Prevention and Prediction of Preterm Birth-Status Quo in the Last 50 Years

Emilija Jasovic-Siveska
Specialist of Gynecology and Obstetrics, Bitola, Macedonia

Corresponding author: Emilija Jasovic-Siveska, MD, PhD, Specialist of Gynecology and Obstetrics, Bitola, Macedonia, Tel: 38972222256, E-mail: medihelp@t-home.mk

Received: April 21, 2014; Accepted: April 23, 2014; Published: April 30, 2014

Copyright: © 2014 Jasovic-Siveska E. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Editorial

Preterm Birth (PB) is a major public health problem worldwide. It’s the leading cause of perinatal morbidity and mortality. PB usually affects 5 to 7 percent of births, but is estimated to be substantially higher in developing countries [1]. Despite four decades the rate of premature births has not changed. Survival rates have increased, and morbidity has decreased because of technological advances in perinatal and neonatal medicine.

PB, 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 [2,3].

The main direct causes of neonatal death globally are PB, severe infections and asphyxia. In developed countries preterm delivery is responsible for about half of all neonatal deaths. Children who are born prematurely have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term [4]. The morbidity associated with PB often extends to later life, resulting in enormous physical, psychological and economic costs [5].

No data have been published on the global incidence of PB. PB rates have not decreased in the last 50 years and in most developed countries continue to rise despite advances in knowledge of the risk factors and mechanisms related to preterm labour. Factors possibly contributing to but not completely explaining this upward trend include increasing rates of multiple births, greater use of assisted reproduction techniques, increases in the proportion of births among women over 34 years of age and changes in clinicalpractices [6].

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 [7]. Reduction of the risk of PB among asymptomatic pregnant women and those symptomatic with threatened preterm labour may offer the opportunity to target care at those most likely to benefit [7,8].

PB is multifactorial disorder in which creationare involved various exogenous and endogenous risk factors whose interactions initiated early, start asynchronous delivery mechanism. PB is now thought to be a syndrome initiated by multiple mechanisms, including infection or inflammation, uteroplacental ischaemia or haemorrhage, uterine overdistension, stress, and other immunologically mediated processes [9,10].

In most cases, the causes of PB are not diagnosed, and the etiology is likely to be multifactorial. All risk factors for PB can be classified into the following categories: maternal characteristics, reproductive history and characteristics of the actual pregnancy.

Pregnant outside marriage and without antenatal care are at higher risk for PB. These conditions are often associated with low socioeconomic status, smoking, alcohol or drugs abuse and poor nutritional status all independent risk factors of PB as well [10]. Other maternal risk factors are: psychological and social stress or depression, genetic factors, inflammatory and immune response, cervical insufficiency, etc [10,11].

About 50% of all preterm delivery occur in primiparous women. History of previous PB is actually the strongest single risk factor. It has been reported that risk of PB ranges from 15% to more than 50%, depending on the number of previous preterm deliveries (for each previous preterm delivery the risk of a subsequent PB increases). There is also an increased risk of PB in pregnancies arising in close proximity to previous delivery. In some studies the induced abortions increase the risk of PB due to cervical damageduring termination of pregnancy [11,12].

Multiple gestations have a increased risk for PB, 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 [10].

Infections are one most often risk factors of PB. 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, infection is difficult to detect due to the limitations of conventional microbial techniques and the difficulties in obtaining appropriate diagnostic samples during pregnancy [10]. Spontaneous preterm deliveries that occur before the 34th week of gestation, have been strongly associated to intrauterine infection. The earlier the PB the stronger the association. Infection is rare in late PB (>34weeks) [11].

The history of vaginal bleeding at any time of pregnancy is associated with PB and also other adverse perinatal outcomes. Vaginal bleeding is a manifestation of decidual damage, but can also be idiopathic. It may be a sign of retrolaplacental haematoma detected by...
ultrasound examination in the first trimester. In late pregnancy vaginal bleeding is associated with placental abruption which is a major obstetrical emergency. General risk factors for placental abruption are maternal smoking, use of alcohol, placenta previa, pre-eclampsia and chorion amnionitis [11,13].

Accurate prediction of PB among asymptomatic pregnant women and those with threatened PB 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. Primary prevention is prevention of the onset of spontaneous PB 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 pregastational agents, or use of cervical cerclage. Secondary prevention involves steps that can be taken to attenuate, stop or reverse the progress of spontaneous PB in its early stages, before advanced cervical dilatation by using tocolytic agents. Tertiary prevention means measures aimed at preventing neonatal complications associated with prematurity by using antenatal corticosteroids to accelerate fetal lung maturity [14].

In the 1990s, two biologic markers were discovered that improve the precision of preterm birth risk assessment: fetal fibronectin and transvaginal ultrasonography [15].

The most accurate and reproducible method of cervical evaluation is trans vaginal ultrasonography, with higher positive predictive value than digital palpation. Measurement of cervical length at 20 to 24 weeks is first marker for identification of the cervical incompetence. Certainly in women who had a previous preterm birth or second-trimester loss, cervical cerclages 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 (<25mm) than in those delivering after 34 weeks and the risk of early delivery was inversely related to cervical length [16,17].

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 & plasma, and are used for prediction of PB. 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 PB but may serve as predictors [17].

The alternative to sonographic measurement of cervical length in predicting the outcome of women presenting in threatened preterm labor is biochemical assessment for the presence of fetal fibronectin in cervicovaginal secretions [18].

Three preventive interventions had a high level of evidence (smoking cessation, progesterone, and zinc supplementation), but only smoking cessation and progesterone, were strongly recommended for implementation for prevention of PB [14].

Preventing tools for PB are:

Cervical cerclage 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 circumstances diagnosed with cervical incompetence. Cerclage may have a beneficial effect in preventing preterm delivery when there is a history of PB 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 [17].

Progesteron: The optimal progesterone formulation, route of delivery, and dose for the prevention of preterm birth has not yet been determined [19]. The vast majority of such clinical trials were performed with diverse formulations of progesterone (vaginal route by using two different pharmaceutical preparations, i.e. 8% gel or 100–400 mg micronized hormone, or intramuscular injection of 17 OHP-C in doses ranging 250-682 mg/week). The most part of randomized subjects is represented by women with a history of at least one previous spontaneous PB or by multiple pregnancies. 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 OHP-C treatment does not 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 [17].

Clinical predictors of PB in 2012 are similar to those mentioned in the 2001 practice bulletin. May be in the future can decreased rate of PB by improved appropriate classification for the causes of preterm birth, with better diagnosis and risk stratification, and by development of new preventive interventions based on better understanding of the underlying aetiologic, intergenerational, and genetics studies.

Finally, all strategies and therapies must improve outcomes for the baby, not only to prevent PB. Little research has assessed perinatal mortality or longer term outcomes since this is difficult and expensive. 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 PB. Funding bodies must resource the collection of these outcomes. Until then, preterm births will remain a major public health issue wide-world [19-21].

References


