RESEARCH ARTICLE

Risk factors and clinical follow-up of patients with preterm births in a tertiary referral maternity unit in Bucharest, Romania

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Abstract

Objective: To analyse the historical risk factors associated with preterm birth, and the potential benefit of correct prenatal care for prevention.

Methods: This prospective study was performed in 2011-12 at the Department of Obstetrics and Gynaecology, Dr. I. Cantacuzino Hospital, Bucharest, Romania, and comprised women who gave birth at the hospital during the study period. The pregnancy was considered clinically cared if a pregnant woman underwent the following exams: first trimester ultrasound, maternal serum tests, screening tests, second trimester ultrasound, and amniocentesis if deemed necessary. The women with multiple pregnancies (twins or more) were excluded. Data collection was conducted according to the guidelines of the Mother and Child Health Research Network. IMB SPSS 21 was used for data analyses.

Results: Of the 4,078 cases, the prevalence of preterm births was 477(11.7%). Women giving birth to preterm babies had significantly less prenatal visits during pregnancy compared to women giving birth at term ($p<0.05$). High body mass index for 34-36 gestational weeks, a previous history of spontaneous abortion, a family history of preterm births and smoking were the most important risk factors for preterm birth ($p<0.05$ each).

Conclusions: The preterm delivery risk factors can be reduced at least partially by taking correct preventive measures during pregnancy.

Keywords: Preterm birth; Risk factors, Smoking, Body mass index, Prenatal care, Pregnancy follow-up. (JPMA 68: 559; 2018)

Introduction

Preterm birth is still a significant medical and social problem, affecting 5-8% of births in Europe[1] and 12-13% in the United States,[2] being an important cause of infant mortality, neurological deficits, developmental retard,[2] pulmonary or ophthalmologic pathologies,[3] and so on. According to the World Health Organisation (WHO), preterm birth is defined as the delivery of an infant before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period.[4] There are many known causes of preterm birth, including infection or inflammation of the amniotic fluid, thrombophilias, haemorrhage during pregnancy or thrombosis, placental abruption, stress, multiple pregnancy, polyhydramnios, cervical incontinence, environment factors (carbon monoxide, organophosphates, smoking), and so on.[5]

While some risk factors are unpreventable or have an unpredictable appearance, others can be identified and corrected through prenatal medical examination associated with follow-up treatments or other preventive measures. Therefore prenatal medical examination — including clinical examination, abdominal/transvaginal ultrasound examination, vaginal examination, genetic and laboratory tests — is essential for a correct identification and prevention of the risk factors associated with premature birth and for decreasing the number of premature births.

At present time in Romania complete population data on preterm birth does not exist, but limited number of articles can be searched on the internet using preterm, birth and Romania as keywords (6-12).

The current study was planned to investigate the benefit of monitoring pregnant women with high-risk pregnancy for preventing preterm birth. The secondary objective was to analyse the main risk factors associated with preterm birth at a tertiary level regional emergency referral maternity centre.

Patients and Methods

This prospective study was performed in 2011-12 at the Department of Obstetrics and Gynaecology, Dr. I. Cantacuzino Hospital, Bucharest, Romania, and comprised women who gave birth at the hospital during the study period. The hospital is a tertiary-level maternity unit and a referral centre for a large sector of Bucharest and other counties (Calarasi, Ilfov-about 5% of the Romanian population) in the south-eastern part of the

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country. Data collection was conducted according to the guidelines of the Regional Cooperation (RECOOP) in the Fields of Health, Science and Technology (HST) Association Mother and Child Health Research Network.

The pregnancy was considered clinically cared if a pregnant woman underwent the following exams: first trimester ultrasound (US), maternal serum tests, screening tests, second trimester US, and amniocentesis if deemed necessary. According to the customary prenatal care in Romania at least two examinations performed by an obstetrician and including US examination should be made for a proper monitoring. Women with multiple pregnancies (twins or more) were excluded from the study. The main risk factors analysed before pregnancy were: body mass index (BMI) — only quantified before pregnancy in our study, because during pregnancy disposition for obesity could be influenced by diabetes or many other factors(BMI categories: underweight = <18.5, normal weight = 18.5-24.9, overweight = 25-29.9 , obesity = >30 or greater), age, weight, height, family history of preterm birth, personal history of spontaneous abortion, incontinent cervix, uterine surgery, chronic hypertension, asthma, diabetes, kidney disease and smoking. Factors analysed during pregnancy were: vaginal bleeding, anaemia, incontinent cervix, cerclage, pre-eclampsia, asthma, kidney disease (excluding infection), urinary tract infections, diabetes and smoking.

Informed consent was obtained from each subject, and the study was approved by the institutional ethics committee.

Data was first entered into Excel sheets and then transferred to an SPSS database. IMB SPSS Statistics 21 Programme was used for statistical analysis. The following methods have been used: univariate analysis, Mann Whitney U test, Chi square test, binary and multi-nominal logistic regression. Odds Ratios (ORs) were rounded to the first decimal by rounding to the superior number when the value was above 0.05 and the inferior number when the value was below 0.5 except for the cases in which OR was around 1 when the rounding was done according to the p value. P value below 0.005 was considered significant.

Results

Of the 4,078 subjects, 3,601(88.3%) had term births and 477(11.7%) had preterm births, among whom 13(0.3%) were extremely preterm (below 28 weeks), 88(2.2%) were very preterm (28-31 weeks), 143(3.5%) were preterm (32-34 weeks) and 233 (5.7%) were late preterm (35-36 weeks).

There was no significant difference related to mean age, weight and BMI values between the preterm and term subjects (p>0.05 each).

For all preterm birth the increase in odds ratio (OR) was not significant for any type of BMI compared to the normal weight group (p>0.05). The increase was significant, for both overweight and obese women giving birth at 34-36 weeks (p<0.05).

Height was significantly lower in the preterm compared to the term group (Table-1).

Babies born at term had a significantly higher mean weight and Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score (Table-2).

Table-1: Maternal characteristics.

Characteristic	Preterm birth	Term birth	Total	Mann-Whitney -U Test	P value
Age	28.2±6.5*	28.0±5.6	28.0±5.8	843.754	0.502
Weight (kg)	67.3±12.4	67.3±12.0	67.3±12.1	852.493,5	0.792
BMI	23.2±4.7	24.8±4.5	24.8±4.5	811.355	0.49
Height (cm)	163.6±6.9	164.8±6.1	164.7±6.2	943,239,5	<0.001

*± Standard Deviation.
BMI: Body Mass Index.

Table-2: Newborn characteristics.

Characteristic	Preterm birth	Term birth	Total	Mann-Whitney -U Test	p value
Weight (g)	2350±734	3266±460	3159±580	1.467.321,5	<0.001
APGAR Score	8.1±1.2	8.7±0.7	8.6±0.8	1.158.835,5	<0.001

*± Standard Deviation.
APGAR: Appearance, Pulse, Grimace, Activity, and Respiration.

Table-3: Monitoring characteristics.

PME	Preterm birth (No.)	Preterm birth (%)	Term birth (No)	Term birth (%)	Missing (No)	Chi^2	p value
1st Trimester US	168	34.4	1573	44.1	37	13.06	<0.001
Genetic screening	26	5.5	136	3.8	7	3.10	0.055
First Trimester Biomarkers	100	21.1	1009	28.1	6	10.370	0.001
Chorionic Villi Sampling	0	0	12	0.3	5	1.596	0.206
2nd Trimester US	318	67.2	3023	84.7	40	94.40	<0.001
Amniocentesis	3	0.6	62	1.7	6	3.20	0.074

PME: Prenatal medical examination
US: Ultrasound.

Table-4: Risk factors for preterm delivery.

Risk factor	Preterm birth (No.)	Preterm birth (%)	Term birth (No)	Term birth (%)	Missing (No)	Wald	OR (95% CI) Adjusted OR1* Adjusted OR2**	p value
Before Pregnancy								
Incompetent	10	2.1	10	0.3	4	20.5	7.7 (3.2-18.5)	<0.001
cervix							8.2 (3.2-20.6)	<0.001
							6.5(0.3-136)	0.223
Chronic HTN	10	2.1	37	1	2	4.1	2.0 (1.0-4.2)	0.044
							2.2 (1.1-4.6)	0.926
							1.1(0.3-4.7)	0.043
Diabetes	16	3.4	43	1.2	0	12.6	2.9 (1.6-5.1)	<0.001
							3.3 (1.8-5.9)	<0.001
							2.4(0.8-7.1)	0.125
Smoking	162	34	748	20.8	0	41.4	2.0 (1.6-2.4)	<0.001
							1.7 (1.4-2.1)	<0.001
							1.7 (1.1-2.4)	0.012
During pregnancy								
Incompetent cervix	11	2.3	11	0.3	6	22.6	7.7 (3.3-17.8)	<0.001
							9.1 (3.8-21.9)	<0.001
							11.2(0.9-145)	0.064
Need of Cerclage	9	1.9	16	0.4	8	12.1	4.3 (1.9-9.8)	<0.001
							5.7(2.5-13.2)	<0.001
							0.8(0.1-10)	0.855
Vaginal bleeding	24	5	103	2.9	5	6.4	1.8 (1.1-2.8)	0.012
							1.8 (1.2-3)	<0.001
							0.3 (0.1-1.3)	0.1
Infections Kidney Disease	19	4	80	2.2	10	5.3	1.8 (1.1-3.0)	0.021
							2.0(1.2-3.3)	0.009
							0.3 (0.1-1.2)	0.082
Diabetes	33	6.9	110	3.1	3	17.5	2.4 (1.6-3.5)	<0.001
							2.6 (1.8-4)	<0.001
							1.3(0.6-2.9)	0.534
Smoking	142	29.8	650	18.1	4	35.8	1.9 (1.5-2.4)	<0.001
							1.7 (1.3-2.1)	<0.001
							1.6 (1.1-2.4)	0.026

*adjusted with clinical monitoring during pregnancy **adjusted with anaemia during pregnancy, chronic hypertension, diabetes (both before and gestational induced), smoking (before and during), kidney disease, infectious kidney disease, vaginal bleeding, BMI before pregnancy.
HTN: Hypertension.
BMI: Body mass index
OR: Odds ratio
CI: Confidence interval.

Women who gave birth to preterm babies had less prenatal visits to their physicians or none compared to women giving birth to term babies (p<0.001). From 477(11.7%) preterm births only 329(69%) were monitored while from 3,601(88.3%) term birth 3075(85.39%) were followed up.

Genetic screening represented the only exception, but the difference was not statistically significant (p>0.05). First and second trimester US and first trimester biomarkers were conducted significantly more often on women giving birth at term (Table-3).

Family history and a history of spontaneous abortion were significantly associated with premature delivery (p<0.05 each).

Using logistic regression, the unadjusted risk factors being identified were diabetes diagnosed before and during the pregnancy, smoking before and during pregnancy), chronic hypertension before pregnancy, `vaginal bleeding and infectious kidney disease during pregnancy. There was a significant association between the number of smoked cigars and the risk for premature delivery, both for smoking before and during pregnancy (p<0.001).

When adjusting the obtained ORs for clinical follow-up of the patient, unmonitored pregnancies tended to have a slight increase in OR for almost all risk factors except for smoking. However, when adjusting for anaemia during pregnancy, chronic hypertension, diabetes, smoking, kidney disease, urinary tract infections, vaginal bleeding, and BMI, only smoking was positively identified as a risk factor, while all others were confounding factors. The main variable which, when added, caused the above-mentioned variables to become statistically not significant (p>0.05) was BMI (Table-4).

Special attention was paid to incontinent cervix, and need of cerclage. Therefore, 168(35%) women with preterm birth where subjected to US scans in the first trimester, 163(34%) during the second trimester and 144(30%) were not examined at all. There was a significant gap between the number of women who did not have US scans and subsequently gave birth prematurely (in less than 28 weeks) and the number of women with term birth (p<0.001). A similar difference existed for the very premature group and the term children (p<0.001). There was no significant difference between the US examinations and pregnancy age at preterm births of 32-37 weeks (p>0.05).

Discussions

The study analysed the importance of clinical follow-up and the main risk factors for preterm birth in a Romanian cohort of 4,078 pregnancies.

Until 2010 Romania had a preterm birth rate below 10%;[13] this study has shown a higher rate at 11.7%), possibly caused by the function of the study centre as tertiary level regional emergency referral maternity centre with more premature babies being born in our hospital. The first hypothesis was more likely as this is a reference hospital, receiving a high number of complicated cases from all around the country, and because of the higher number of assisted reproductive procedures performed (known to be associated with an increased risk for preterm births).[14,15] Also, according to WHO guidelines,[4] the deliveries starting with 24 weeks of gestation were considered preterm, (until 2010 Romanian law declared the birth after 28 weeks of gestation) and this could be another reason for the higher incidence of prematurity.

Epidemiologic data shows that women who have previously delivered prematurely or have family history of preterm birth influence the incidence of preterm birth (PTB).[16] In this study family history of PTB was significantly associated with premature delivery: 4.6% of women who gave birth prematurely and had a family history of preterm births compared to only 1.1% of women who gave birth at term that had a family history of preterm births. A previous history of spontaneous abortion was also significantly associated with a preterm birth: 88(18.4%) women who gave birth prematurely had a history of spontaneous abortion compared to 344(9.6%) women who gave birth at term and had a history of spontaneous abortion.

BMI has often been analysed in association with preterm birth. However, some studies did not show a significant increase in risk for preterm birth in obese and/or overweight compared to normal weight women.[17] Overweight and obese women are, however, known to have an increased risk for preterm birth before 33 weeks.[17] Nevertheless, in our study group, the before-33 weeks subgroup was not associated with a significant increase in risk, but there was a statistically significant risk increase for both overweight and obese women for a preterm delivery at 34-36 gestational weeks.

A possible cause for this apparent discrepancy might be the multiple pathology associated with obesity, like diabetes mellitus, gestational diabetes mellitus, pre-eclampsia, intrauterine growth restriction and foetal macrosomia. All these diseases could be causes for medically-induced PTB but not for spontaneous PTB.[18]

As most PTBs occur in the 34-36 weeks age group, this association may cause the particular pattern identified in our study. A low height is known to be associated with an increased risk for preterm delivery, especially for births at gestational weeks below 32.[19] In our study the low-height group was associated significantly with PTB, but there were no statistically significant differences on subtypes of PTBs.

Our study shows that with better follow-up during pregnancy and first trimester screening will reduce the incidence of PTB.

The incorrect clinical follow-up of patients was associated with increases in the OR for most significant risk factors analysed in this study, emphasising its usefulness in reducing PTBs.

The association between diabetes and the risk of PTB has been studied before, with contradictory results. For example, Hedderson et al. have identified a correlation between spontaneous preterm birth and high glucose values of the mothers, independent of other perinatal complications.[20] Ray et al., in a study analysing the outcome of mothers with type 2 diabetes and gestational diabetes mellitus (GDM), identified an increased risk of PTBs associated with diabetes mellitus, but the results were considered to be caused by increased adiposity of the mothers.[21] Nordin et al. haven't identified a significant increase in the risk of PTB in diabetic/hyperglycaemic mothers.[22] In our study, diabetes, both before and during pregnancy, seemed to be associated with a significant increase in the risk for preterm births. However, after controlling for additional risk factors (especially BMI) the association could be no longer identified. Nevertheless our team should continue in our cohort to follow up the newborns of obese women with diabetes to investigate the role of intrauterine growth and GDM as a major antenatal factor for later overweight.[23,24]

Smoking is known to be significantly associated with preterm delivery.[25] The relation, even if statistically significant, is, however, weak[26] as also proven by our study, that showed only a minor increase in the risk associated with smoking either before (Adjusted OR=1.7) or during pregnancy (Adjusted OR=1.6).

In terms of limitation, the study was conducted at a single centre which happened to be a referral maternity unit for high-risk pregnancies. However, as the patients came from all over the country, and as the aim of the study was not to analyse the prevalence of preterm delivery across Romania, the geographical bias was not considered relevant.

Conclusions

Appropriate clinical follow-up in pregnancy was found to be associated with a decrease in the risk of preterm births. An improper follow-up, a previous history of spontaneous abortion, a family history of PTBs, height and smoking were the most important risk factors for PTB.

Preventive measures during pregnancy are integral to minimising the risk for PTBs.

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Conflict of Interest: None.

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