

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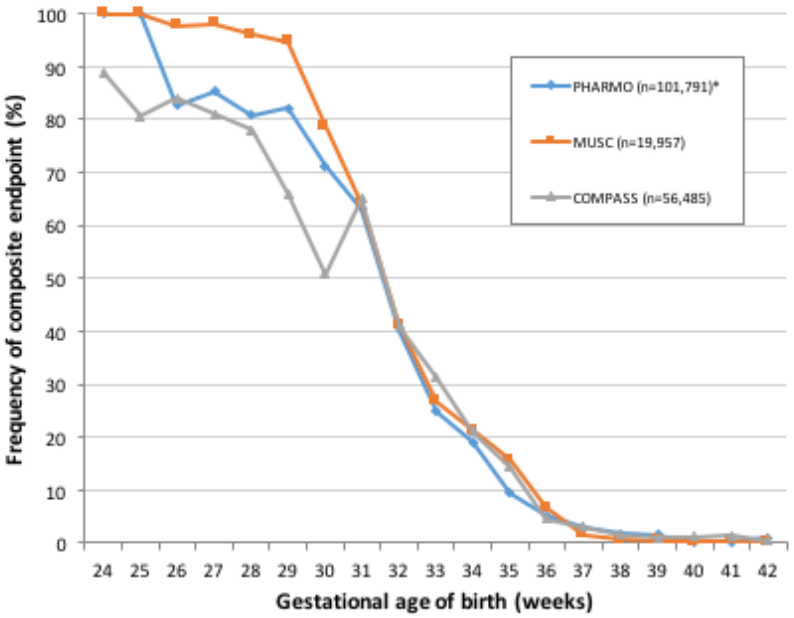
Background

Neonatal benefit is a required endpoint by the FDA in RCTs of new tocolytics. We previously defined a composite endpoint (CE) of neonatal mortality and morbidity (RDS, BPD, IVH, PVL, NEC, ROP, cerebellar haemorrage, sepsis, meningitis) for use in Phase-3-RCTs. Initially, CE frequency was assessed in US settings (Medical University South Carolina (MUSC): single-site 3° hospital [n=19,957]; COMPASS Research Network: numerous hospitals across 7 states [n=56,485]). To understand CE frequency across different geographies, we compared US settings with a Dutch population.

Figure 1. Comparison of composite endpoint frequency between PHARMO-PRIN, MUSC and COMPASS databases



**Neonatal mortality excluded from composite as PHARMO Database Network contains live infants only, hence deaths could not be linked between PRN-PHARMO databases*

Material/Methods

Retrospective analyses were conducted using mother-infant linked pairs from a combined dataset of the Netherlands Perinatal Registry (PRN) and the PHARMO Database Network (2000-2010), funded by GSK. CE frequency was assessed among live singleton infants ≥24 weeks gestational age (GA) without congenital abnormalities and excluding those born to women with specific pregnancy complications (including eclampsia/HELLP, placental conditions, infection).

Results

Among the PHARMO-PRN cohort (n=101,791), 2 infants died before birth hospital discharge; 2,446 infants had ≥1 CE morbidity variables. Overall, CE distribution was similar between datasets (Figure 1); between 24-28w GA, CE frequency in PHARMO was up to 20% lower than MUSC but more comparable to COMPASS; this was reversed between 29-31w. After 32w, frequency between datasets merged.

Conclusions
Differences in exact composite definition, patient populations, medical coding and country-specific treatment protocols (lack of resuscitation for <26 weeks GA) are important factors when comparing datasets. However, we conclude that CE rates are broadly analogous between US and European settings, allowing confidence in sample size estimation in ongoing RCTs.
Word count (excluding title): 250

P20 – RISK FACTORS FOR MORTALITY OF OFFSPRING IN PPROM AND DELIVERY BEFORE 30 WEEKS OF GESTATION

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Background
Preterm premature rupture of membranes (PPROM) occurs in one third of preterm deliveries. The outcome of very preterm PPROM is often poor, but it may be difficult to predict the outcome in individual cases. The aim of this study was to analyze clinical risk factors and placental histological findings in PPROM cases and relate them with neonatal outcome.

Methods
Cases of PPROM and delivery before 30 weeks of gestation were collected from Tampere University Hospital's database between 2004 and 2014.

Cases where delivery occurred within 24 hours of PPROM or placental histology was not available were excluded. Total of 81 mothers and 92 newborns were included in the study. We divided newborns into two groups: survivors and nonsurvivors.

Binary logistic regression was used to identify risk factors for mortality of offspring.

Results
In the nonsurvivors' group the gestational age at PPROM and delivery were lower (23+1 vs. 26+1 days and 25+3 vs. 27+5 days, respectively), but latency from PROM to delivery was longer (13.0 vs. 5.0 days).

Maternal BMI was higher in the group of nonsurvivors (28.3 vs. 25.4). CRP and leukocyte count at different stages of hospital stay were higher, histological chorioamnionitis and funisitis were found more often in nonsurvivors (92,0% vs. 70,1% and 76% vs. 34%).

Conclusion
Gestational age at PPROM, histological finding of funisitis and CRP at admission to hospital were independent risk factors for mortality of offspring in PPROM and delivery before 30 weeks of gestation.

P21 – BIOCHEMICAL AND BIOPHYSICAL MARKERS OF PRETERM BIRTH; THEIR POTENTIAL TO PREDICT UNDERLYING AETIOLOGY.

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Background
Fetal fibronectin (fFN) and cervical length (CL) are reliable predictors of preterm birth (PTB). The underlying aetiology of PTB is frequently associated with inflammation and infection, which can be detected by placental histopathology. We evaluated the relationship between predictive markers and aetiology to elucidate their relationship.

Methods
The relationship between placental histopathology, fFN and CL was examined in 105 women with preterm birth (50ng/mL) was significantly correlated with placental inflammation (42/48, 87%, odds ratio 8.96, Pearson's chi square coefficient 21.49, p=0.000004). Equivalent odds ratio for short cervical length and placental inflammation was 2.81 (95% CI 1.73-15.04).

Significantly fewer women with a negative fFN had evidence of placental inflammation (44%, 25/57, odds ratio 0.112, 95% CI 0.04-0.30).

fFN is more strongly associated with inflammation than CL (fFN wald test 3.00, p=0.046, CL wald test 1.399, p=0.237).

Conclusion
There is significant association between positive fFN and inflammatory placental histology, greater than CL. A false negative fFN result is more likely to correspond with non-inflammatory pathology (normal placental pathology or vascular lesions). Infective morbidity may be increased in women and neonates with positive fFN who deliver preterm.

P22 – THREATENED PRETERM LABOUR MANAGEMENT: RESULTS OF A DELPHI CONSENSUS ON BEST PRACTICE.

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Background
Many women with symptoms of threatened preterm labour (TPTL) do not deliver early. Interventions can reduce mortality and morbidity associated with preterm birth but are not without risk and cost, e.g. repeated antenatal steroids and in utero transfer. TPTL management appears to vary around the UK (Stock et al., 2014).

Aim
To explore variation in UK TPTL management and to reach expert consensus on best practice.

Method
Members of the UK Preterm Clinical Network were invited by e-mail to participate in a Delphi process. In round one, participants considered different scenarios and were asked to indicate which interventions they would recommend dependent on TPTL test results and % risk of delivery within 48 hours. Collated results were distributed to participants, who were invited to repeat the survey following consideration of the report.

Results
Thirty-one respondents completed the first survey (71% were consultants). 74% indicated availability of quantitative fetal fibronectin (fFN), 48% transvaginal cervical length measurement, 39% a PTB % risk prediction tool, 32% qualitative fFN, 13% used Actim Partus, and 6% Partosure. Twenty respondents agreed to continue the Delphi process. Opinions on management varied dependent on test used, intervention offered and gestation at presentation. Thresholds for admission and steroid use were lower than for in utero transfer, despite scenarios stating 'no cots are available in your unit'.

Discussion
A further survey has been distributed and the outcome of a final meeting to establish consensus will be presented.

P23 – EVALUATION OF PHOSPHORYLATED INSULIN LIKE GROWTH FACTOR BINDING PROTEIN-1 AND SONOGRAPHICALLY MEASURED CERVICAL LENGTH FOR PREDICTION OF PRETERM BIRTH IN THREATENED PRETERM LABOR.

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Background and objectives
Measurement of cervical length using Transvaginal Sonography (TVS) is commonly used to identify those patients of threatened preterm labor who are likely to deliver. Biochemical markers in cervical secretions namely fetal fibronectin and phosphorylated Insulin Growth Factor Binding Protein - 1 (phIGFBP-1) have also been used to improve predictability.

This study evaluated bedside kit test for phIGFBP-1 and cervical length measurement by TVS, individually and in combination, for prediction of preterm birth in patients with threatened preterm labour.

Material and method
A prospective observational study was conducted at a tertiary centre in India where women between 28+1 and 36+6 weeks period of gestation with threatened preterm labour were recruited and rapid bed-side test for phIGFBP-1 and TVS for measurement of cervical length were done. Patients were followed till delivery and data was collected and analysed.

Results
468 patients completed the study. Statistical analysis of sensitivity, specificity, PPV and NPV showed that phIGFBP-1 was a better predictor of preterm birth compared to cervical length. There was very good correlation of phIGFBP-1 for prediction of delivery in the crucial period of next 7 days with a kappa of 0.833 (0.780-0.886). Cervical length and phIGFBP-1 were shown to be independent of each other on multivariate regression analysis.

Conclusion
A negative result for phIGFBP-1 can predict the outcome of threatened preterm labour quite accurately. Evaluation of cervical length does not add improve predictability. In cases with a positive test for phIGFBP-1, cervical length may be measured and incorporated in the management algorithm. This would result in a more economical approach and optimization of resources.

P24 – INFLAMMATION IN CHORIO-DECIDUA AND AMNION IN PRETERM BIRTH SUBTYPES.

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Background

Labour is an inflammatory process that involves secretion of cytokines/chemokines from both resident and infiltrating immune cells. Preterm birth (PB) is a consequence of untimely mechanisms that elicit pro-inflammatory pathways within the uterus. The inflammatory contribution of amnion and choriodecidua (CD) in PB subtypes are unclear and a direct comparison of these tissues would enhance understanding.

Material/Methods

40 matched samples of amnion and CD were collected at preterm caesarean sections and grouped into PB subtypes (preterm no labour [PTNL], chorioamnionitis, idiopathic, twins no labour [TwNL], and twins labour [TwL]) based on clinical indication for delivery. Samples were stored at -800C. Protein lysates were generated and concentrations determined using a Biorad protein assay. A Bio-Plex cytokine assay was undertaken on a single human inflammation panel (37 analytes). Data was analysed using GraphPad Prism®.

Results

Comparison of analyte concentrations were undertaken using amnion as the baseline. In PTNL, only 13% analytes were increased in CD, with 50% analytes showing no significant difference between the two tissues. In chorioamnionitis and idiopathic subtypes, 68% and 13% of analytes were increased significantly in the CD compared to the amnion respectively. Interestingly, in TwNL and TwL, 16% of analytes and nearly 45% analytes were significantly raised in CD compared to amnion respectively.

Conclusion

Pro-inflammatory analytes were more raised in CD in chorioamnionitis and TwL than in amnion, suggesting CD is highly enriched with these analytes during infection and possibly in stretch associated PB. Further work could determine whether this influx of analytes alters the immune cell populations of CD.

P25 – REAL-WORLD EVIDENCE OF POSTNATAL OUTCOMES IN INFANTS WITH COMORBIDITY COMPOSITE ENDPOINT AT BIRTH.

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Background

Neonatal benefit is a required endpoint by the FDA in RCTs of new tocolytics for women in spontaneous preterm labour (SPTL). A composite endpoint (CE) of neonatal mortality and morbidities (RDS, BPD, IVH, PVL, ROP, NEC, cerebellar haemorrage, sepsis, meningitis) is being used in ongoing Phase-3-RCTs; furthermore, all infants are enrolled into a long-term follow-up study. To understand how the CE impacts postnatal morbidities, we conducted a longitudinal assessment of infants.

Material/Methods

Retrospective analyses were conducted using mother-infant linked pairs combining data from the Netherlands Perinatal Registry and PHARMO Database Network (2000-2010), funded by GSK. The morbidity CE (excluding mortality as PHARMO Database Network contains live infants only) was assessed among infants of women reflecting the RCT population (SPTL, uncomplicated singleton pregnancies). Postnatal outcomes (using ICD-9/10, ICPC codes) were assessed in a subcohort with GP data to enable long-term follow-up.

Results

Within the linked mother-infant cohort (n=134,006), 17,903 had GP data; of these, 847 infants were born to mothers with uncomplicated SPTL. CE was present in 64 (7.6%) infants; average (±SD) follow-up time was 5.7 (±2.5) years. Outcomes with significantly increased incidence rates in children with versus without the CE included valvulopathy (adjusted HR [95% CI] 14.76 [1.22-178.69], only observed in first year), adverse respiratory outcomes including asthma (2.94 [1.46-5.92]), failure to thrive (7.12 [1.73-29.21]), any infectious disease (9.90 [5.67-17.28]) and cognitive impairment (36.25 [1.33-988.54]).

Conclusions

These real-world retrospective analyses allow proactive contextualization and interpretation of safety signals that may arise from ongoing RCTs over the next 5-10 years.

P26 – THE ROLE OF DIGITAL VAGINAL PH SELF-ASSESSMENT AS A PREDICTOR OF PRETERM BIRTH.

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Background
Vaginal infection including bacterial vaginosis (BV) has a proven association with preterm birth (PTB). Vaginal pH >4.5, one of the diagnostic criteria for BV, is independently thought to be associated with PTB. Digital self-testing with the "pH Glove" offers an antenatal screening opportunity to identify those with possible infection who are therefore at increased risk of PTB.

We set out to identify whether a vaginal pH >4.5, in a high-risk antenatal population, is a valid self-assessment screening tool for identifying women at increased risk of PTB.

Methods
243 singleton pregnant women attending general antenatal and high-risk Prematurity Surveillance Clinic from October 2014 to February 2015 used a pH Glove to self-test vaginal pH. Primary outcomes were gestation at delivery and birth weight.

Results
The rate of PTB within the high risk cohort was similar in those with a pH>4.5 compared to 4.5 does not appear to be a valid screening tool for increased risk of PTB in a high risk asymptomatic cohort.

P27 – THE ANTISECRETORY FACTOR IN PLACENTA AFTER TERM AND PRETERM BIRTH.

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Background
Inflammation may play a role in the mechanisms behind preterm birth (PTB) and its complications. The pathophysiology of PTB is unclear and effective treatment is lacking. Antisecretory factor (AF) is involved in the regulation of secretory processes and inflammation, and might be of importance. The study objective was to determine AF and inflammatory markers in placenta after term and preterm birth.

Material/methods
61placenta biopsies collected after birth: 31 preterm (< 36 weeks of gestation); 30 term (37 - 41 weeks of gestation). Inclusion: Women ≥ 18 years, spontaneous delivery onset. Exclusion: tobacco use, preeclampsia, diabetes, other systemic disease or fetal malformation. Determination of AF and CD68 (inflammatory marker) was performed using immunohistochemistry with result graded into an ordinal scale of seven grades according to the assessment method.

Results
AF is present in the outer, syncytiotrophoblast, layer of the placenta villi. Results showed differences in AF and CD68 between preterm and term placental tissue ($p<0.05$). In preterm placenta there were a low presence of AF and high of CD68 while in term placentas high presence of AF and low of CD68.

Conclusion
The level of AF differed between preterm and term placentas. The results indicate a link between AF levels in placenta and preterm delivery with an inverse relationship to inflammation. It is a novel finding that may contribute to unravel the pathophysiology of preterm birth and a basis for future research aiming to develop new treatment to prevent preterm birth and its consequences.

P28 – TREATMENT OF BACTERIAL VAGINOSIS IN EARLY PREGNANCY AND ITS EFFECT ON SPONTANEOUS PRETERM DELIVERY.

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[3] Associate Professor, Örebro University, Sweden, Tönsberg, Norway
[4] MD, Athens, Greece
[5] MD, Skövde, Sweden

Background
This study was conducted to investigate whether screening and treatment of bacterial vaginosis in early pregnancy reduces the risk for preterm delivery.

Material and methods
Women were screened for BV during their first visits to the maternal health care unit. After the vaginal samples were air dried, they were sent to the gynaecological department and analyzed using Hay/Ison modified classification. Eligible women were women who lived in Skaraborg county and delivered at Skaraborg Hospital in Skövde, Sweden. Women were divided into screened (with BV or with lactobacilli flora) or unscreened. Women with BV were offered treatment with vaginal clindamycin.

Results
During 2007–2015, a total of 6 896 women were screened for BV, 10,7% of whom had it. Survival analysis showed that women with BV had spontaneous preterm delivered significantly earlier than women with normal lactobacilli flora even after treatment with vaginal clindamycin. During the same year, 15 357 women delivered at Skaraborg Hospital who were not screened for BV. These women delivered significantly earlier than the screened women.

Conclusion
Even though patients with BV had been treated with clindamycin, they still had an increased risk for preterm delivery compared to women with normal lactobacilli flora. The difference between the screened women and the unscreened women could be due to the positive effect of treatment with clindamycin. Treatment of BV will not reduce the risk of spontaneous premature delivery to the same level as women with normal lactobacilli flora.

P29 – VALIDATION OF MULTIPLEX PCR FOR DIAGNOSING BACTERIAL VAGINOSIS.

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Background
After candidiasis, bacterial vaginosis (BV) is the most common cause of fluor vaginalis. During pregnancy bacterial vaginosis can cause preterm labor, intra-uterine infections and post-partum fever. For diagnosing BV multiplex PCR assays are upcoming and seem to be more sensitive compared with the known tests.

Methods/materials
Eighty premenopausal women were included. Sixty patients were complaining of vaginal discharge and twenty patients were visiting the outpatient department for other reasons than discharge. Medical history was taken, three vaginal swabs were taken for culture and PCR analysis. Test characteristics of culture, PCR and the Amsel criteria were determined using the Nugent score as reference standard.

Results
Among all 80 patients 17 (23%) Nugent score, 35 (47%) BV PCR, 12 (15%) culture and 19 (26%) Amsel criteria outcomes were positive. In total sample size sensitivity of BV PCR (100%) was significantly higher (difference 47%, 95% CI 23% to 71%) compared with the culture of G. vaginalis (53%). Specificity of G. vaginalis culture (96%) compared with BV PCR (73%) was significantly higher in total sample size (difference 23%, 95% CI -34% to -6%).

Conclusions
The PCR was the most sensitive and rapid method to diagnose BV. The specificity of the culture was significantly higher than the BV PCR. However, the sensitivity of the culture is too low to use it as a diagnostic method. The BV PCR is the method of choice to diagnose BV. Further research should be done to determine whether its low PPV is due to a relatively low sensitivity of the Nugent score.

P30 – NOVEL BIOMARKERS FOR DETECTION OF INTRA-AMNIOTIC INFECTION IN PRETERM PREGNANCIES WITH INTACT MEMBRANES.

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Background

Intra-amniotic infection (IAI), i.e. microbial invasion of the amniotic cavity (MIAC) with inflammation, is a major single etiologic factor of preterm delivery. IAI occurs equally in women with or without preterm prelabor rupture of membranes (PPROM). Infection produces more intense fetal response than inflammation without MIAC. This justifies seeking for rapid amniotic fluid biomarkers associated with MIAC. We studied the diagnostic performance of inflammatory proteases in the IAI diagnostics in cases and controls with intact membranes.

Material / methods

Amniocentesis was performed in 26 singleton pregnancies with suspected IAI between 22+0 and 31+0 weeks of gestation and in 54 pregnant controls between 17+0 and 36+0, all with intact membranes. Amniotic fluid matrix metalloproteinase (MMP) – 8 was quantitated with a solid-phase immunoenzymometric assay (MMP-8 IEMA, Medix Biochemica, Espoo, Finland) and others by using commercial enzyme-linked immunosorbent assay according to manufacturer´s instructions. Microbiologic analyses were performed with 16S rRNA sequencing (am-PCR) (n= 72).

Results

The median concentrations (ng/mL) of MMP-8, MMP-9 and tissue inhibitor of matrix metalloproteinase -1 (Timp-1) were higher in cases with suspected IAI compared to controls (10.3 vs. 4.5, p<0.001; 8.7 vs. 2.6, p<0.001; and 1292 vs. 1112, p=0.020, respectively). MIAC was detected in six (23%) cases. Among these women, the median concentrations (ng/mL) of MMP-8, MMP-9 and Timp-1 were significantly higher than in cases without MIAC (2542 vs. 7.5, p<0.001; 2182.5 vs. 3.4, p<0.001; 3298 vs. 1178, p=0.004, respectively).

Conclusion

Am-MMP-9 and am-Timp-1 are new promising biomarkers for the diagnosis of IAI.

P31 – WOMEN WITH PRETERM LABOR AND HIGH CERVICAL LENGTH AND NEGATIVE FIBRONECTING WHO DELIVER PRETERM HAVE A DIFFERENT VAGINAL MICROBIOTA THAN THOSE DELIVERING AT TERM.

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Objective

Women delivering preterm have different vaginal microbiota than those delivering at term. We aimed to identify whether the vaginal microbiota of low risk women (high cervical length [CL >25 mm] and negative fibronectin [ffn] tests) with preterm labor (PTL) was different of those delivering at term.

Material and Methods

Secondary analysis of women included in a former study assessing the value of quantitative ffn test in women with PTL in the University Hospitals of Geneva, Switzerland. Women were included if having regular contractions at <37 weeks and had qualitative and quantitative ffn tests and vaginal ultrasound measured CL. Women consented to use the vaginal swab for analysis of the microbiota using Next Generation Sequencing techniques. For each sample we performed principal coordinate analysis (PCoA) based on the presence and absence of 100%-ID or 97%-ID phylotypes.

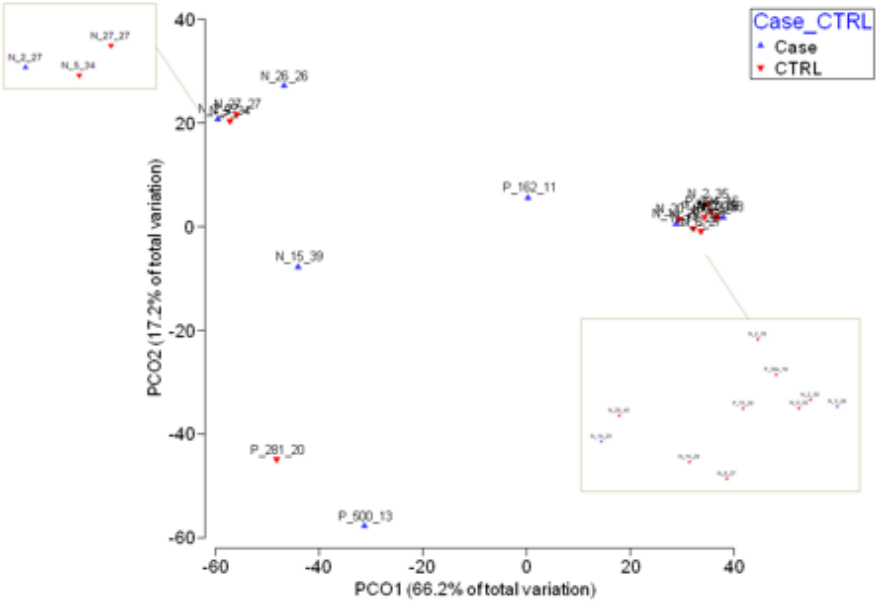
Results

We included 7 women delivering preterm and 11 delivering at term. Figure 1 shows results based on PCoA values, qualitative and quantitative ffn tests and CL). Most women cluster on a particular type of microbiota with high lactobacilli (So called "protective microbiota"). PCoA showed that the microbiota from the preterm women had greater within-group dispersions. Women delivering preterm who were considered at low risk had a vaginal microbiota not clustering with the "protective one. There was one low-risk woman with long CL and negative ffn tests who delivered preterm but who had a prior preterm birth.

Conclusion

Vaginal microbiota might help identifying women with negative ffn results and high CL who end up delivering preterm.

Figure 1. Principal coordinate analysis (PCoA), qualitative and quantitative fibronectin results and vaginal ultrasound cervical length in cases (women delivery preterm) and controls (women delivering at term.



*Each women is identified by the results of the qualitative ffn test (N: negative, P: positive), the quantitative ffn test and the cervical length.

P32 – THE PRETERM CLINICAL NETWORK DATABASE: A STANDARDISED AND SYSTEMATIC DATA COLLECTION METHOD FOR PRETERM CLINICS.

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Introduction

Despite much research effort, there is a paucity of conclusive evidence for preterm birth prediction and prevention. Monitoring and interventions offered to women at risk varies considerably around the UK and depends on local maternity care provision (Sharp and Alfirevic, 2014).

Where empirical evidence is lacking, clinicians use their experience and knowledge gained over time, to guide them in management of individual patients. This experience and knowledge, if captured on a larger scale, could be utilized as a valuable source of evidence, particularly in areas where empirical evidence is lacking (Hay et al, 2008; Owtad et al 2013).

Methods and results

The UK Preterm Clinical Network was established with the aim of improving care and outcomes for women at risk of preterm birth through the sharing of a wealth of experience and knowledge, and the building of clinical and research collaborations. It was agreed that an online accessible database was needed to facilitate this. We have designed a web-based data collection and storage platform that provides a standardised and systematic method of collecting clinical data for both local audit and larger studies using combined data. The database has been constructed and piloted, governance

approvals are in progress and 25 members, including three international contributors, are ready to begin collecting data.

Discussion
This Preterm Clinical Network platform has significant potential to generate a better understanding of effectiveness of current surveillance practices and preterm birth prevention strategies on a national and international scale, as well as initiating innovation and research collaborations.

P33 – THE ASSOCIATION BETWEEN PROGESTERONE AND PRETERM BIRTH

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Background
Preterm birth is the leading cause of perinatal morbidity and mortality worldwide. Progesterone is a steroid hormone that plays a fundamental role in maintaining pregnancy. It has been used in treating conditions such as miscarriage and preterm labour, although its mechanisms of action remain unclear. We hypothesize that serum progesterone levels are different in women who have preterm births from women who have term births.

Methods
Serum progesterone levels were measured in 708 women with singleton pregnancies within four visits: visit 1, 9 -14 weeks; visit 2, 18 - 22 weeks; visit 3, 28 - 32 weeks; and visit 4, > 34 weeks. Levels were compared between preterm and term groups; and among term, spontaneous preterm, and iatrogenic preterm subgroups.

Results
Serum progesterone level (nmol/L) at visit 3 in preterm group (mean, 374.4; 95% CI, 332.1- 416.8) was significantly higher than in term group (mean, 335.5; 95% CI, 328.1 to 342.9) (p=0.025). The levels did not differ significantly between the two groups for visits 1, 2 and 4. In subgroup analysis, progesterone level was significantly higher in iatrogenic preterm birth subgroup compared to term subgroup for visit 1 and visit 3. At 304.5nmol/L, progesterone as a predictor of preterm birth has: 81.8% sensitivity, 40.1% specificity, NPV 97.5%, PPV 7.2%.

Conclusion
This is the first large prospective study in an Asian population to investigate association between progesterone level and preterm birth. We found higher serum progesterone levels at 28 – 32 weeks in women with preterm births, and it was weakly predictive of preterm birth.

P34 – LONG-TERM OUTCOMES AND HEALTHCARE RESOURCE USE (HRU) OF INFANTS BORN TO MOTHERS WITH SPONTANEOUS PRETERM LABOR (SPTL) IN THE LINKED PHARMO-PRN COHORT.

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Background
As new tocolytics for SPTL are in development, detailed real-world information on long-term outcomes of infants born to women with SPTL is needed to contextualize outcomes of infants born to trial participants.

Material/Methods
The study (funded by GSK) used a cohort of children with linked information from 2 data sources; The Netherlands Perinatal Registry (PRN) and the PHARMO Database Network (2000-2010). A cohort design was used to assess rates of outcomes from birth until the end of follow-up. Outcomes were based on hospitalizations, dispensing records, general practitioner (GP) referrals to other healthcare providers.

Results
The cohort included 134,006 singleton infants. Of these, GP data was available for 17,903 children, with a follow-up of 5.7-6.1 years. A SPTL subcohort was defined as children born to mothers with an uncomplicated pregnancy and either a diagnosis of preterm labor or a delivery < 37 weeks GA. There were 847 children in the SPTL cohort and 16,393 children in a full-term (FT) cohort. SPTL children had increased risk for health events and HRU vs. FT children in the follow-up period, with significantly higher rates of referrals for: any specialist (adjusted HR 1.52); therapies, e.g. speech therapy (adjusted HR 1.52); mental health (adjusted HR 2.12); and surgical (adjusted HR 1.48). SPTL children also had higher rates of postnatal hospitalizations and pharmacy dispensing (Table 1).

Conclusions
This study provides insight into risk of health outcomes of SPTL infants compared to FT infans and how this changes in the years following delivery.
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Table 1. Rates of HRU any time during the postnatal follow-up, for pregnancies with FTL and SPTL

	FT N at risk = 16,393			STPL N at risk = 847			RR crude	RR adjusted*
Postnatal HRU	**N**	**PY**	**Rates per 1,000 PY (95%CI)**	**N**	**PY**	**Rates per 1,000 PY (95%CI)**	**(95% CI)**	**(95% CI)**
Postnatal hospitalizations								
At least one hospitalization	44,344	828,866	5.3 (5.3-5.4)	3,016	43,450	6.9 (6.7-7.2)	1.30 (1.26-1.34)	1.24 (1.20-1.28)
Total number of hospitalizations	97,276	828,866	12 (12-12)	7,866	43,450	18 (18-19)	1.54 (1.46-1.63)	1.45 (1.36-1.54)
Total days of hospitalization	247,875	828,866	30 (30-30)	32,872	43,450	76 (75-76)	2.53 (2.36-2.71)	1.66 (1.45-1.91)
Out-patient medication use								
At least one dispensing	120,878	828,866	15 (14-15)	6,490	43,450	15 (15-15)	1.02 (1.01-1.04)	1.00 (1.00-1.01)
Total number of dispensings	2,374,291	828,866	286 (286-287)	157,921	43,450	363 (362-365)	1.27 (1.23-1.31)	1.21 (1.17-1.25)

*Relevant characteristics present in at least 5% of the population and with univariate p-values <0.1 were considered eligible for the multivariable (adjusted) regression model, using a backward stepwise approach.

P35 - CLINICAL IMPORTANCE OF MICROBIAL INVASION OF THE AMNIOTIC CAVITY AFTER INTRODUCTION OF AMNIOCENTESIS IN THE MANAGEMENT OF WOMEN WITH PRETERM LABOR AND INTACT MEMBRANES.

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Introduction
The objective was to determinate clinical significance of microbial invasion of the amniotic cavity (MIAC) after the introduction of the amniocentesis in the management of women with preterm labor (PTL).

Material and methods
Prospective cohort study. From September 2013 to February 2015 a transabdominal amniocentesis was performed in women with PTL between 22.0 to 34.0 weeks. MIAC was defined as positive amniotic fluid culture for aerobic/anaerobic/genital Mycoplasma. Main clinical outcome evaluated were gestational age at sampling, at delivery, Apgar score at 5 minutes, umbilical artery pH, days in neonatal intensive care unit, intraventricular hemorrage grade III or IV, respiratory distress syndrome, early-onset neonatal sepsis, stillbirth, neonatal death and the occurrence of clinical chorioamnionitis, postpartum endometritis. We also recorded funisitis and histologic chorioamnionitis as placental findings. Neonatal outcomes were adjusted for gestational age at delivery.

Results
52 women with PTL between 23.1 and 33.5 gestational weeks were included. MIAC was found in 11,5% of women. GA at sampling was similar between groups. However, a significantly earlier GA at delivery was observed in the MIAC group. No statistical differences were observed in short-term neonatal outcome after adjustment for GA. In addition, a similar rate of clinical chorioamnionitis and puerperal endometritis was found between groups.

Conclusions
MIAC complicates 11.5% of women with PTL below 34.0 weeks. A significantly earlier gestational age at delivery was observed in women with MIAC. However, no differences in neonatal outcome were observed after adjustment for gestational age at delivery.

Table 1

	MIAC group n=6	No MIAC N=46	p (<0.05)
Maternal age (y), mean (SD)	28.5 (5.9)	31.2 (5.9)	0,298
Nulliparity n(%)	4 (66.7)	29 (63)	1,000
GA at admission (amniocentesis) (wk), mean (SD)	28.1 (2.8)	29.5 (2.4)	0,194
GA at delivery (wk), mean (SD)	32.5 (0.5)	36.3 (3.5)	0,031
Birthweight (g), mean (SD)	1998 (1159)	2683 (771)	0,999*
1-min Apgar score, mean (SD)	7.5 (1.8)	8.2 (1.9)	0,999*
5-min Apgar score, mean (SD)	9.3 (1.6)	9.4 (1.0)	1,000*
UA pH, mean (SD)	7.26 (0.02)	7.23 (0.05)	0,998*
UV pH, mean (SD)	7.27 (0.09)	7.32 (0.05)	0,999*
Histologic chorioamnionitis n (%)	4/4 (100)	1/10 (10)	0,005
Histologic funisitis (%)	1/4 (25)	0/10 (0)	0,286
Puerperal endometritis	0 (0)	2 (4.5)	1,000
Clinical choriamnionitis n(%)	0 (0)	3 (6.8)	1,000
Days in NICU, mean (SD)	42.1 (37.2)	5.6 (12.5)	0,998*
Distress respiratory syndrome n(%)	2 (33.3)	6 (14)	0,999*
IVH grade III or IV n(%)	1 (16.7)	0 (0)	1,000*
Neonatal sepsis n(%)	2 (33.3)	1 (2.2)	0,256*
Enterocolitis n(%)	0 (0)	0 (0)	--
Stillbirth n(%)	0 (0)	0 (0)	--
Neonatal death n(%)	0 (0)	1 (2.4)	1,000*

Continuous variables were compared using a Student T-test presented as mean (standard deviation). Categorical variables were compared using Chi-square or Fisher exact tests and presented as number (%). p compares women with MIAC and the "No-MIAC" group (unadjusted analysis). p*compares women with MIAC and the "No-MIACI" group (+ variables adjusted for gestational age at delivery)

P36 – EFFECTS OF HIGH GLUCOSE AND METABOLIC STRESS ON PLACENTAL MACROPHAGE ACTIVATION

Lisa M. Rogers, Linda Englund Ogge, Bo Jacobsson, Kasey Vickers, David M. Aronoff

Background

Gestational diabetes mellitus (GDM) is associated with placental inflammation. Macrophages (Mϕs) modulate placental inflammation while microRNAs (miRNAs) regulate Mϕ activation. Our hypothesis is that hyperglycemia activates placental Mϕs (PM) to a more inflammatory phenotype, which is associated with alterations in miRNA expression.

Methods

Three macrophage sources were used: the macrophage-like THP-1 cell line (differentiated with phorbol ester), human peripheral blood monocyte-derived macrophages (MDMs) differentiated for 7d with M-CSF, and PM from healthy donors undergoing term non-laboring C-sections. Mϕs were exposed to 2mM (hypoglycemia), 5mM (euglycemia), 10mM (intermediate hyperglycemia), or 25mM glucose (hyperglycemia) for 3d ± 10-100 ng/mL lipopolysaccharide (LPS) for 24h. To mimic metabolic stress, Mϕs were exposed to a metabolic cocktail (MetaC) comprised of 30mM glucose, 0.4mM palmitate, and 10nM human insulin for 1h, then ± LPS for 24h. Supernatants were collected for ELISA and RNA harvested for miRNA assessment.

Results

Glucose alone did not modulate macrophage activation in the absence of LPS. In the presence of LPS, glucose suppressed proinflammatory cytokine expression

(IL-1β, TNF-α, and MCP-1) in a dose-dependent manner. The results were statistically significant only in THP-1 cells. Studies of the effect of MetaC on Mϕ activation and correlations with miRNA are pending.

Conclusion

Glucose appears to modulate macrophage inflammatory responses to LPS but more studies are pending.

Funding

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P37 – CERVICAL PESSARY AND MICRONIZED PROGESTERONE VAGINAL TABLETS FOR THE PREVENTION OF SPONTANEOUS PRETERM BIRTH IN PATIENTS WITH CCI ≤ 5TH PERCENTILE IN ROUTINE ULTRASOUND SCAN AT 11 TO 13.6 WEEKS.

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Objective

To present our experience in the use of combination therapy with cervical pessary (CP) and vaginal micronized progesterone tablets (VMP) for the prevention of preterm birth (PP) in singleton pregnancies with cervical consistency index (CCI) ≤ 5th percentile in first trimester, routine scan, compared with historical matched controls.

Methods

Prospectively, between January 1st, 2015 to December 31th, 2015,all singleton pregnancies evaluated in our unit institution, with cervical consistency index ≤ 5th percentile at 11 to 13.6, were offered combined treatment with CP and VMP 200mg bid. The VMP was continued until 34 weeks, the CP retired at 36 weeks or at the onset of labor. Pregnancy with contractions, bleeding or RPM were excluded. The result was compared with historical controls matched week of gestation and CCI, 1: 1 ratio.

Results

In the study group 10 patients, the mean gestational age at admission was 12.3 weeks, cervical length 37.4 mm and the average CCI was 51% in the group of historical controls 10 patients, the mean gestational age at enrollment was 12.1 weeks, cervical length 40.4mm and the CCI average was 53%.

The mean gestational age at delivery in the study group compared to the historical control group was higher, 34.5 vs 28.7 weeks respectively, p = 0.013

Conclusion

Combined treatment with CP and VMP in patients with singleton pregnancies with CCI ≤ 5th percentile in 11-13.6 week, is feasible and shows a trend toward and fewer PTB Compared to historical controls.

P39 – THE PREDICTIVE VALUE OF QUANTITATIVE FIBRONECTIN TESTING IN COMBINATION WITH CERVICAL LENGTH MEASUREMENT IN SYMPTOMATIC WOMEN.

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Background
To evaluate whether quantitative fetal fibronectin testing improves the prediction of spontaneous preterm birth within seven days in symptomatic women undergoing cervical length measurement as compared to qualitative fetal fibronectin testing.

Methods
We performed a European multicentre cohort study in ten perinatal centres in five countries. Women between 24 and 34 weeks of gestation with signs of active labour and intact membranes underwent fetal fibronectin testing and cervical length measurement. We assessed the risk of preterm birth within seven days in predefined strata based on fibronectin concentration and cervical length. Furthermore, we used logistic regression to construct a model including quantitative fibronectin and cervical length, and one including qualitative fibronectin and cervical length. We compared the models' capability to identify women at low risk (500ng/mL). Using a threshold of 10 ng/mL in women with a cervix 500 ng/mL in women with a cervix >30mm (n=82), six women at high risk (33%) were identified. Use of quantitative fibronectin instead of qualitative fibronectin resulted in reclassification of 37 women from high risk to low risk, of whom four (11%) delivered within seven days.

Conclusion
Quantitative fibronectin testing in combination with cervical length measurement gives a more accurate prediction of spontaneous preterm birth within seven days in symptomatic women, compared to qualitative fibronectin testing.

P40 – IMPROVING PREDICTION OF PRETERM AND TERM BIRTH – DEVELOPMENT OF TOOLS FOR QUANTIFICATION OF CERVICAL STIFFNESS DURING ROUTINE PREGNANCY CONSULTATION

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Introduction
During pregnancy the cervix remains firm and closed. At term, the cervix must allow delivery, which requires it to soften, shorten and dilate. Critical problems occur when the timing and extent of the mechanical changes are altered. Their identification by an objective assessment carries great potential for improving the prediction of preterm birth, as well as the successful management of delivery. The goal is to quantitatively describe the changes in cervical stiffness and thus contributing to a better understanding of these processes in normal pregnancy.

Method
A device has been developed to measure the consistency of cervical tissue using the aspiration method. The probe is vaginally positioned on the cervix. The device applies a weak vacuum and measures the negative pressure necessary for a standardised displacement of the tissue. This negative pressure (pcl) is proportional to cervical stiffness.

Results
448 aspiration measurements were carried out on 50 pregnant women at each routine consultation and on 50 non-pregnant subjects. Stiffness in the first trimester is significantly lower than for the non-pregnant group, by a factor >2 for the mean value. pcl continuously decreases during gestation, with significant differences between first and second trimester. After delivery, consistency recovers to early pregnancy levels.

Conclusions
The aspiration method allows an objective description of the cervical consistency during pregnancy, indicating that the tissue softens already at the beginning of gestation, transforms continuously to lower consistency and recovers its stiffness after delivery. A clinical study is currently ongoing to determine the usefulness of the device in preterm birth diagnosis.

P42 – PERINATAL OUTCOMES AFTER CONSERVATIVE MANAGEMENT IN MULTIPLE PREGNANCIES COMPLICATED BY PROLONGED EARLY PRETERM PREMATURE RUPTURE OF MEMBRANES (EPPROM) PRIOR TO 24 WEEKS.

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Background

Since availability of assisted reproductive techniques, multiple pregnancies have become common in obstetric practice. Better perinatal care has allowed improvement on neonatal survival and morbidity. EPPROM is a rare complication that usually affects just one of the fetuses, bringing challenge towards medical counseling and obstetric management in those pregnancies. There are a few studies concerning conservative management in this clinical situation.

Objective

To evaluate perinatal outcomes in twin gestations complicated with EPPROM prior to 24 weeks which were managed conservatively.

Material and methods

Retrospective study in a tertiary center between 2001 and 2015. Inclusion: multiple pregnancies complicated by EPPROM below 24 weeks of gestational age and managed conservatively. Exclusion: Women requiring TOP and pregnancies in which one of the fetus was not alive at the time of the EPPROM. Basal characteristics of the women included and perinatal outcomes were evaluated. Composite morbidity was defined as presence of one or more of the following: respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, periventricular leukomalacia, pulmonary hypoplasia or skeletal deformities.

Results

30 women were included. Maternal characteristics are described in Table 1. Neonatal outcomes comparing neonates with and without EPPROM are described in Table 2. The interdelivery lapse of time in the case of delayed delivery of the second

Table 1. Baseline characteristics

	n: 30
Maternal age (years)	33.7 (+- 5.1)
Nulliparity	16 (53.3%)
Prior invasive procedure	18 (60%)
GA at EPPROM (weeks)	19.1 (+- 3.4)
Cervical length at admission (mm)	31.8 (+-12.5)
Delayed delivery of the second twin	1/30 (3.3%)
At least one surviving twin	14/30 (46.7%)
Two surviving twins	5/30 (16.7%)
Clinical chorioamnionitis	39,2 (0,1)
GA at delivery (weeks)	7/27 (25.9%)
27.9 (±4.8)	22 (4,7)
Delivery < 24 weeks	6/29 (20.7%)
Delivery ≥ 28 weeks	15/29 (51.7%)
Delivery ≥ 32 weeks	7/29 (24.1 %)
Latency EPPROM to delivery (median in days, minimum –maximum value)	60 (5-189)

GA: Gestational age
EPPROM: Early preterm premature rupture of membranes
LVP: Largest vertical pocket of amniotic fluid.
Continuous variables were presented as median (minimum value-maximum value). Categorical variables were presented as number (%).

Table 2. Perinatal outcomes

	EPPROM	**No EPPROM**	**OR**	**p-value**
LVP at admission	1.3 (+-0.9)	3.6 (+-1.5)	0.257	<0.001
Second trimester miscarriage	4/30 (13.3%)	3/30 (10%)	1.385	0.688
Stillbirth	1/30 (3.3%)	2/30 (6.7%)	0.483	0.561
Neonatal death	8/30 (26.7%)	3/30 (10%)	3.273	0.107
Pulmonary hypoplasia	4/30 (15.4%)	0	-	0.041
Skeletal deformities	4/27 (14.8%)	0	-	0.038
Composite morbidity	20/24 (83.3%)	17/22 (77.3%)	1.471	0.606
Mortality	11/29 (37.9%)	8/29 (27.6%)	1.750	0.092

twin was 46 days. Composite morbidity was similar in the two groups, although only EPPROM twins presented pulmonary hypoplasia or skeletal deformities. There were no cases of maternal death.

Conclusions

Conservative management of multiple pregnancies after EPPROM is associated with high perinatal mortality. However, a 50% of pregnancies progressed beyond 28 weeks and in 46% cases one of two neonates survived.

P43 – CHARACTERISATION OF CYTOKINE INFLAMMATORY NETWORKS IN PRETERM BIRTH - THE ROLE OF SYSTEMS BIOLOGY

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Background

Preterm birth (PTB) is a persistent and expensive global health problem. There is strong evidence to support a role for cytokines in the initiation of inflammation/infection-induced PTB, however individual cytokine analysis has been unable to consistently identify those predictive of PTB or their operant pathways. As it is likely that they behave as an interactive network, we set out to characterise the patterns of inflammatory activity in asymptomatic women within the midtrimester who subsequently delivered preterm or at term.

Methods

A nested case-control study - samples were obtained from the SCOPE biobank, which prospectively acquired demographic information and biologic samples from a cohort of healthy primiparous women. Plasma samples were taken at 20 weeks gestation from women who subsequently developed spontaneous preterm labour and delivered at 37 weeks. Bayesian network analysis revealed key differences in the cytokine networks operating in each group. Classifier analysis identified the five most discriminatory analytes as being (in order of importance) IL-4, IFN-gamma, MIP-1alpha, IL-6, IL-17a. Receiver-operator curves constructed using these ranked analytes showed modest predictive performance.

Conclusion

The use of multiplex technology, allied with network and classifier analysis, has identified differing underlying patterns of inflammatory network activity in asymptomatic women within the midtrimester. Validation of these findings and refinement of these interrogative techniques is required before clinical application can be considered.

P44 - OUTCOMES OF WOMEN WHO EXPERIENCE SPONTANEOUS PRETERM LABOUR (SPTL) IN THE LINKED PHARMOPRN COHORT.

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Background

In order to contextualize results of tocolytic clinical trials among women with SPTL, it is import to understand outcomes and healthcare utilization of women with SPTL in a real-world setting.

Material/Methods

Outcomes were assessed in women with SPTL (women with an uncomplicated pregnancy and either a diagnosis of preterm labour or who delivered a preterm infant) vs. women with full-term delivery (FT). Two data sources were used (2000-2010, funded by GSK); The Netherlands Perinatal Registry (PRN): nationwide registry of pregnancies and neonatal care, and the PHARMO Database Network: population-based network of healthcare databases (combining hospitals, pharmacies, other settings).

Results

The study cohort contained 134,006 singleton pregnancies. Of these 122,894 (92%) were FT and 6,599 (5%) were SPTL with 4,527 (69%) delivering < 37 weeks GA. More women with SPTL were aged 18-25 vs. FT (18% vs. 13%) and had first births (53% vs. 43%).

Women with SPTL spent more days hospitalized during the delivery visit vs. FT women (rate per 100 PY 201 vs. 83, adjusted RR 1.23). Excluding the delivery visit, women with SPTL had 1.67 times more hospital days (95% CI 1.56-1.80), mean ±SD 1.8 (±5.4) vs. 0.5 (±2.2) hospital days per pregnancy. There was significantly more out-patient dispensing during pregnancy in SPTL vs. FT women (rate per 100 PY 552 vs. 436, adjusted RR 1.27).

Conclusions

These analyses provide real-world outcome data of SPTL women, providing further understanding and interpretation of expected healthcare use and safety signals from ongoing and future clinical trials.

P45 – ABNORMAL VAGINAL FLORA AMONG SOUTH INDIAN PREGNANT WOMEN – A PILOT STUDY TO ELUCIDATE THE BACTERIAL ETIOLOGY AND THEIR IMPLICATIONS ON PREGNANCY OUTCOMES.

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Background

Causal relationship between bacterial vaginosis (BV) and/or abnormal vaginal flora (AVF) with preterm delivery is well acknowledged. However, the exact microbial etiology of BV and AVF remains unclear. Considering the ethnical variation in the bacterial etiology of BV, the present pilot study was undertaken to elucidate the detection rates of seven vaginal bacterial species among Indian pregnant women and their association with BV, AVF and preterm delivery.

Materials and Methods

High-vaginal swabs obtained from 245 pregnant women attending an obstetrics clinic for routine antenatal checkup at a secondary level hospital in south India were used for the present study. Nugent's scoring system (NSS) was used to diagnose BV. A qualitative multiplex PCR was used to detect seven bacterial species namely: Atopobium spp, G.vaginalis, Prevotella spp., Leptotrichia spp., Peptinophilus spp., Ureaplasma urealyticum and Mycoplasma hominis. Further, association of these bacterial species with BV, AVF and preterm delivery was determined.

Results

Overall, AVF was observed among 43 (17.5%) women, of which, BV could be diagnosed using NSS in 12 (4.9%) women. Vaginal colonization of G.vaginalis (11%), U.urealyticum (11%), Atopobium spp (10.2%) and Leptotrichia spp (10.2%) were commonly observed in the present study population. Preterm delivery was observed among 26 (10.8%) women. Colonization of G. vaginalis, Atopobium spp., M. hominis and Leptotrichia spp., had statistically significant association with BV and AVF. Colonization of G.vaginalis, Atopobium spp., and M.hominis during pregnancy had significant association with preterm delivery.

Conclusion

Our study findings underscore the need for microbiological characterization of AVF among Indian pregnant women using culture independent techniques.

P46 – EMERGENCY CERCLAGE: OBSTETRIC AND PERINATAL OUTCOMES.

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Background

The aim of the study is to describe gestational and neonatal outcomes of women with second-trimester cervical insufficiency treated with an emergency cervical cerclage between July 2009 and November 2015.

Material/methods

A retrospective observational study was conducted. We collected information of all emergency cerclages performed in our centre before 26 completed weeks. Multiple pregnancies were excluded from analysis.

Results

Nineteen cases were reviewed during the study period: sixteen were cerclages performed in singletons and three in multiple pregnancies, which were excluded from the study. One case was lost to follow-up at 226 weeks of gestation.

Gestational age at cerclage "median (range)" was 230 (18-256) weeks. Of all cases reviewed, 31% presented prolapse and ballooning of membranes. Median gestational age at delivery and cerclage-to-delivery interval were 305 (211-393) weeks and 51 (3-111) days, respectively.

Amniocentesis was performed before cerclage placement in 81,3% of cases (13/16).

Neonatal survival rate was 80%. All deaths occurred in previable deliveries (two before 22 weeks and one at 20 weeks of gestation), no perinatal deaths were described in single pregnancies.

62% (10/15) and 33% (5/15) of women delivered beyond 28 and 34 weeks, respectively. 83% (10/12) who reached 24 weeks delivered after 28 weeks.

Eight neonates were admitted in the intensive care unit with median 34 (5-120) days of stay.

Conclusion

Emergency cerclage placement was related with high neonatal survival rate. Achieving fetal viability was associated with delivery beyond 28 weeks in more than 80% of cases.

P47 – PERINATAL OUTCOME IN WOMEN AFTER IVF-ET AND PRETERM DELIVERY.

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Background

IVF-ET is the standard procedure for infertile pairs and accounts for about 3-5% of all pregnancies in European countries. There is a slight higher literature data pointing on worse perinatal outcome in neonates after IVF-ET, especially when adjusted to maternal age and parity. Thus, we aimed to compare our perinatology results in singleton and twin-pregnancies after IVF-ET compared to control pregnancies after spontaneous conception.

Material and Methods

Retrospective, case-control based study for 5 years at Dpt. of Obstetrics and Gynecology, Martin. Inclusion criterion was a viable pregnancy after 24th g.w.

Results

Observed group consisted of 62 singleton and 26 twin-pregnancies, control group included 6775 singleton and 111 twin-pregnancies. The singleton pregnancies after IVF-ET showed significant trend to higher operative deliveries (79% vs 31%, $p<0.05$), higher risk of preterm labor (≤ 37gw OR 1.7 or ≤ 32gw OR 2.6), low birth weight (≤ 1500g OR 2.9) and risk of preeclampsia (OR 3.1), $p<0.05$). The twins after IVF-ET showed nonsignificant lower risk of preterm delivery, significant lower risk for low birth weight and significant higher risk of preeclampsia, Diabetes mellitus, and operative deliveries, $p<0.05$.

Conclusion

Adverse perinatal outcomes in neonates after IVF-ET have been confirmed only for singleton pregnancies, whereas twin pregnancies after IVF-ET showed more favourable outcomes compared to control group.

P48 – PREGNANCY AND NEONATAL OUTCOME IN EARLY PRETERM PREMATURE RUPTURE OF MEMBRANES.

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Introduction

The aim of the study was to evaluate gestational and neonatal outcome in women with early preterm premature rupture of membranes (EPPROM).

Material and methods

A retrospective observational study including singleton pregnancies admitted in our centre with EPPROM (<24 weeks) was performed between 2001 and 2014.

Results

Eighty-two cases of EPPROM were reviewed during a 14-years period. Seventy-one were single pregnancies: twenty-seven cases were secondary to an invasive procedure and forty-four were spontaneous. Only spontaneous were considered and two cases were lost to follow-up at 190 and 241 weeks of gestation.

Expectant management was decided in 69% of women and 31% of patients requested a termination of pregnancy after being informed of fetal prognosis.

Of all on-going pregnancies, 69% (20/29) of women had a miscarriage, none stillbirth and 31% (9/29) of pregnancies achieved fetal viability.

Gestational age at preterm premature rupture of membranes and gestational age at delivery "median (range)" in ongoing pregnancies were 214 (191-236) weeks and 346 (272-412) weeks, respectively.

Only nine cases of clinical chorioamnionitis were reported (three in viable pregnancies and six in miscarriages) and no maternal deaths were described.

Neonatal survival rate was 31%, increasing to 100% if pregnancies reached 240 weeks of gestation.

The most common neonatal complications reported were respiratory distress syndrome (3/12) and necrotizing enterocolitis (2/12). No cases of sepsis were reported.

Conclusions

Prognosis of previable preterm premature rupture of membranes is poor but pregnancies that achieve 240 weeks of gestation have a survival rate around 100%.

P49 – OUTCOMES FOR RESCUE CERVICAL CERCLAGES AT A SINGLE INSTITUTION.

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Background

Rescue cerclage is performed in the presence of premature cervical dilatation and exposed fetal membranes to restore cervical integrity, protect the membranes and reduce the risk of miscarriage and preterm birth.

Methods

We present a retrospective study of rescue cerclages performed at Queen Charlotte's and Chelsea Hospital, London between 2005-2015.

Results

31 singleton pregnancies were identified. Cerclages inserted in asymptomatic women resulted in higher latency 93 vs 21 days (p28 weeks were associated with lower cervical dilatation at insertion; 2 vs 3.5cm (p=0.005), lower prevalence of symptoms (14% vs 76%), an average latency of 113 days and an average gestation of 38+2 weeks at delivery. Cerclages that failed did so within 10 days in 76% of cases with significantly higher levels of histological chorioamnionitis. There was a single case of iatrogenic membrane rupture. Suture removal was uncomplicated in all cases.

Conclusion

Rescue cerclage is more likely to be successful if inserted in asymptomatic women, prior to 20 weeks gestation with cervical dilatation of ≤3cm. Intraoperative rupture of the membranes was rare. The majority of sutures that failed did so within 10 days and were associated with chorioamnionitis, whilst successful stitches all resulted in delivery >36 weeks.

P50 – BEE HONEY, ROYAL JELLY AND PROPOLIS FOR THE PREVENTION OF PRETERM LABOR.

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Background

In-vitro work showed that bee honey (BH) and royal jelly (RJ) had "improvement effect" on the mechanical performance of fetal membranes. Propolis is known of its anti-infection properties. Consequently, we tested the possible prophylactic effect of these products against preterm labor (PL).

Material/Methods

Fifty-nine gravidas with history of recurrent PL were quasi-randomly assigned into 2 groups: group I (30 women) received daily ingestion of 20 ml of cotton-trifolium BH, 400 mg propolis and 2 grams of RJ from the 15th gestation week till the onset of labor or completion of 38 weeks' gestation; group II (29 women) served as controls. Primary outcomes assessed were: 1) incidence of PL, and, 2) gestation age at birth, and, 2). Secondary outcomes were: 1) ultrasonic evidence of cervical changes of threatening PL, and, 2) total leucocytic count and C-reactive protein.

Results

Twenty-two pregnancies of group I went to term as compared to 13 of controls (75.9 %, 44.8%; $P < 0.01$). Average gestation weeks at birth were 36.3 and 31.1 ($P < 0.01$ %). Cervical ultrasonographic signs of PL threat were elicited in 11 and 19 cases of groups I and II respectively (36.7, 65.5%; $P < 0.01$). High leucocytic counts and C-reactive protein were found in 10 and 15 women of cases and controls respectively (33.3, 51.7%; $P < 0.05$).

Conclusion

Bee honey, royal jelly and propolis may be effective for reducing the risk of PL. Further studies are required to elucidate the possible mechanisms and the best application route.

P51 – THE EFFECTS OF BEE HONEY AND ROYAL JELLY ON THE MECHANICAL PROPERTIES OF THE FETAL MEMBRANES.

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Background
Premature rupture of fetal membranes (PROM) carries high risk for preterm labor. Improving the mechanical efficiency of the membranes might be of prophylactic value. The effects of bee honey (H) and royal jelly (RJ) on the mechanical properties of fetal membranes were in-vitro tested.

Material/Methods
Amnion (A) and amnion/chorion complexes (B) were collected from 138 deliveries. Comparative membrane pieces were treated with either H, RJ, H/RJ mixture, or physiologic saline. These were subsequently evaluated by: a) manometric device for their mechanical properties, and, b) histological examination for collagen content.

Results
Tearing pressure and elastic extension yield were significantly improved for both A (pressure of 105.7 with H and 146.5 for RJ versus 50.3 mm Hg for the controls; and elastic extension yield of 1.73 with H and 1.93 for RJ versus 1.46 cm for the controls); and B membranes (pressure of 190.7 mm Hg with H and 246.5 for RJ versus 121.2 mm Hg for the controls; elastic extension yield of 2.01 with H, 2.05 with RJ, versus 1.83 cm for the controls). Histological examination and image-analysis quantification revealed significantly increased collagen staining pattern, too.

Conclusion
H, H/RJ had positive effect on the mechanical properties of fetal membranes. This may be through "collagen promoting action". Further studies are required to: 1) define the exact mechanism involved (e.g. effects on proline/hydroxyproline content, collagen cross-linkage), and, 2) test the efficacy of different methods for clinical extrapolation; i.e. whether ingesting these nutrients, or using them in some form of "local application".

P52 – SIMPLE COMPOSITE SONOGRAPHIC PARAMETERS OF THE SECOND TRIMESTER CERVIX FOR THE PREDICTION OF SPONTANEOUS PRETERM LABOR.

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Background
There is need for simple, cheap and highly predictive test for spontaneous preterm labor (SPL). The "zone of endocervical crypts (ZEC)" is a well-defined sonographic landmark corresponding to enfolding of the endocervical mucosa. Early loss of ZEC might be considered as indicative of "premature effacement". We tested a "composite" parameter of cervical length plus ZEC loss for predicting SPL.

Material/Methods
The study included singleton pregnant women attending Asyout Clinic for Gynecology and Obstetrics between 20 and <24 weeks' gestation.

Transvaginal ultrasonography was used for assessing: a) the cervical length, and, b) existence of ZEC. Monoechoic appearance of the cervix corresponded to loss of ZEC.

The sensitivity, specificity, positive and negative predictive values (PPV, NPV) were calculated for: 1) cervical shortening 2) ZEC loss, 3) combined 1 & 2, and, 4) funneling

Results
Two thousand and one pregnancies were evaluated for incidence and sonographic prediction of SPL (24 - <32 weeks, and 32-36 weeks). The overall SPL rate was 9%. Loss of ZEC and the combined ZEC loss and shortened cervix were found to have a better specificity and PPV than the shortened cervix alone. ZEC loss had better PPV for early PL rather than late. "Funneling" had poor PPV, but, is still a good "negative".

Conclusion
The composite parameter of the "lost ZEC" and short cervix is superior to the cervical length alone for the early prediction of SPL. It might be required to correlate the ZEC to other clinical criteria as infection.

P53 – PLASMA FROM GESTATIONAL DIABETES MELLITUS INCREASE THE LEVEL OF FABP4 IN ADIPOCYTE

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Background
Gestational diabetes mellitus (GDM) results in complicated pregnancy as macrosomia, birth injury, still birth, iatrogenic preterm birth in uncontrolled GDM. Even though the incidence of GDM is increasing in Korea, the precise pathogenesis of GDM is unknown.Fatty acid–binding proteins (FABPs) constitute a family of highly homologous cytosolic proteins and can bind a variety of hydrophobic compounds, including fatty acids. FABP4 was first detected in adipose tissue and mature adipocytes. FABP4 is highly expressed in adipocytes. The aim of this study investigated whether plasma obtained from pregnant woman with GDM may increase the FABP4 expression in adipocyte

Material and Methods
We obtained plasma from pregnant woman with GDM and normal pregnant woman on 32 weeks of gestation respectively. Adipocyte bought from ATCC were cultured for 17 days. We put FBS media, plasma from GDM patients, and plasma from normal pregnancy in the adipocyte. We underwent ELISA, qPCR.

Results and conclusion
Plasma from pregnant woman with GDM increase the protein level of FABP4 in adipocyte more than plasma from normal pregnancy. Our results suggest that some material in GDM plasma make adipocyte to increase the FABP4 that stimulate

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P54 – INFLUENCE ON PERINATAL OUTCOMES OF A VAGINAL FLORA STABILIZER IN WOMEN WITH PRETERM PRELABOUR RUPTURE OF MEMBRANES.

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Background
To evaluate the effect on perinatal outcomes of a vaginal flora stabilizer containing lactic acid and glycogen (Geliofil®) in women with preterm prelabour rupture of membranes (PPROM) before 30.0 weeks.

Material and methods
From 2011-2014, vaginal Geliofil® was added to the standard management (prophylactic antibiotics 5 days and corticosteroids) of women with singleton pregnancies and diagnosis of PPROM between 24.0 and 29.6 weeks. Geliofil® was administered with a frequency of one application per day during the first 5 days of admission and once a week until delivery.

Maternal and neonatal outcomes were compared with a control group of women admitted during a previous period of time (2008-2011).

Standard management included also induction of labor after 32.0 weeks if lung maturity was confirmed, or after 34.0 weeks if not.

Results
Twenty-five women were treated with Geliofil® and 24 were considered the control group. Maternal characteristics were comparable between groups. No statistically differences were observed at gestational age at delivery, latency from PPROM-delivery or the occurrence of either clinical or histological chorioamnionitis after use of Geliofil®. In addition, we did not observed differences in either composite maternal or neonatal morbidity.

Conclusion
Geliofil®, as a vaginal flora stabilizer, did not have any effect on perinatal outcomes in women with PPROM below 30.0 weeks.

P55 – PERINATAL OUTCOME IN WOMEN WITH PREECLAMPSIA AND PRETERM DELIVERY.

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Background
Preeclampsia is a hypertensive disorder of pregnancy that affects 3% to 5% of all

pregnancies in general. When present in severe form it have the adverse effect on pregnancy and newborn.

Material and methods
We have done a retrospective study to describe perinatal outcomes among the singleton pregnancies complicated with preeclampsia and eclampsia.The study groups consisted of women delivering at Department of Obstetrics and Gynecology, University hospital Martin,Slovakia in 2014 and 2015.

Results
Out of 2772 deliveries only 28 were admitted as suspected PE and out of this number only 21 (0.75%) were confirmed with diagnosis of preeclampsia during their hospitalization. Perinatal mortality rate was similar among the studied groups (mild, severe vs.non-specified forms of PE and healthy controls). However, we have observed the higher rates of caesarean-section in these patients, nonsignificant lower Apgar scores, trend to preterm birth and lower birth weight ($p<0.05$) compared controls. Additionally, preterm deliveries were significant associated with the severity of PE and proteinury.

Conclusion
The results between our groups were quite similar, even though most of the deliveries were pre-term, we did not detect adverse low Apgar score despite the fact that the deliveries in some cases were born before 30th gestation week.

P56 – PREMATURE LABOR WITH TRAVELER'S DIARRHEA.

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Background
Diarrhea, in general, is a risk for the pregnant women. It entails the possibility of inducing "uterine irritation" by intense bowl cramps. We tried to define the incidence of preterm labor in association with traveler's diarrhea and the subsequent effect on neonatal health.

Material/methods
Ninety-nine pregnant women suffering from traveler's diarrhea (group I) and one-hundred one matched control cases (group II) were compared for: 1) the incidence of preterm labor, and, 2) neonatal outcome.

Results
Twenty-three patients of group I (23.2%) gave birth preterm as compared to 8 cases of group II (8%); P 0.05). Average term neonatal birth weight for group I was 2611 g versus 2993 g for group II ($P<0.05$). 13 of group I infants (13.2%) were admitted to the neonatal intensive care, versus 5 (5%) of group II, ($P<0.05$) and the average hospital stay was 7.3 and 3.9 days, respectively ($P<0.05$). 4 and 1 neonatal deaths took place in groups I and II, respectively; the cases of group I were: 2 due to septicemia, one due to respiratory failure and one due to enterocolitis, and that of group II was due to respiratory failure. There was no congenital anomaly in either group.

Conclusion
Traveler's diarrhea is associated with a considerable risk of preterm labor and second trimester miscarriage, and, consequently, increased risks of poor neonatal outcomes. Active treatment is recommended for the prevention of these complications

P58 – VAGINAL LIPOIC ACID STIMULATES THE CERVICAL SECRETION OF ANTI-INFLAMMATORY INTERLEUKINS, IN WOMEN AT RISK FOR PRETERM BIRTH.

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Background
Inflammatory activation is associated with cervical ripening and fetal membrane weakening leading to spontaneous preterm birth (PTB). Lipoic acid (ALA) is known to have anti-inflammatory activity in several experimental models. Our aim is to demonstrate whether ALA vaginal administration affect cervical inflammation.

Material&Methods
Nulliparous women with singleton pregnancy hospitalized at 24 and 30 weeks for a first episode of preterm labor were enrolled at discharge. They were randomly allocated to receive placebo (20 women, 15 analyzed) or ALA (20 women, 17 analyzed) through vaginal capsules for 30 days. A cervical swab and TVU cervical length (CL) were performed before and after treatment. A pool of citokynes (IL-1, IL-2, IL-4, IL-6, IL-8, IL-10, TNF-α) were measured.

Results
Overall, there was a non statistically significant reduction of CL in both groups. Subgroup analysis of women with baseline CL<21mm showed a statistically significant CL shortening with placebo while not with ALA. There was a statistically significant variation for IL-4 and IL-10 between the two group after the treatment (IL-4: ALA group 118.0% vs placebo 23.9%, p=0.012; IL-10: ALA group 481.9% vs placebo group 124.3%, p=0.058). Pro-inflammatory ILs showed similar variation between the two groups. Anti-inflammatory ILs variation (IL-4 plus IL-10) was statistically significantly higher in the ALA group (490.4%) vs placebo (64.4%; p=0.03).

Conclusion
The administration of ALA through vaginal suppository significantly stimulates the cervical secretion of anti-inflammatory ILs. In women with short CL, vaginal ALA treatment seems also associated with stabilization of the cervix.

P59 – MEAL PATTERNS AND GLYCEMIC PROPERTIES OF MATERNAL DIET IN RELATION TO PRETERM DELIVERY; RESULTS FROM A LARGE PROSPECTIVE COHORT STUDY.

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Background
Maternal diet may affect the risk of preterm delivery, but relation to meal frequency and carbohydrate quality is unknown. The objectives of this study were to examine associations between meal patterns and selected glycemic properties of maternal diet in relation to preterm delivery.

Method
A prospective cohort study including 66,000 pregnancies from the Norwegian Mother and Child Cohort Study (MoBa). Information about women's meal frequency and food intake was obtained from a validated food frequency questionnaire in mid-pregnancy. Using principal component analysis, three meal patterns were identified: "snack meal", "main meal" and "evening meal". Pattern scores were ranked in quartiles for analyses. Dietary glycemic index and glycemic load were calculated based on international tables. Food intakes were converted into grams per day of carbohydrates, added sugar and dietary fiber. Gestational age was obtained from the Medical Birth Registry of Norway and preterm delivery was defined as birth before 37 gestational weeks.

Results
After adjustment for covariates, high adherence to the "main meal" pattern, was associated with reduced prevalence of preterm delivery, hazard ratios for the third and fourth quartiles were 0.89 (95% CI: 0.80, 0.98) and 0.90 (95% CI: 0.81, 0.99), p for trend 0.028. High glycemic load was associated with increased prevalence of late preterm delivery (34+0–36+6 wks.); hazard ratio for the highest vs. lowest quartile was 1.31 (95% CI 1.06 to 1.63) p-for trend 0.015. We found no significant association between glycemic index, carbohydrates, added sugar, dietary fiber or the remaining two meal patterns in relation to preterm delivery.

Conclusion
Eating regular main meals throughout the day were associated with lower prevalence of preterm delivery. High glycemic load was associated with higher prevalence of late preterm delivery. Dietary habits in pregnancy should be further studied as potential components in development of preterm delivery.

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