

WOMENS HEALTH, REPRODUCTION AND FERTILITY

April 08-09, 2019 Abu Dhabi, UAE

Prediction of preterm delivery at symptomatic and asymptomatic women

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Preterm delivery is the leading cause of neonatal mortality and morbidity in the world. Its worldwide incidence ranges from around 5%-15%, depending on the population. The worldwide rates of preterm birth have increased in the past couple of decades in spite of the efforts to alleviate the problems associated with preterm delivery and the medical advances made. Preterm deliveries and associated complications account for over 75% of the neonatal mortality rates and for around half of the neurological sequelae in newborn children. Consequently, women presenting with threatened preterm labor are often treated with hospitalization and the administration of tocolytics to avoid preterm delivery. Randomized studies on the use of tocolytics in threatened preterm labor have demonstrated a significant prolongation of pregnancy by about 7 days but no significant reduction in the incidence of preterm delivery, perinatal morbidity or mortality. Preterm delivery exerts numerous negative effects on the neonate: a substantially higher risk of neurological complications, chronic lung disease, respiratory distress syndrome, necrotizing enterocolitis and increases the social burden of these children. This is especially true for extremely preterm neonates, i.e. neonates delivered before 28 gestational weeks. According to Romero and colleagues, preterm labor (PRL) can be considered a syndrome that is initiated by a myriad of mechanisms, such as inflammation, uterine over-distension, utero-placental hemorrhage and ischemia and other immunologic and non-immunologic processes. The author also published that all these different initiation mechanisms converge into a single terminal inflammatory pathway that results in increased uterine contractility, cervical ripening and decidua activation. Timely prediction and prevention at asymptomatic patient is important for reducing preterm delivery. Transvaginal ultra-sonographic cervical length measurement is a commonly used and powerful method for prediction of preterm delivery and its combination with vaginal progesterone, significantly contributes to the prevention of premature delivery. In 2013, Romero published a meta-analysis of individual data from randomized clinical trials who shows that vaginal progesterone reduces the rate of preterm birth in singleton gestation <33 weeks by 44%, reduction of the NICU hospitalization rate by 25%, respiratory distress syndrome by 52%, mechanical ventilation by 34%, neonatal morbidity / mortality by 43%, and delivery of newborns <1500 grams by 45%. According to the new meta-analysis of individual patient data of randomized controlled trials of Romero from 2017, administration of vaginal progesterone in asymptomatic women with a twin gestation and a sonographic CL \leq 25mm in the mid-trimester lead to significantly decrease in the risk of preterm delivery from 31 % in pregnancy <33 gestation weeks, respiratory distress syndrome for 33%, birth weight <1500 g for 47%, use of mechanical ventilation for 46 % and morbidity and mortality for 47%. Treatment with progesterone is only one of the solutions to prevent preterm delivery, we can expect the intervention to be successful only if specific pathways leading to premature delivery are discontinued, and this should be considered in all further clinical trials. Research aimed to reduce the incidence and consequences of PTD has been focused either on early detection and prediction through the identification of risk factors or on the treatment of symptomatic and clinically manifest patients by mitigating PTD via tocolytic agents. The latter approach, however, has a limited effectiveness and only prolongs PTD by 48 hours, which provides clinicians with adequate time to administer corticosteroids to accelerate fetal lung maturation and transfer

the patient to a tertiary health care center equipped with a neonatal intensive care unit, which in turn improves the outcome of prematurely delivered neonates. However, only a small portion, 8-38% of patients admitted because of clinical symptoms of PTL will go on to deliver prematurely. The ability to distinguish between these two groups of patients (high-risk and low-risk patients) is of paramount importance for the reduction of unnecessary hospitalization and treatment of low-risk patients. Recently, biomedical research has been rapidly developing newer tools such as genomics and proteomics^{21, 22}, with promising results. In order to contribute to the efforts for prediction of preterm delivery, we conducted a prospective cohort study at the Clinic for Gynecology and Obstetrics, Skopje. Patients were eligible to join this prospective cohort study if they attended the University Clinic for Gynecology and Obstetrics, Skopje and were admitted to Department of High Risk Pregnancy Unit with symptoms of preterm labor (symptoms of uterine activity, three regular uterine contractions in 10 minutes). The aim of this study was to determine the relationship between sonographic cervical length, fetal fibronectin (fFN), pHIGFBP-1 (Actim partus test), cytokines (IL-6, IL-2R and TNF-alpha) and spontaneous preterm birth (SPTB) up to 14 days from sampling. In this study we included symptomatic and asymptomatic patients at 24.0 to 36.6 gestation weeks. The studied biochemical markers in our study were only moderately successful in the prediction of preterm delivery. The best predictor model in our study was the combination of the fFN test, Actim partus test, concentration of IL-6 in the cervical fluid, the cervical length <21.5 mm, concentration of CRP and IL-6 in the serum. Our study is only the beginning of this type of research in our population. Further research is required in terms of the evaluation of cost-benefit of using such test to prevent subsequent unnecessary interventions in the low-risk group, as well as achieve the benefits from such intervention in the high-risk groups of patients.

Biography

Marija Hadji Lega has earned her Medical degree from St. Cyril & Methodius University, Medical Faculty, FYRO Macedonia (1997). She has completed her Specialization in Obstetrics & Gynecology from the same university in 2005 and also sub-specialization in Perinatal Medicine (Maternal-Fetal Medicine) in 2014 also from the same university. She has obtained her PhD degree in Clinical Medicine (Prediction of Preterm Deliveries) from Medical Faculty, University of Nish, Serbia. She has more than 21 years of experience in obstetrics, gynecology and especially in fetal medicine (first trimester screening, anomaly scans, growth scan). She was the Chief of High Risk Pregnancy Unit at University Clinic for Gynecology and Obstetrics (Unique Tertiary level Clinic for Gynecology and Obstetrics), Skopje, FYRO Macedonia.

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