

Mother and Child Health Oral  
Presentation  
Senior Scientists' Forum

# Role of vitamin D in modulating gestational diabetes

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**Background:** Presence of vitamin D receptors in pancreatic cells suggests the role of vitamin D in augmenting gestational diabetes mellitus (GDM). Autocrine metabolism of vitamin D promotes anti-inflammatory response to maternal decidua and fetal trophoblasts. Immunomodulatory actions of vitamin D are likely to be compromised under conditions of low vitamin D levels with potential detrimental physiological consequences.

**Objective:** This article aims at exploring the possible mechanisms underlying GDM that could be regulated or affected by pleiotropic effects of vitamin D.

**RESULTS:** In spite of the unique capacity of placenta to produce active vitamin D, recent data are now available to implicate autocrine/paracrine impact of maternal vitamin D status can result in both increased insulin resistance and reduced insulin secretion, linking inflammation to metabolic disorder in the mother. Insulin and cytokines are the main contributors to the cascade of events and potential regulators of placental function in GDM.

**Conclusion:** Low maternal levels of major circulating form of vitamin D could be a perplexing factor that leads to expression of GDM. Deficient or even insufficient levels of vitamin D may allow diabetic insult during pregnancy and inducing changes in a variety of key functional molecules and gene expression leading to gestational diabetes. Large cohort studies, assessing Vitamin D status both pre-pregnancy and during pregnancy are required to confirm the development of GDM.

# Metabolic syndrome is inversely related to soluble receptor for advanced glycation end products: a study in mother-infant pairs

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**Background:** Advanced glycation end products (AGEs) are formed on proteins by nonenzymatic glycation/glyoxidation. Their natural accumulation is accelerated under pathologic conditions (hyperglycemia, increased oxidative-/carbonyl- stress). AGEs alter the structure and function of proteins. Interaction with their specific cell surface receptor (receptor for AGEs - RAGE) results in overexpression of cytokines, adhesion molecules, growth factors, and induction of oxidative stress. Circulating soluble RAGE (sRAGE) consists of only extracellular ligand binding domain. It acts as a natural competitive inhibitor of signaling pathways, removing or neutralizing the circulating RAGE ligands. In the elderly subjects metabolic syndrome (MetS) seems to be associated with low plasma levels of circulating sRAGE.

**Aim:** The prevalence of MetS is highly age-dependent. We asked whether low sRAGE is per se associated with MetS, or represents an age-dependent feature. Data obtained in ICARE study from 73 apparently healthy mothers and their 77 infants (4- to-12-months of age) were subjected to secondary analysis. Mothers were classified according to the presence of MetS components as negative (n=32), those with pre-MetS (insulin resistance + 1 sign of MetS, n=27) and overt MetS (n=14). Signs of MetS and sRAGE levels were determined in the mothers and the infants.

**Results:** Infants of the negative mothers were more insulin sensitive than those of pre- or overt MetS mothers (QUICKI:  $0.448 \pm 0.067$ ,  $0.418 \pm 0.047$ , and  $0.415 \pm 0.072$ , respectively,  $p < 0.05$ ). Mothers with pre- ( $1627 \pm 628$  pg/ml,  $p < 0.01$ ) and overt MetS ( $1120 \pm 421$  pg/ml,  $p < 0.001$ ) displayed lower sRAGE levels if compared with those without any sign of MetS ( $1851 \pm 720$  pg/ml). In their children only a trend towards decline was observed ( $1801 \pm 808$  pg/ml,  $1611 \pm 492$  pg/ml, and  $2159 \pm 1033$  pg/ml, respectively). In the mothers sRAGE levels inversely correlated with insulin sensitivity (i.e. QUICKI,  $r = 0.40$ ,  $p < 0.001$ ), and BMI ( $r = -0.40$ ,  $p < 0.001$ ). In the infants negative relationship between sRAGE and body weight was revealed ( $r = -0.23$ ,  $p < 0.05$ ).

**Conclusion:** Infants of mothers with MetS maintain normoglycemia on the account of higher insulin levels. MetS is associated with decreased levels of sRAGE in the mothers and a tendency towards decline of sRAGE in their offsprings.

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Mother and Child Health Oral  
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# Spontaneous and induced preterm births have different obstetric characteristics and risk factors

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**Introduction:** Preterm birth (PTB) is often described as a single entity. Prevention is based on identification and elimination of risk factors that are observed in the entire pregnant population delivering before 37 weeks gestation. PTB is mostly viewed as an outcome despite the fact that, in many cases, it is a method of obstetric intervention to reduce fetal, maternal and neonatal morbidity and mortality. Therefore, we decided to test the notion that there might be important differences between spontaneous and induced cases of PTB with regards to both risk factors and outcome measures.

**Methods and patients:** Retrospective analysis of 1500 consecutive cases was carried out by collecting demographic, obstetric and outcome data. PTB was defined as delivery before the 37<sup>th</sup> completed gestational week based on Naegele calculation corrected by first trimester CRL measurement. Comparisons were made between cases of spontaneous and induced deliveries. The delivery was considered spontaneous if tocolysis was required to attain time for fetal therapy or there was no need for measures aiming at cervical ripening or inducing uterine activity with oxytocin. Continuous variables were compared by t-test and the frequency of categorical variables was compared by  $\chi^2$ -test.

**Results:** According to our selection criteria 571 cases were spontaneous and 929 cases were induced PTBs. The mean age and pre-pregnancy weight of patients with induced and spontaneous delivery were significantly different (30.2 vs. 28.4 years; 68.8 vs. 64.4 kg). There was no difference between the two groups in the number of spontaneous and artificial abortions. Among multiparous patients there was a significant difference in the frequency of previous Caesarean section between induced and spontaneous cases of PTB (82/163 vs. 30/141). No differences were found between our groups with regards to history of hypertension, asthma, diabetes and renal disease but significantly more patients were smokers among cases with induced PTB (92/565 vs. 227/916). In the index pregnancy, significantly more patients had preeclampsia in the induced group but there was no difference in the frequency of asthma, diabetes, renal disease and urinary tract infection. However, preterm premature rupture of membranes was significantly less common in the induced group than among spontaneous PTBs (213/571 vs. 567/929). Caesarean frequency was significantly higher in the induced group compared to that in spontaneous PTBs (402/571 vs. 312/928). Despite mean gestational age at birth was not different in the two groups (32.7 vs. 33.0 weeks); the mean birth weight was significantly higher in the spontaneous group than in induced PTBs (2173 vs. 1979 g).

**Conclusion:** Induced PTBs have significantly different demographic and obstetric background as well as different outcome when compared to those of spontaneous PTBs. Our results show that a genome wide search for risk factors of preterm delivery may need to take these differences into account.

# The relationship between preterm birth and risk factors in Slovak republic

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**Background:** Preterm birth (PTB), defined as childbirth occurring at less than 37 completed weeks or 259 days of gestation, is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health. Genetic, environmental, social and behavioral factors interact in complex pathogeneses leading to PTB.

**Objective:** To investigate and evaluate risk factors associated with PTB.

**Material and Methods:** The RECOOP HST Consortium Mother and Child Health (MOCHEA) Research Network retrospective study was conducted among 315 women between 24-36 weeks of gestation with singleton pregnancies. Excluded were labors with multiple pregnancy, artificial PTB (preeclampsia, placental abruption) and pregnancy with more than 36 weeks of gestation. Data were extracted from patient records from January 2007 to June 2010 in the University Hospital in Bratislava. Questionnaire was included medical history, developing problems and special procedures performed during pregnancy.

**Results:** The mean age of the pregnant women was 30 years, mean weight 62.7 kg, BMI 22.7 and height 166.2 cm (Table 1).

Table 1. Maternal characteristics

	Age (years)	Pre-pregnancy weight (kg)	BMI	Height (cm)	Gestational age (weeks)
<b>No.</b>	315	304	303	307	31.5
<b>Mean</b>	30.0	62.7	22.7	166.2	33.5
<b>SD</b>	5.8	12.6	4.5	6.8	2.8
<b>Min</b>	15.0	33.0	14.5	143.0	24.0
<b>25<sup>th</sup> percentile</b>	26.0	55.0	19.8	162.0	32.0
<b>Med</b>	30.0	60.0	21.5	167.0	35.0
<b>75<sup>th</sup> percentile</b>	34.0	68.0	24.2	171.0	36.0
<b>Max</b>	47.0	115.0	42.8	183.0	36.0

Out of our cohort of 315 subjects, 192 women were primipara (Table 2). We observed a statistically significant correlation between BMI and preeclampsia ( $p=0.006$ ), weight and smoking ( $p=0.037$ ), gestational diabetes and chronic hypertension ( $p=0.001$ ). We found data from prior pregnancy with spontaneous abortion at 58 (18.4%), elective termination at 40 (12.7%), incompetent cervix at 9 (2.9%), caesarian section at 36 (11.4%) and myomectomy at 8 (2.5%) women in our dataset. 32 (10.2%) women smoked 7-8 cigarettes in average per day before and during pregnancy. We found highly statistically significant associations between age and smoking ( $p=0.001$ ) and between age and election termination ( $p=0.009$ ).

Table 2. Maternal and pregnancy characteristics for preterm birth

<b>Maternal status (no. (%))</b>	Married	190 (60.32)
	Single	110 (34.92)
	Divorced	15 (4.76)
<b>Maternal education (no. (%))</b>	Primary	15 (4.76)
	Secondary	174 (55.23)
	University	106 (33.65)
<b>Parity (no. (%))</b>	0	192 (60.96)
	1	79 (25.07)
	2+	44 (13.97)
<b>Infant sex (no. (%))</b>	Male	161 (51.11)
	Female	154 (48.89)

**Conclusion:** Many of the suspected risk factors listed above are significant for PTB in our group, also interrelated with each other and probably with some other co-factors.

# Epidemiologic impact of the new diagnosis criteria in gestational diabetes mellitus

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**Background:** Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study showed the impact of hyperglycemia for maternal and fetal outcome.

**Aim:** With regard to the new glycemic thresholds for the diagnosis of gestational diabetes mellitus (GDM) we performed the 75g oral glucose tolerance test (OGTT) on 60 pregnant women during 24-28 weeks of gestation.

**Methods:** The subjects' characteristics (means) before conception were: age 26.75 years, BMI 22.78 kg/m<sup>2</sup>, with 65% normal weight and 26.7% overweight or obese. The mean weight gain in pregnancy was 15.59 kg.

**Results:** A comparative analysis has been performed for the new diagnosis criteria of GDM with regard of the old WHO criteria, highlighting an increment of GDM with 10.4%. Statistically significant differences between normal weight subjects and overweight and obese subjects were obtained for: age ( $p < 0.005$ ) – the overweight and obese were older; fasting, 1 hour and 2 hours glycaemia ( $p < 0.05$ ) – the overweight and obese had higher values. In the overweight and obese group the weight gain in pregnancy correlated with the 1 and 2 hours glycaemia ( $r 0.47$ ), and there was a higher prevalence of premature babies, cesareans, arterial hypertension and GDM.

**Conclusion:** The present study underlines the importance of new diagnosis criteria on the prevalence of GDM and demonstrates that excessive weight is one of the main risk factors for GDM and other related complications.



# Ultrasound transverse diameter of fetal thymus as a marker of histological chorioamnionitis in women with preterm prelabor rupture of the membrane-

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**Background:** The thymus is a bi-lobed, key organ of the cellular branch of the immune system that plays an important role in the differentiation, selection and maturation of T-cell lymphocytes. It is a well known fact that thymus is susceptible to involution, which can occur in two different ways. First, age related involution begins in the puberty and the thymus size and its activity are dramatically reduced. Second, stress involution may appear during the prenatal period in response to different forms of acute stress stimuli such as infection, trauma, sepsis, and physical stress. This type of the thymic involution is initiated by the activation of the hypothalamo-pituitary-adrenal axis, which in turn cause glucocorticoids induced apoptosis of cortical thymocytes. The stress thymic involution was reported in the presence of histological chorioamnionitis in a radiologic study and recently in an ultrasound study and also along with intrauterine growth restricted fetuses.

**Objectives:** To determine whether measurement of the transverse diameter of fetal thymus is of value in identification PPRM women with the presence of histological chorioamnionitis and microbial invasion of the amniotic cavity.

**Results:** We enrolled eighty-nine patients between 24<sup>th</sup> and 36<sup>th</sup> weeks of gestation with PPRM in our study. Histological chorioamnionitis was found in 46% (40/87), and microbial invasion of the amniotic cavity was identified in 34% (30/87).

The small transverse diameter (< 5<sup>th</sup> percentile for gestation age) of fetal thymus was recorded in 29 of 40 women with the presence histological chorioamnionitis ( $p < 0.0001$ , sensitivity 71%, specificity 76%, PPV 73%, NPV 74%, likelihood ratio 3.0, RR 2.8, odds ratio 7,7). We did not find the difference in the presence of the small transverse diameter of fetal thymus between groups with and without microbial invasion of the amniotic cavity ( $p = 0.11$ )

**Conclusion:** The transverse diameter of fetal thymus in women with preterm prelabor rupture of membrane might be a rapid and non-invasive marker of histological chorioamnionitis.

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## Maternal factors related to preterm birth

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The rate of preterm birth (<37 gestational weeks) continues to rise worldwide despite using the novel diagnostic and therapeutic methods of medical care. As being part of the Mother and Child Health Research Network (MOCHEA) we collected data to identify the risk factors of preterm birth in the Southern part of Hungary. Data were extracted from 163 preterm births in a retrospective study, 2009. Our department is a tertiary referral center of the region, having 1720 deliveries in the study period. We examined historical risk factors, problems during pregnancy and special, pregnancy-related tests. Mean maternal pre-pregnant BMI was 23.9; mean maternal age was 30.4 years. Prior spontaneous abortion was found in 26.4% of the cases. The frequency of pre-pregnant hypertension, asthma, and diabetes was low (1.2-0.6-3.1%, respectively), but during pregnancy 11.7% of the mothers developed gestational diabetes. During pregnancy 12.3% of the mothers smoked, preeclampsia was present in 14.7% of the cases. Cervical cerclage was placed in 4.3% of the cases. Our data are consistent with those found in other countries of the network, but more and detailed examinations are necessary and going on to describe all the possible risk factors for preterm birth.

# Amniotic fluid concentrations of soluble scavenger receptor for hemoglobin (sCD163) in pregnancy complicated by preterm prelabor rupture of the membranes and histologic chorioamnionitis

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**Background:** The inflammation of the fetal membranes, characterized by immunocyte infiltration of fetal membranes, the placenta, and the umbilical cord, is termed *histological chorioamnionitis*, and it represents a clinically important outcome in pregnancies complicated by preterm labor or preterm prelabor rupture of the membrane (PPROM). Histological chorioamnionitis (HCA) is one of the measures of intrauterine infection that correlates to the presence of microbes in the amniotic fluid, and it is accompanied by a high concentration of inflammatory mediators in this compartment.

Scavenger receptor for hemoglobin (CD163) is a membrane glycoprotein involved in endocytosis of haptoglobin-hemoglobin complexes. Its expression seems to be restricted to the monocyte/macrophage lineage. As CD163 has been proposed to function in the innate immune response and in the resolution of inflammation, this monocyte/macrophage-specific glycoprotein is likely involved at various stages of the inflammatory response. The expression of the membrane CD163 is unregulated by interleukin (IL)-10, IL-6, and glucocorticoids. As a consequence of activation of Toll-like receptor (TLR), a soluble form of CD163 (sCD163) is shed from cell surfaces. This shedding is also possible in response to stimulation by other proinflammatory factors. Plasma sCD163 level has been previously determined in asymptomatic pregnant women in the first trimester and from women with symptoms of preterm labor. However, its potential (patho) physiologic role in spontaneous labor at term and in PPRM complicated by HCA is still not known.

**Objectives:** To determine changes in the amniotic fluid sCD163 concentrations during advancing gestation, and in patients with PPRM complicated by the presence of HCA. 152 women with singleton pregnancies were enrolled in the study.

**Results:** Women in the midtrimester had a significantly higher median amniotic fluid sCD163 concentration than those at term not in labor (308 ng/mL vs. 217 ng/mL;  $p=0.04$ ). Patients with PPRM and HCA had a higher median amniotic fluid sCD163 level than those with PPRM without histological signs of inflammation (885 ng/mL vs. 288 ng/mL;  $p < 0.0001$ ).

**Conclusion:** Amniotic fluid sCD163 concentrations decrease with advancing gestation. Amniotic fluid sCD163 concentrations are significantly higher in women with PPRM between 24 and 36 gestational weeks with HCA than those without histological signs of inflammation.

## **Coxsackievirus infections during pregnancy**

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**Background:** Human enteroviruses may cause serious clinical symptoms in newborns and immunocompromised patients. Aseptic meningitis, myocarditis, serious newborn sepsis and mild paralysis are few serious illnesses caused by enteroviruses. They may cause chronic diseases such as dilated cardiomyopathy and type 1 diabetes. A few reports indicate that infection during pregnancy may cause congenital anomalies, stillborn babies or miscarriages. Serological studies show that infection during pregnancy and association to juvenile diabetes.

**Aims:** One of the aims of our work was to determine the prevalence of anti-coxsackievirus antibodies during pregnancy. 217 serum samples were tested for antibodies by virus neutralization test against coxsackieviruses (CV) B1 –B5, A7 and A9. The other aim was to investigate an experimental model infection, to study the effect of infection with coxsackievirus B4-E2 (diabetogenic strain) in the different trimesters of pregnancy on the course of pregnancy and on the offspring.

**Results:** In the serological study paired blood serum samples from 217 pregnant women were studied for antibodies against coxsackievirus serotypes (CVB1-CVB6, CVA7 and CVA9) in sera of pregnant women from selected areas of the Slovak Republic. Coxsackievirus B4 (CVB4) infection (75.12%) was prevalent in the monitored population, followed by CVB3, CVA7, CVA9, CVB5, CVB2, CVB1 while coxsackievirus B6 (CVB6) was scarce. In 30 out of 217 cases (13.82%) current infection (4 fold rise in antibody titer) was recorded. In the experimental study, mice infected in the first and third week of the gravidity showed a normal course of the pregnancy similar to that of the sham infected control mice. Whereas, of three infected mice (in the second week of gravidity) one mouse showed sudden loss of weight indicating miscarriage and the second mouse showed lethargy and absence of gain in weight. Pancreases and hearts of the unborn fetuses showed presence of enteroviral RNA detected by RT-PCR. One of the mice from this group infected in the second trimester delivered normally, but only 8 offsprings as compared to 12 -15 delivered by control and mice infected in the first and third weeks of pregnancy.

**Conclusion:** We conclude that the most significant influence of the infection is in the second trimester of the pregnancy. Presence of virus RNA proves the possibility of transfer of the coxsackievirus B4-E2 infection from mother to child during antenatal development.

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## Preconceptional risk factors and preterm birth

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**Backgrounds:** Preterm birth (PTB) is estimated to account for 6-10% of all births worldwide with 13 million PTBs occurring annually and 1 million resulting in death. The diagnosis of spontaneous preterm labor and accurate prediction of preterm delivery is extremely difficult. Advances in perinatal medicine have not reduced PTB. Identification of effective risk assessment markers can potentially improve. Measures that can reduce PTB are yet to be established. Identifying risk factors for PTB is one of these measures.

**Aims:** The aim of the study was to investigate possible connection between risk factors and PTB.

**Results:** During three years (from 2007 – 2009) in our Department Split there were 465 (3.5%) preterm births. The mean ages of the mothers were 29.19 years (+/- 5.62). The mean BMI was 26.69 (+/- 3.65). Six mothers (1,3%) have positive family history of preterm birth. Sixty-six of 465 women had one, ten had two and two had three spontaneous abortions. Hundred and thirty-one women had one, thirty-nine had two, nine had three deliveries and two four-term deliveries. Short cervix was prenatal diagnosed only in one woman. Uterine surgery had been performed in thirty-three women and in one uterine surgery of the leiomyoma. Chronic hypertension had not been estimated before pregnancy in any women. Asthma has been diagnosed in two and diabetes in four women. Kidney disease had been identified in thirteen women; kidney infection in five and one of them had fever with infection. There were twenty-four smokers. The mean number of cigarettes per day was 10 (+/- 0). Narcotics used only one mother before pregnancy.

**Conclusion:** In our study risk factor observed are not significant in assessing risk of preterm birth.

# Preterm birth in women with vaginal disbiosis -prediction and prevention

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**Objective.** Preterm birth (PTB) is the defining challenge to modern perinatal medicine. Frequency of premature birth, from data of the Lviv clinical regional perinatal center, last year's (2007 – 2010) hesitates from 10,7 % to 11,5 % and does not have a tendency to the decline. PTB are principal reason of perinatal morbidity and death rate in a region. It is now clear that preterm birth is not caused by any one pathological process but many of them, some are not even identified.

**Materials and Methods.** We analyzed pregnancy proceeding in 55 pregnant women with the presence of risk factors of PTB. Following criteria's were mat history of spontaneous preterm birth (<37 wks.), singleton pregnancy. Contraindications criteria's were multi-fetal pregnancy, pregnancy after ART, past history of thrombophlebitis or thromboembolic disorders, vaginal bleeding, markedly impaired liver function. As the control group were examination 15 women with a first pregnancy without risk factors of PTB. At 19-21 weeks of gestation pregnant were testing of the vaginal pH level with MERCK pH indicator rods (pH 4.0 – 7.0) and study microbiocenosis of vagina from PCR at real-time (Femoflor 16, Russia). Detekciya was conducted Lactobacillus spp., Enterobacterium spp., Streptococcus spp., Staphylococcus spp., Gardnerella vaginalis, Eubacterium spp., Fusobacterium spp., Veilonella spp., Clostridium spp., Mobiluncus spp., Peptostreptococcus spp., Atopobium vaginae, Mycoplasma hominis and genitalium, Ureaplasma (urealyticum and parvum), Candida spp. The material was carried out from a back vault by vagina.

**Results.** The symptoms of bacterial vaginitis (BV) are exposed for 27.3% women. Vaginal pH level on the average  $6,8 \pm 0,4$  was diagnosed at 70,9 % pregnant. At 61.8% pregnant the spectrum of the selected microorganisms was form by G.vaginalis 9.1%, Clostridium spp. 5.5%, A.vaginalae 36.4%, Peptostreptococcus spp. 5.5%, Bacteroides spp. 14,6%, Fusobacterium spp. 52,7 %, Mobiluncus spp. 36.4 %, Staphylococcus spp. 9.1%, Streptococcus spp. 9.1 %, Enterobacteriaceae 30.9%, M.hominis 18.2 %, U.urealyticum 9.1 %, Candida 27.2 %. In this group symptoms of PTB appear from 61.8 % pregnant after 24 weeks of gestation. At the rest 38.2% women with normal condition of vaginal biocenosis symptoms of PTB appear only from 28.6 % ( $p < 0,05$ ). At control group vaginal disbiosis was exposed in the 20 % observed cases and symptoms of PTB were only in 6.7 % women.

**Conclusion.** More than half of pregnant women with the risk factors had an asymptomatic flow of BV, at 61.8 % and developed symptoms of PTB. Findings testify the presence of reserve in the decline of frequency and of unfavourable perinatal results by the study of the state of vagina biotopes and its timely treatment.

## **Risk factors of PTB. Survey based on the retrospective analysis of PTBs at our clinic between 2007 and 2009**

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**Background.** The most numerous group of patients liable to perinatal morbidity and mortality is still that of those born early. They are the most vulnerable as regards both fetal complications during birth and later neurological adverse outcomes. In order to prevent and treat the causes of premature birth efficiently it is important to know the factors leading to it.

**Objectives.** The aim of our study is to contribute to the knowledge of the Hungarian gynecologists and neonatologists through the international survey conducted within the framework of the RECOOP HST Consortium about the risk factors typical of Hungary. Our aim is to offer a reliable picture about the factors of premature birth in our country.

We analyzed the 747 PTBs out of the 8649 births at our clinic between 2007 and 2009 on the basis of the criteria determined by the RECOOP HST Consortium. The subject matter of the analysis included the case histories of the pregnant women in question, their gestational anamneses, the complications during the current pregnancy, and the methods of the diagnosis of premature birth. Births prior to the 37th week of gestation and newborn babies under 2500 grams were considered to belong to the category of PTB.

**Results.** We have found that premature births were the most frequent between the 27th and 36th years of age of the mothers (32 years in average). The mothers' earlier spontaneous abortions (22.2%), PTBs (6.3 %), and surgeries of the uterus (18.3 % altogether) including caesarean sections (12.6%), myomectomies (1.3%) and others, cervix insufficiency (3.5%), and current asthma bronchiale (2.3%) involve a greater risk from the point of view of PTB. Anemia during the early stage of pregnancy (44.4%), pre-eclampsia (16.3%), and gestational diabetes (8.6%) also belongs to the risk factors, but urinary tract infections (1.2%) are of minor importance from this respect. Invasive diagnostic interventions (GAC and CVS) were applied in 2.0 and 0.7%, respectively. 3.3% of the pregnant mothers were treated against imminent PTB. As regards harmful habits the supply of data has been insufficient.

**Conclusion.** The analysis revealed that the most frequent diseases during pregnancy typical among Hungarian women and earlier surgeries belong to the primary risk factors. With these pieces of information at hand the national health policy can improve conditions leading to PTB. The old axiom is valid in the case of premature birth as well, namely that it is easier to prevent it than to treat it.



# Mother and Child Health Young Scientists' Poster Presentation

# Healthy mother–child–pairs study on the impact of heritability and prenatal factors on blood chemistry parameters

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**Background:** Heritability and environmental factors play an essential role in determining phenotypic expression. Adults living in the same household share similar lifestyle habits and consume the same diets. However diets consumed by mothers differ from those of exclusively breast- or formula-fed, and weaning infants. We investigated the effect of familial and prenatal factors on blood chemistry parameters in 2-to-12 month-olds healthy infants. **Materials and methods:** Plasma samples obtained from 133 healthy mother-child pairs in frames of ICARE study were analyzed for 22 standard and 7 special blood chemistry parameters. Using general linear model (GLM) we assessed the impact of mother's weight gain during pregnancy, concentration/activity of the analyte in the mother, child's age and feeding regimen on the corresponding analyte in the infants. **Results:** Prenatal and/or genetic factors exert significant impact on plasma levels of sodium, creatinine, bilirubin, HDL-cholesterol, glycaemia, phosphatemia, albumin, uric acid, cholesterol, CRP, sRAGE, sICAM, sVCAM, AST and GMT activity, and CML/albumin ratio, independently of child's age and feeding regimen. After correction for feeding and child's age GLM confirmed the sole impact of heritability on plasma levels of sodium, creatinine, bilirubin and HDL-cholesterol, impact of familial and prenatal factors on variability of sRAGE and CRP levels. Plasma activity/concentration of AST and sICAM-1 were affected except for mother's analyte level also by child's age, and concentration of sVCAM-1 by feeding regimen of infants. Child's age and the concentration/activity of the analyte in mother's plasma showed comparable impact on the concentration of albumin and activity of GMT in the infants, and in case of plasma uric acid concentration, child's age showed slightly higher impact than the mother's plasma level. Except for genetic and prenatal factors, child's plasma phosphate levels were mainly affected by the child's feeding regimen. Mother's glycaemia (had the highest impact), weight gain during pregnancy and child's feeding regimen accounted for 12% in the variability of child's glycaemia. 12.4% of the variability in plasma cholesterol was explained by child's age, mother's cholesterol concentration, and namely by child's feeding regimen. **Conclusion:** 16 blood chemistry parameters in infants were significantly affected by heritable factors, which may play a role in manifestation of different diseases in their later life.

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## **Retrospective data of PTB 2007–2010 in the Osijek university hospital centre**

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**Background:** Croatian rate of preterm birth is 8-10% in the last two decades. **Aims:** During the last three years at Ob/Gyn Dept., Osijek Clinical Hospital Centre there was 7609 births, 640 were premature births (8,41%). Our aim is to present our results during the first phase of the multicentric study in MOCHEA Network Research “PTB risk factor research” project. **Results:** At Osijek University Hospital Centre there were 640 premature births in years 2007–2010 (8.41%). The first group of the processed data addressed risk factors not related to pregnancy. The mean age of the patients was 28.9. The mean body weight of the patients before pregnancy was 64.72. The mean BMI was 23.66. All patients were Caucasians. Seventy patients (10.9%) had previous history of spontaneous abortion. In this subgroup, most patients had one spontaneous abortion (86, 13.4%). Premature births included in the study were in the first pregnancy in 353 (55.2%) cases, in the second pregnancy in 165 (11.7%) cases, in the third pregnancy in 18 (2.8%) cases, and in the fourth pregnancy in 29 (4.5%) cases. Previous surgical procedures involving the uterus were recorded in 35 (5.5%) patients. Myomectomy was performed in 12 patients (1.9%). Arterial hypertension was noted in 10 patients (1.6%), 8 of which used antihypertensive therapy. Two patients had asthma, while 4 (0.6%) had controlled diabetes, 6 (0.9%) had renal disease, inflammatory in 2 (0.3%), and with increased body temperature in one case. Smoking prior to pregnancy was in 119 patients (18.6%), 1 (0.2%) had history of narcotic and cannabis abuse prior to pregnancy. The second group of the processed data addressed risk factors related to pregnancy. Vaginal hemorrhage in the first trimester was recorded in 36 patients (5.6%), anemia was noted in 64 (9.7%), prenatal ultrasound was performed in 599 patients (93.6%), cervical incompetence was diagnosed in 27 (4.2%). In 26 of these patients cerclage was performed. Vaginal hemorrhage in the third trimester was in 11 patients (1.7%). Preeclampsia was recorded in 63 patients (9.8%). Asthma related to pregnancy was reported in 2 patients (0.3%), gestational diabetes was recorded in 29 (4.5%), six requiring therapy. Renal disease in 11 patients (1.7%), smoking in pregnancy in 119 (18.6%). The third of the processed data addressed Medical interventions and special tests during pregnancy. Genetic screening underwent 27 patients (4.2%). obstetric ultrasound in the first trimester was performed in 538 (8.41%), obstetric ultrasound in the second trimester was performed in 609 (95.2%). In 20 patients (3.1%), an amniocentesis was performed. Cerclage was necessary in 25 patients (3.9%). Progesterone was applied in 121 patients (18.9%). **Conclusion:** There appears to be a correlation between percentage of women who smoke in pregnancy (18.6%) and percentage of women with history of spontaneous abortions (16.1%), what emphasizes the possible role of smoking in spontaneous abortion. The percentage of patients with gestational diabetes (4.5%) is comparable to the proportion of patients with BMI of 30 or more. The percentage of patients screened by obstetric ultrasound is high, what undoubtedly contributes to the early detection of genetic abnormalities. We emphasize the correlation between the number of patients with previous spontaneous abortions and premature births in earlier pregnancies (16.1 % to 10.9 %).

## **Neonatal hypoxia induces the changes in presynaptic modulation of GABAergic transmission.**

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In human infants, hypoxia is the most common cause of seizures. There are certain sensitive time windows during development when an initial insult is more likely to initiate epileptogenesis. In a rat model of this process, the state of hypoxia was induced by exposure of 10- to 12-day-old rats to a respiratory medium with low O<sub>2</sub> content (4% O<sub>2</sub> and 96% N<sub>2</sub>) for 12 min (up to the initiation of tonic-clonic seizures). Although neonatal seizures often do not immediately progress to chronic epilepsy, they do cause increased susceptibility to seizures and a risk of epilepsy later in life.

Here, we report the data obtained in rats exposed to hypoxia and seizures at age 10–12 postnatal days and taken in experiments 8–9 weeks after hypoxia treatment. We are particularly interested in presynaptic modulatory systems that selectively alter the release of glutamate as well as of inhibitory neurotransmitters such as GABA and that may be up regulated either by seizures or by the epileptogenic process. We characterize the events induced by glutamate receptors agonists in isolated hippocampal nerve terminals by analyzing [<sup>3</sup>H] GABA release from nerve terminals in control and rats exposed to hypoxia/seizures. In control animals, the time-course of [<sup>3</sup>H] GABA release is a curve with a maximal point at 2<sup>nd</sup> min gradually descended up to baseline of 10<sup>th</sup> min. Using specific blocker of GABA transporters NO-711, we have shown that [<sup>3</sup>H] GABA release induced by glutamate receptors activation was a result of stimulation of exocytotic process and following gradual decrease in intracellular GABA is due to transporter-mediated [<sup>3</sup>H] GABA uptake. It seems likely that the response to glutamate includes two processes: a rapid release of [<sup>3</sup>H] GABA that is followed by its reuptake into nerve terminals. This modulatory effect of glutamate on GABA release changes after hypoxia/seizures expose. While exocytotic release was similar to that observed in the control experiments subsequent reuptake was significant depress. This suggests that carrier-mediated GABA release is greatest after neonatal hypoxia/seizures and act to reduce excitability.

# **Umbilical cord blood concentration of soluble scavenger receptor for hemoglobin, but not pentraxin 3, is of value for the early postpartum identification of the presence of histological chorioamnionitis**

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**Background:** Histological chorioamnionitis (HCA), characterized by high-grade polymorphonuclears infiltration in placental tissue and fetal membranes, habitually indicates the presence of intrauterine infection, and thus, represents a clinically important outcome in pregnancies complicated by preterm labor or preterm prelabor rupture of membranes (PPROM). Unfortunately, the diagnosis of HCA is not known to the obstetricians and the neonatologists until after delivery, and therefore, cannot be used for clinical management.

Recent studies have identified increasing plasma concentration of pentraxin 3 (PTX3) and soluble scavenger receptor for hemoglobin (sCD163) in several pathologic conditions including bacteremia, systemic inflammatory response syndrome, sepsis, and septic shock. Interestingly, the presence of intraamniotic inflammation was also associated with significantly higher amniotic fluid PTX3 concentrations.

**Objectives:** To determine whether umbilical cord blood concentrations of PTX3 and sCD163 are of value in the early postpartum diagnosis of HCA in PPRM patients. Eighty-three women with pregnancies complicated by PPRM between 24 and 36 weeks of gestation with ( $n = 38$ ) and without ( $n = 45$ ) HCA were included in the study.

**Results:** The presence of HCA was associated with a significantly higher median umbilical cord blood sCD163, but not PTX3 concentration, to compare with the absence of HCA [sCD163: 1466 ng/mL, interquartile range (IQR) 1187-1828 vs. 1168 ng/mL, IQR 887-1595;  $p = 0.01$ ; PTX3: 3.96 ng/mL, IQR 2.24-6.77 vs. 2.95 ng/mL, IQR 1.74-6.93;  $p = 0.49$ ].

**Conclusion:** HCA is associated with a significant increasing of umbilical cord blood sCD163, but not PTX3 concentration. Umbilical cord blood sCD163 seems to be a postpartum marker of the presence of HCA.

# Preterm birth – epidemiologic analyzes of birth between 2007-2009 in “Dr. I. Cantacuzino” Ob-Gyn Department

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**Background:** Prematurity is a leading cause of neonatal mortality and a global health problem that affects high, middle and low-income countries. Several factors may increase the risk of preterm birth and some of them are purported to predict it.

**Objective:** This study was undertaken to determine the relationship between traditional risk factors (maternal history of preterm birth, number of spontaneous abortum, drugs in pregnancy, smoking during pregnancy, hypertension, urinary tract infections etc.) and preterm birth.

**Results:** This study is a retrospective one, from 2007-2009. We analyzed the data of 1071 preterm birth (< 37 weeks of gestational age) at „Dr. I. Cantacuzino Hospital, Bucharest, Romania, in a third level (highest in rank) emergency referral maternity. These data are part of a larger multinational RECOOP MOCHEA Research Network.

Mean maternal age was 28.06 years. Mean BMI was 23.38.

In our analysis the factors that remained significantly associated with preterm birth were smoking (45%), anemia( 18.5%), vaginal bleeding (16.4%), inferior urinary tract infections (6.5%), diabetes(3.8%).

10.6 % from all the women includes have had uterine surgery in antecedents, from which 1.4% myomectomies.

At 82.3% was not administrated oral or intra-vaginal progesterone. On the other hand, 9.8% have had previous spontaneous abortion. There was no evidence of effect modification by income and no clear difference between the socioeconomic statuses.

**Conclusion:** Screening tests with prediction model for preterm delivery risk should be used for all pregnant women.

Further studies are required to understand the causes of the epidemic of preterm births in Romania.

# Incidence and risk factors of preterm birth in Szt. György Hospital, Székesfehérvár

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**Introduction:** Preterm birth (PTB), defined as childbirth occurring at less than 37 completed weeks of gestation or infants are under 2500g, is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health. Preterm babies have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses and the risk for other diseases like obesity, hypertension and acute myocardial infarction compared with children born at term.

**Object:** The aim of our study was to investigate the incidence of PTB and the frequency of its risk factors in our hospital.

**Methods:** We analyzed our database of birth from 1<sup>st</sup> January 2010 to 31<sup>st</sup> December 2010. In this year there was 2599 delivery in our hospital, from which 257 were PTB. 15 of these babies were born after the completed 37<sup>th</sup> gestational week, but were under 2500g. Risk factors of PTB can exist before the pregnancy or develop during it. In our work we studied the presence of the risk factors described in the literature in our hospital.

**Results:** The average weight of preterm babies was 2312g, and they were born during the 34<sup>th</sup> gestational week. We examined the age of the pregnant (<17=9, >35=48), the presence of maternal diseases such as hypertension (14), diabetes mellitus (14), anemia (8). Other risk factors are preeclampsia (12), abortion (71), previous PTB (9) or delivery (126) in the history, assisted reproduction (11), surgery performed on the uterus or uterine abnormalities (38). During the pregnancy developing risk factors are abnormalities of the placenta (25), intrauterine growth restriction, oligohydramnios (25), acute fetal distress (25), irregularities of the umbilical cord (13), pre-labor premature rupture of membrane (102) and the multiple gestations (32). 48% of the cases were spontaneous delivery, and 52% caesarean section.

**Conclusion:** The infant mortality and morbidity (IMMR) rate is one of the most important indicators of a country's level of health or development, and is a component of the physical quality of life index. In Hungary 64% of these cases are PTB, which is in our country as well as in our hospital 10%, higher than the average of the EU. Successful reduction of IMMR may require the implementation of effective risk identification, the development of effective screening system and behavioral modification programs for the prevention of PTB.

# Expression of genes encoding the enzymes of transsulfuration pathway and taurine biosynthesis in human placenta at the first and the third trimesters of gestation

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**Background:** Cysteine is synthesized from homocysteine by cystathionine  $\beta$ -synthase (CBS) and cystathionine  $\gamma$ -lyase (CSE) and used for the syntheses of taurine by cysteine dioxygenase (CDO) and cysteine sulfinic acid decarboxylase (CSAD). Taurine is necessary for normal development of fetal central nervous system and endocrine glands. Cysteine also is used for the syntheses of hydrogen sulfide by CBS and CSE, which may play a role as smooth muscle relaxant, endogenous neuromodulator in brain tissue, vasodilator, which reduces blood pressure. As transsulfuration pathway and further fate of cysteine in human placenta were scarcely addressed, the main goal of our research was to fill this gap.

**Materials and Methods:** Expression of *CBS*, *CSE*, *CDO*, *CSAD* at the mRNA level was determined by reverse transcriptase and polymerase chain reaction (RT-PCR), at protein level – with Western blot analysis. Enzymatic activity of CBS was assessed by radiobiological method. The objects of the study were placentas of the first and the third trimesters of gestation.

**Results:** We detected specific mRNAs encoding CBS and CSE in human placenta at the first and the third trimesters of pregnancy. Western blot analysis revealed the expression of CBS full-size protein (63 kDa) in placental samples from the both terms of gestation. We also confirmed the catalytic activity of CBS at both terms of gestation. Taken together, these data confirm the functioning of transsulfuration pathway in placenta. The amount of CDO-specific mRNA was higher in term placenta than in the first trimester one. In contrast, the amount of CSAD mRNA was much lower in the samples from term placenta in comparison with placenta from the first trimester of pregnancy. We suggest that taurine is preferentially synthesized in human placenta during the first trimester of gestation.

**Conclusions:** Identification of *CBS* and *CSE* genes expression at mRNA level and discovery of catalytically active CBS protein point to the functional activity of transsulfuration pathway in human placenta for the first time. The discrepancy in the amounts of CDO and CSAD mRNAs in both terms of gestation allows us to suggest more active taurine synthesis during the first trimester of gestation than in the third one.