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Editorial

Preterm Birth as a Global Health Issue- What do we know?

Emilija Jasovic-Siveska*

Specialist of Gynecology and Obstetrics in PHO for Gynecology and Obstetrics "Medihelp" Bitola and Professor of Gynecology and Obstetrics, College for Nursing, University St. Clement of Ohrid, Bitola, Macedonia

***Corresponding Author:** Emilija Jasovic-Siveska, Specialist of Gynecology and Obstetrics in PHO for Gynecology and Obstetrics "Medihelp" Bitola and Professor of Gynecology and Obstetrics, College for Nursing, University St. Clement of Ohrid, Bitola, Macedonia.

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Preterm births (PTBs) are all births before 37 completed weeks or 259 days of gestation. It is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health [1,2]. PTBs are a significant global health issue worldwide and a leading cause of perinatal morbidity and mortality. The incidence of PTB has not changed during the last 50 years. Every year about 15 million babies are born preterm. PTB usually affects 5 - 7% of births, but most of them are in developing countries [3]. The incidence of PTB has increased worldwide. In 2010, 11% of all live births were born preterm [4]. Survival rates have increased, and morbidity has decreased because of technologic advances in perinatal and neonatal medicine [5].

The serious neonatal complications and consequences can be avoided by early identification of the pregnant woman at risk for PTB, timely implementation of appropriate intervention and treatment. The leading causes of neonatal death worldwide are PTB, severe infections and asphyxia. Children who are born prematurely have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term [6]. The morbidity associated with PTB often extends to later life, resulting in enormous physical, psychological and economic costs [5,7].

Possible factors which contribute to this upward trend include increasing rates of multiple pregnancies, greater use of assisted reproduction techniques, increases in the proportion of births among women ≥ 34 years of age and changes in clinical practices (increased incidence of elective Caesarean Section; high risk pregnancies; Iatrogenic PBs etc.) [8,9].

Etiology

PTB is a highly complex and incompletely understood syndrome, and it's etiology is likely to be multifactorial which creation involves various exogenous and endogenous risk factors. All risk factors for PTB can be classified into the following categories: maternal characteristics, reproductive history and characteristics of the actual pregnancy. PTB is now thought to be a syndrome initiated by multiple mechanisms, including infection, inflammation, uteroplacental ischaemia, haemorrhage, placental malperfusion, uterine anomalies, uterine overdistension, stress, and other immunologically mediated processes [5,9-14].

Maternal characteristics and reproductive history. Pregnant outside marriage and without antenatal care are at higher risk for PTB (these conditions are often associated with low socioeconomic status, smoking, alcohol or drug abuse and poor nutritional status etc) [10]. Other maternal risk factors are: psychological stress or depression, genetic factors, primiparity, inflammatory and immune response, cervical insufficiency, etc [1,15]. Baer., *et al*. report that a change in partner seemed to be protective against PTB [16].

Previous PTB is actually the strongest single risk factor. It has been reported that risk of PTB ranges from 15% to more than 50%, depending on the number of previous preterm deliveries. In some studies the induced abortions increase the risk of PTB due to cervical damage during termination of pregnancy [17].

Characteristics of actual pregnancy. Multiple pregnancies are at increased risk of maternal, perinatal and infant morbidity and mortality. Multiple gestations have an increased risk for PTB, and result in 12 - 27% of all preterm deliveries. In the past decades, there was a great increase in the incidence of multiple deliveries, above all as a result of the use of assisted reproduction technologies [18,19].

The intrauterine infections are the leading cause of PTBs (at least 40%) [1]. In individual cases it is often difficult to determine whether an infection is the cause or consequence of the processes leading to preterm delivery. Genital tract infections account for about 25 - 40% of preterm deliveries. Women with *Chlamydia trachomatis, Gardnerella vaginalis, Trichomonas vaginalis, Neisseria gonorrhoeae, Treponema pallidum*, have a higher rate of preterm births. Still, the infection is difficult to detect due to the limitations of conventional microbial techniques and the difficulties in obtaining appropriate diagnostic samples during pregnancy [9,20]. Experimental models also suggest the possible induction of labour by viral infection [5].

An investigation regarding the relationship between intrauterine infection and fetal inflammation, has shown that preterm infants with funisitis had higher cord blood IL-6 concentrations than those without funisitis. Fetal plasma IL-6 levels have also been shown to be significantly associated with inflammatory lesions in the chorioamnion [21].

Vaginal bleeding is a manifestation of decidual damage, but can also be idiopathic. The history of vaginal bleeding at any time of pregnancy is associated with PTB and also other adverse perinatal outcomes. In late pregnancy vaginal bleeding is associated with placental abruption. General risk factors for placental abruption are maternal smoking, use of alcohol, placenta preavia, pre-eclampsia and chorioamnionitis [9,22,23].

Evaluation and Prevention of PTBs

Accurate prediction of PTB among asymptomatic pregnant women and those with threatened PTB might offer an opportunity to target more intensive antenatal surveillance and prophylactic measures to those most likely to benefit from primary, secondary or tertiary prevention [5].

Primary prevention is prevention of the onset of spontaneous PTB in asymptomatic women by cessation of smoking and/or alcohol use, by maintaining a healthy genitourinary tract and periodontal status or by administration of maternal progestational agents, or use of cervical cerclage [5,9].

Secondary prevention involves steps that can be taken to attenuate, stop or reverse the progress of spontaneous PTB in its early stages, before advanced cervical dilatation by using tocolytic agents [5,9].

Tertiary prevention means measures aimed at preventing neonatal complications associated with prematurity by using antenatal corticosteroids (ACs) to accelerate fetal lung maturity and for reducing neonatal respiratory distress syndrome (RDS) [5,9]. Numerous studies have shown that ACs therapy reduced mortality by 31%, risk of RDS by 44%, and the risk of intraventricular haemorrhage by 46%. Also, ACs treatment reduced a risk of necrotizing enterocolitis, incidence of intensive care and sepsis during the first 48 hours of life [24]. ACOG Committee recommended ACs between 24+0 and 33+6 week of gestation who are at risk for preterm delivery within 7 days, including for those with a ruptured membrane and multiple pregnancies. A single repeat course of ACs Should be considered in women who are less than 34+0 wg who are at risk for preterm delivery within 7 days, and whose prior course of ACs was administrated more than 14 days previously. A single course of betamethasone is recommended for pregnant women between 34+0 to 36+6 weeks of gestation at risk of PTB within 7 days and who haven't received a previous of ACs [25]. A single course includes two intramuscular injections of betamethasone given 24h apart or dexamethasone, four doses of 6 mg, given 12h apart [24].

Two biologic markers improved the precision of preterm birth risk assessment: fetal fibronectin and transvaginal ultrasonography [23,26].

Cervical evaluation by transvaginal ultrasonography is the most accurate and reproducible method, with higher positive predictive value than digital palpation. The measurement of cervical length at 20 to 24 weeks is the first marker for identification of the cervical incompetence. Certainly in women who had a previous preterm birth or second-trimester loss, cervical cerclage is either carried out electively in the first trimester, or it is reserved for those where serial scans, starting from the first-trimester, demonstrate cervical shortening. At 11 to 13 weeks, the endocervical length in pregnancies complicated by subsequent spontaneous delivery before 34 weeks was shorter (< 25 mm) than in those delivering after 34 weeks and the risk of early delivery was inversely related to cervical length [23,26,27].

Biomarkers in serum or plasma are easy to collect, with minimal discomfort to the patient. Alpha fetoprotein, ferritin, C-reactive protein, various cytokines and relaxin are examples of biomarkers that can be measured in serum and plasma, and are used for prediction of PTB. Inflammation-associated proteins are produced in response to inflammation in the choriodecidual space and also in extra-uterine tissues. Proteins of the choriodecidua are thought to leak into the amniotic fluid, plasma or into cervical and vaginal fluid from the placenta or choriodecidual space as a result of tissue disruption. Some proteins, IGFBP-1, FFN and prolactin, may have no actual role in the pathway leading to PTB, but may serve as predictors [28].

Preventing tools for PTB are:

Cervical cerclage: It has been one of the preventive strategies used for many years, but there are no studies that show overall evidence except in very specific cases. The literature shows evidence that cerclage provides clear and proven benefits only in pregnant women with diagnosed cervical incompetence. Cerclage may have a beneficial effect in preventing preterm delivery when there is a history of PTB and an objective decrease in cervical length or increase cervix dilatation in non-symptomatic patients. In cases with uterine abnormalities and multiple pregnancies, cerclage has failed to show evidence of improvement in perinatal results. In singleton gestations without prior spontaneous PTB but with transvaginal cervicometry less than 25 mm in the second trimester, cerclage does not seem to prevent PTB. However, in these pregnancies, cerclage seems to be efficacious at lower cervical length, such as < 10 mm, and when tocolytics or antibiotics are used as additional therapy [29].

Progesterone: The optimal progesterone formulation, route of administration, and dose for the prevention of PTB has not yet been determined. The vast majority of such clinical trials were performed with diverse formulations of progesterone: vaginal route (8% gel or 100 - 400 mg micronized hormone) or intramuscular injection (17 OHP-C 250-682 mg/week). Asymptomatic mid-second trimester women with a very short cervix as well as third-trimester patients having had a successful treatment of a preterm labor episode were also admitted to 'progesterone' supplementation. Micronized progesterone capsules (200 mg vaginally daily) were used in the trial of P4 for asymptomatic women with a very short cervix (less than 15 mm), and appeared to be effective for such an indication. Supplemental 17 OHPC treatment doesn't benefit women with short cervix and previous preterm birth submitted to cervical cerclage for suspected cervical insufficiency. The latter study suggests that treatment with 17-OHP-C may be associated also with increased maternal morbidity that is an additional safety flag [29-31].

Clinical predictors of PTB in 2017 are similar to those mentioned in the last decades. The delivery of a preterm infant brings considerable health care costs which are strongly gestational age-dependent. The costs are not just those incurred while in the hospital's neonatal intensive care unit. Some health problems that develop at this time can persist for years, leading to long-lasting use of healthcare and social services, including special education and rehabilitation for those with physical handicaps. Maternal hospitalization before and after delivery and an increased number of Caesarean sections also increase costs. Reduction of the risk of PTB among asymptomatic pregnant women and those symptomatic with threatened preterm labour may offer the opportunity to target care at those most likely to benefit [5,6,9].

Finally, all strategies and therapies must improve outcomes for the baby, not only to prevent PB. Effect of progesterone on long-term health of offspring is largely unknown, and should be assessed before widespread adoption of any new intervention to prevent PTB. Funding bodies must resource the collection of these outcomes. Until then, preterm births will remain a major public health issue worldwide [9,29,32].

Bibliography

1. Goldenberg RL., *et al.* "Epidemiology and causes of preterm birth". *Lancet* 371.9606 (2008): 75-84.

2. Wang ML., *et al*. "Clinical outcomes of near- term infants". *Pediatrics* 114.2 (2004): 372-376.

3. Lawn JE., *et al.* "One year after The Lancet Neonatal Survival Series- was the call for action heard?" *Lancet* 367.9521 (2006): 1541-1547.

4. Blencowe H., *et al.* "National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications". *Lancet* 379.9832 (2012): 2162-2172.

5. Jasovic-Siveska E. "Editorial: Etiology, Prevention and Prediction of Preterm Birth- What is New?" *Obstetrics and Gynecology International Journal* 8.3 (2017): 00291.

6. Petrou S. "The economic consequences of preterm birth during the first 10 years of life". *BJOG: An International Journal of Obstetrics and Gynaecology* 112.1 (2005): 110-115.

7. Tommiska V., *et al.* "No improvement in outcome of nationwide extremely low birth weight infant populations between 1996-1997 and 1999-2000". *Pediatrics* 119.1 (2007): 29-36.

8. Davidoff MJ., *et al.* "Changes in the gestational age distribution among U.S. singleton births: impact on rates of late preterm birth, 1992 to 2002". *Seminar in Perinatology* 30.1 (2006): 8-15.

9. Jasovic-Siveska E. "Prevention and Prediction of Preterm Birth-Status Quo in the Last 50 Years". *Reproductive System and Sexual Disorders* 3 (2014): e117.

10. Escobar GJ., *et al.* "Unstudied Infants: Outcomes of moderately premature infants in the NICU". *Archives of Disease in Childhood. Fetal and Neonatal Edition* 91.4 (2006): F238-244.

11. Hodek., *et al.* "Measuring economic consequences of preterm birth - Methodological recommendations for the evaluation of personal burden on children and their caregivers". *Health Economics Review* 1 (2011): 6.

12. Meis PJ., *et al.* "Prevention of recurrent preterm delivery by 17 alpha–hydroxyprogesterone caproate". *The New England Journal of Medicine* 348 (2003): 2379-2385.

13. Lekovich J., *et al.* "Placental malperfusion as a possible mechanism of preterm birth in patients with Mullerian anomalies". *Journal of Perinatal Medicine* 45.1 (2017): 45-49.

14. Karahanoglu E., *et al.* "Nifedipine increased fetoplacental perfusion". *Journal of Perinatal Medicine* 45.1 (2017): 51-55.

15. Romero R., *et al.* "The preterm parturition syndrome". *BJOG: An International Journal of Obstetrics and Gynaecology* 113.3 (2006b): 17-42.

16. Baer RJ., *et al.* "Risk of preterm birth among women according to change in partner". *Journal of Perinatal Medicine* 45.1 (2017): 63-70.

17. McCormack RA., *et al.* "Antepartum bleeding of unknown origin in the second half of pregnancy and pregnancy outcomes". *BJOG: An International Journal of Obstetrics and Gynaecology* 115.11 (2008): 1451-1457.

18. Chang HH., *et al.* "Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index". *Lancet* 381.9862 (2013): 223-234.

19. Romero R., *et al.* "Vaginal progesterone decreases preterm birth and neonatal morbidity and mortality in women with a twin gestation and a short cervix: an updated meta-analysis of individual patient data". *Ultrasound in Obstetrics and Gynecology* 49.3 (2017): 303-314.

20. Lamont RF. "Infection in the prediction and antibiotics in the prevention of spontaneous preterm labour and preterm birth". *BJOG: An International Journal of Obstetrics and Gynaecology* 110.20 (2003): 71-75.

21. Kemp MW. "Preterm Birth, Intrauterine Infection, and Fetal Inflammation". *Frontiers in Immunology* 5 (2014): 574.

22. Thorp JM. "Predicting and preventing preterm birth". *OBG Management* 17.6 (2005): 49-53.

23. Greco E., et al. "Prediction of spontaneous preterm delivery from endocervical length at 11 to 13 weeks". *Prenatal Diagnosis* 31.1 (2011): 84-89.

24. Blickstein I. "Antenatal corticosteroids: current controversis". *Journal of Perinatal Medicine* 45.1 (2017): 5-9.

25. Committee Opinion. "Antenatal Corticosteroid Therapy". *Obstetrics and Gynecology* 130.2 (2017): e104-e109.

26. Di Renzo Gc., et al. "Guidelines for the management of spontaneous preterm labor: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth". *The Journal of Maternal-Fetal and Neonatal Medicine* 24.5 (2011): 659-667.

27. Tsoi E., *et al.* "Ultrasound assessment of cervical length in threatened preterm labor". *Ultrasound Obstetrics and Gynecology* 21.6 (2003): 552-555.

28. Polettini J., *et al.* "Biomarkers of spontaneous preterm birth: a systematic review of studies using multiplex analysis". *Journal of Perinatal Medicine* 45.1 (2017): 71-84.

29. Society for Maternal Fetal Medicine Publications Committee. "ACOG Committee Opinion number 419 October 2008 (replaces no. 291, November 2003). Use of progesterone to reduce preterm birth". *Obstetrics and Gynecology* 112.4 (2008): 963-965.

30. Likis FE., *et al.* "Progestogens for preterm birth prevention: a systematic review and meta-analysis". *Obstetrics and Gynecology* 120.4 (2012): 897-907.

31. Ahn KH., *et al.* "The safety of progesterone in the prevention of preterm birth: meta-analysis of neonatal mortality". *Journal of Perinatal Medicine* 45.1 (2017): 11-20.

32. Blencowe H., *et al.* "National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications". *Lancet* 379.9832 (2012): 2162-2172.

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