Paper II

Maternal risk factors for preterm birth in Murmansk County, Russia: a registry-based study

Anna A. Usynina, Vitaly A. Postoev, Andrej M. Grjibovski, Alexandra Krettek, Evert Nieboer, Jon Øyvind Odland, and Erik Eik Anda

Paediatric and Perinatal Epidemiology

doi: 10.1111/ppe.12304

Maternal Risk Factors for Preterm Birth in Murmansk County, Russia: A Registry-Based Study

Anna A. Usynina,[a,b] Vitaly A. Postoev,[a,b] Andrej M. Grjibovski,[b,c,d,e] Alexandra Krettek,[a,f,g] Evert Nieboer,[a,h] Jon Øyvind Odland,[a,i] Erik Eik Anda[a]

[a]*Department of Community Medicine, Faculty of Health Sciences, UiT The Arctic University of Norway, Tromsø, Norway*

[b]*International School of Public Health, Northern State Medical University, Arkhangelsk, Russia*

[c]*Department of International Public Health, Norwegian Institute of Public Health, Oslo, Norway*

[d]*Department of Preventive Medicine, International Kazakh-Turkish University, Turkestan, Kazakhstan*

[e]*North-Eastern Federal University, Yakutsk, Russia*

[f]*Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden*

[g]*Department of Biomedicine and Public Health, School of Health and Education, University of Skövde, Skövde, Sweden*

[h]*Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton, ON, Canada*

[i]*Department of Public Health, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa*

Abstract

Background: Globally, about 11% of all liveborn infants are preterm. To date, data on prevalence and risk factors of preterm birth (PTB) in Russia are limited. The aims of this study were to estimate the prevalence of PTB in Murmansk County, Northwestern Russia and to investigate associations between PTB and selected maternal factors using the Murmansk County Birth Registry.

Methods: We conducted a registry-based study of 52 806 births (2006–2011). In total, 51 156 births were included in the prevalence analysis, of which 3546 were PTBs. Odds ratios with 95% confidence intervals of moderate-to-late PTB, very PTB and extremely PTB for a range of maternal characteristics were estimated using multinomial logistic regression, adjusting for potential confounders.

Results: The overall prevalence of PTB in Murmansk County was 6.9%. Unmarried status, prior PTBs, spontaneous and induced abortions were strongly associated with PTB at any gestational age. Maternal low educational level increased the risk of extremely and moderate-to-late PTB. Young (<18 years) or older (≥35 years) mothers, graduates of vocational schools, underweight, overweight/obese mothers, and smokers were at higher risk of moderate-to-late PTB. Secondary education, alcohol abuse, diabetes mellitus, or gestational diabetes were strongly associated with moderate-to-late and very PTB.

Conclusions: The observed prevalence of PTB (6.9%) in Murmansk County, Russia was comparable with data on live PTB from European countries. Adverse prior pregnancy outcomes, maternal low educational level, unmarried status, alcohol abuse, and diabetes mellitus or gestational diabetes were the most common risk factors for PTB.

Keywords: *birth registry, extremely preterm birth, moderate-to-late preterm birth, Northwestern Russia, risk factors, very preterm birth.*

Preterm birth (PTB) is defined as birth before 37 completed weeks or 259 days of gestation.[1] Globally, about 11% of all liveborn infants are preterm,[2] and the prevalence of PTB is region- or country-dependent. In Europe, it comprises 6.2% with a 95% confidence interval of 5.8–6.7 for all births[3] and 5–10% for livebirths.[4] Previous studies in Northwest Russia demonstrate varying prevalence of PTB. In the city of Severodvinsk (Arkhangelsk County), 5.6% of spontaneous live singleton births were preterm,[5] while in Murmansk County the prevalence of PTB was higher (8.7%) but included stillbirths.[6] In Syktyvkar (the capital of Komi Republic, located next to Arkhangelsk County), the PTB prevalence (from 28 weeks of gestation on) comprised 4.9 and 5.8% in 1980–84 and 1995–99, respectively.[7]

Preterm birth is a major contributor to under five-year mortality and morbidity, especially those births

Correspondence:
Anna A. Usynina, Northern State Medical University, 51, Troitsky Ave., Arkhangelsk 163000, Russia.
E-mail: aus002@post.uit.no

© 2016 John Wiley & Sons Ltd

that take place before 34 weeks of gestation.[2] Generally speaking, the mortality and morbidity of preterm infants are inversely proportional to gestational age (GA).[8] Since prognoses are GA-dependent, the World Health Organization (WHO) divides PTB into three categories: extremely preterm (<28 weeks), very preterm (28 to <32 weeks), and moderate-to-late preterm (32 to <37 weeks).[1]

Preterm birth has multiple causes such as chronic genital[9] and urinal tract infections,[10] young maternal age,[11] heavy physical and/or occupational exertion during pregnancy,[12] alcohol abuse,[13] and low educational level.[14] Compared to women with normal body mass index (BMI), underweight[15] and overweight or obese[16] mothers exhibit increased risk of PTB. Previous history of PTB is also associated with the risk of current PTB.[17,18]

Stillbirth, major congenital anomalies, placenta previa and abruption place women at a higher risk of PTB independent of GA.[19] General infection, drug abuse, and mental disorders are all indicated to be major contributors to extremely and very preterm spontaneous PTB with intact membranes,[20] as does maternal tobacco smoking during weeks 27–33.[21] Pre-existing or gestational diabetes, general infection, drug dependence, and mental disorders are known systemic co-morbidities associated with spontaneous PTB at 32–36 weeks,[20] while risks due to maternal young age, incomplete secondary education, and low BMI are enhanced at lower GA.[14]

Internationally published data on prevalence and risk factors of PTB in Russia are limited. Low level of maternal education, maternal stress, placental disorders (abruption/antepartum haemorrhage and placenta previa), and history of antenatal fetal loss have been identified to increase spontaneous PTB risk in Severodvinsk.[5] In the city of Monchegorsk (Murmansk County), the prevalence of PTB is higher in unmarried women, for women with prior PTB and smokers.[22] In a recent paper on BMI among the current study population, maternal obesity was associated with both very and moderate spontaneous PTBs; this risk also increased for underweight mothers.[23] To date, studies on GA-dependent multiple risk factors of PTB in Russia have not been done. Clearly, PTB is a multi-causal process that involves the interaction of multiple factors. In addition, insufficient data on risk factors and their interactions can limit preventive interventions. Accordingly, the aims of this study were to estimate the prevalence of PTB in Murmansk County and to identify pertinent maternal predictive factors. The regional Murmansk County Birth Registry (MCBR) provides the opportunity to conduct such research.

Methods

Data source

Murmansk County is located in the northwestern part of Russia (Figure 1). In 2013, it had 780 400 inhabitants.[24] The MCBR was established in 2006 and its implementation has been described in detail.[25] It contains information about all births, including stillbirths from GA of 22 weeks and onwards. The records also include maternal sociodemographic data and health status information before and during pregnancy, and selected interventions pertaining to pregnancy and delivery. Based on five entries (mother's birth date, delivery type and complications, sex and weight of baby), a review of 410 files in 2006 and 547 in 2007 indicated minimal errors (respectively, 1.1 and 0.15% had missing information and 0.89 and 0.84% errors in transfers from hospital files onto the registry forms; with no errors for transfers from the latter to the registry database).[25]

Study sample

The initial study population included all births registered in MCBR from January 1, 2006 to December 31, 2011 (n = 52 806). We excluded multiple births, births with missing information on birthweight (BW) or GA, and births with GA <154 and >315 days totalling 1564 cases (Figure 2). The distribution of BW by GA showed outliers predominantly with high BW at low GAs, suggesting that some infants with high BW had incorrect GA values and were misclassified as preterm. The same observation is described in previous studies.[26,27] We screened all records with GA 22–32 weeks and applied Tukey's methodology[28] and method proposed by Alexander *et al.*[26] to exclude extreme outliers. In addition, we used internationally recommended growth charts for preterm infants[29] to confirm the decisions. Initially, 164 births were defined as outliers. Births with implausible combinations of gestational age estimated by ultrasound or last menstrual period (LMP), and BW were excluded (n = 104). In the remaining 60 cases, the discrepancy between the recorded LMP and the fetal ultrasound

© 2016 John Wiley & Sons Ltd

Figure 1. Murmansk County, Northwestern Russia.

was greater than 4 weeks. Clinical opinion suggested inaccurate GA estimation (underestimation) by ultrasound for these heavier infants. To reduce misclassification of them as infants with lower GAs, we imputed GA values based on LMP only. Because of the co-occurrence of certain items of missing information for some births, the sum of the total exclusions (1668) shown in Figure 2 exceeds the actual number of 1650. In the end, 51 156 births were included in the analyses, of which 3546 were PTBs.

Measurement of outcome

Preterm birth was defined as birth at or after 22 completed gestational weeks (≥154 days) and before 37 weeks (<259 days). GA was calculated as the difference between the date of delivery predicted by first ultrasound in pregnancy and the actual date of a child's birth and adding 280 days to obtain the final value. For 4001 births, data on ultrasound were not available and GA was therefore determined as the period from the first day of the last menstrual period (LMP) until the date of birth. Respectively, moderate-to-late PTB, very PTB, and extremely PTB were defined as preterm births during days 224–258, 196–223, and 154–195 of gestation.

Measurement of exposure

We treated sociodemographic and life style maternal characteristics as categorical variables, which included: maternal age (<18, 18–34, ≥35 years); education (none or primary [class 1–9], secondary [class 10–11], vocational school, higher); cigarette smoking, and alcohol abuse during pregnancy (yes/no). We categorised civil status as single, married, and cohabiting; the first category included divorced and separated women. Maternal BMI at the first antenatal visit was categorised into four groups according to the WHO classification: underweight (BMI < 18.5 kg/m^2), normal weight (BMI = 18.5–24.9 kg/m^2), overweight (BMI = 25–29.9 kg/m^2), and obese (BMI ≥ 30.0 kg/m^2).[30] Medical covariates included parity (primipara, multipara), history of previous PTB, previous spontaneous and induced abortions, diabetes mellitus, or gestational diabetes. Any birth defects were considered as a potential confounder and were included in the analyses as a binary variable.

Data analysis

We used Chi-squared tests to estimate differences in prevalence of selected factors between the three

© 2016 John Wiley & Sons Ltd

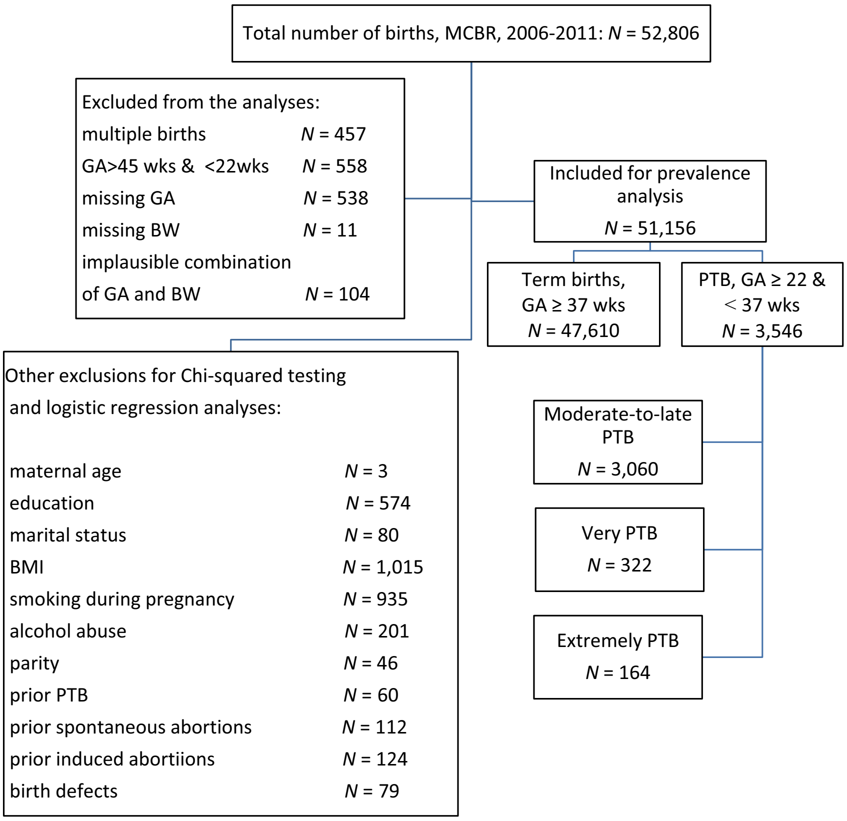

Figure 2. Study flowchart.

defined PTB groups and term births. Multinomial logistic regression models were designed to assess risk for PTB groups, controlling for maternal sociodemographic, life style, and medical covariates (e.g. maternal reproductive history, diabetes mellitus, and fetal birth defects). Odds ratios (ORs) and corresponding 95% confidence intervals were estimated for PTB groups, with term births as reference. All statistical analyses were performed using SPSS 21.0. v.21.0 (Armonk, NY, USA: IBM Corp.).

Ethical considerations

The Ethical Committee of the Northern State Medical University (Arkhangelsk, Russia) and the Regional Committee for Medical and Health Research Ethics in Northern Norway (REK-Nord) approved this study.

Results

The overall prevalence of PTB in Murmansk County was 6.9% (Figure 2), with a distribution of 0.3% (extremely), 0.6% (very), and 6.0% (moderate-to-late) PTB among the three subgroups. We found a downward trend in PTB rate for the 2006–2011 period ($P = 0.007$), which was 7.6, 6.9, 6.9, 7.1, 6.7, and 6.4%, respectively. The prevalence of stillbirth among the PTBs was 3.2% ($n = 115$, of which 37 were in the extremely PTB group). The descriptive statistics for selected maternal sociodemographic, anthropometric, and life style characteristics pertaining to the PTB groups and term births are summarised in Table 1. Compared with term births, all three PTB groups feature higher proportions of unmarried mothers, women with low educational level (none/primary and secondary), smokers, overweight and obese women and those who abused alcohol. Compared to term births, highly educated mothers had a lower prevalence of PTB in the moderate-to-late and very PTB groups. Younger (<18 years) or older (≥35 years) mothers had somewhat higher proportions of PTB at any GA. The proportion of smokers and women identified with alcohol abuse gradually increased from term birth to very PTB groups.

Women who delivered at term reported the lowest percentages of PTBs and spontaneous or induced

© 2016 John Wiley & Sons Ltd

abortions in their medical history (Table 2), whereas the proportion of prior PTB gradually increased from the moderate-to-late group to the extremely PTB group; 11.6% of the women in the latter group had one or more multiple PTBs in their reproductive history. Diabetes mellitus and gestational diabetes were also higher in all PTB groups when compared with term births. We found no differences in the prevalence of chronic genito-urethral infections between term and the PTB groups, and consequently did not include this variable in our final model.

The multinomial logistic regression model results are summarised in Table 3. Compared with women aged 18–34 years, risk of moderate-to-late PTB was respectively 1.4- and 1.3-fold higher among mothers in the <18 years and ≥35 years age groups. Compared to the term birth group, young (<18 years) and older (≥35 years) women exhibited a non-significant increase in very and extremely PTB. Lower education (none or primary) contributed to the risk of moderate-to-late and extremely PTB. Women with secondary education (class 10–11) had higher risk of very and extremely PTB. Single and cohabitation increased the risk in all three PTB groups, but for cohabitants the risk for very PTB was not statistically significant. Alcohol abuse had a robust impact on the moderate-to-late and very PTB groups, and the risk of moderate-to-late PTB was 1.1 times higher in smoking mothers compared to non-smokers. Underweight or overweight and obese women had a higher risk of delivering during weeks 32 to <37 of gestation compared with normal-weight women. Significant associations with prior PTBs, prior spontaneous and induced abortions are indicated in Table 3. These risks increase with decreasing GA. Diabetes mellitus and gestational diabetes respectively increased the risk of moderate-to-late and very PTB 5.5 and 12-fold, while a comparable enhancement in extremely PTBs did not reach significance.

Table 1. Breakdown of PTBs by maternal sociodemographic, anthropometric and life style characteristics for the four MCBR birth groups (2006–2011)

Characteristic	Term birth		Moderate-to-late preterm birth		Very preterm birth		Extremely preterm birth		
	N	%	*N*	%	*N*	%	*N*	%	*P**
Age, years									
<18	734	1.5	77	2.5	8	2.5	6	3.7	<0.001
18–34	42 779	89.9	2634	86.1	269	83.5	134	81.7	
≥35	4094	8.6	349	11.4	45	14.0	24	14.6	
Education									
None or primary (class 1–9)	1542	3.3	163	5.4	14	4.5	15	9.4	<0.001
Secondary (class 10–11)	14 753	31.3	1105	36.7	126	40.3	59	37.1	
Vocational school	14 919	31.7	951	31.6	101	32.2	40	25.2	
Higher	15 885	33.7	792	26.3	72	23.0	45	28.3	
Marital status									
Single	4481	9.4	432	14.1	59	18.5	22	13.4	<0.001
Married	35 135	73.9	1951	63.9	191	59.9	96	58.5	
Cohabitant	7920	16.7	674	22.0	69	21.6	46	28.1	
BMI, kg/m^2									
Underweight (<18.5)	2913	6.2	211	7.2	16	5.3	4	2.6	<0.001
Normal weight (18.5–24.9)	30 824	66.0	1821	61.8	201	66.1	94	62.3	
Overweight and obese (≥25.0)	13 002	27.8	915	31.0	87	28.6	53	35.1	
Smoking during pregnancy									
No	38 310	81.9	2260	75.8	224	71.8	123	76.9	<0.001
Yes	8459	18.1	720	24.2	88	28.2	37	23.1	
Alcohol abuse									
No	47 285	99.7	3003	98.8	313	97.8	162	99.4	<0.001
Yes	147	0.3	37	1.2	7	2.2	1	0.6	

N, number of cases.

*Significant *P*-values indicate that differences in proportion exist between the term and preterm birth groups for the indicated characteristics.

© 2016 John Wiley & Sons Ltd

Table 2. Breakdown of PTBs by maternal reproductive and medical history characteristics, types of birth presentation, and defects for the four MCBR birth groups (2006–2011)

	Term births		Moderate-to-late preterm birth		Very preterm birth		Extremely preterm birth		
Characteristic	*N*	%	*N*	%	*N*	%	*N*	%	*P**
Parity									
Primipara	26 344	55.4	1589	52.0	152	47.2	82	50.0	<0.001
Multipara	21 225	44.6	1466	48.0	170	52.8	82	50.0	
Prior preterm births									
No	46 653	98.1	2892	94.7	292	91.0	145	88.4	<0.001
Yes	905	1.9	161	5.3	29	9.0	19	11.6	
Prior spontaneous abortions (0–22 weeks)									
No	41 956	88.3	2607	85.3	257	79.8	120	73.2	<0.001
Yes	5546	11.7	449	14.7	65	20.2	44	26.8	
Prior induced abortions									
No	27 572	58.1	1638	53.7	151	46.9	68	41.5	<0.001
Yes	19 923	41.9	1413	46.3	171	53.1	96	58.5	
Chronic infections of genitourinary tract									
No	30 551	74.9	1884	73.2	198	75.3	98	71.5	0.2
Yes	10 241	25.1	691	26.8	65	24.7	39	28.5	
Diabetes mellitus or gestational diabetes									
No	47 521	99.8	3028	99.0	314	97.5	163	99.4	<0.001
Yes	89	0.2	32	1.0	8	2.5	1	0.6	
Birth defects									
No	46 273	97.2	2908	95.6	282	91.0	128	94.1	<0.001
Yes	1315	2.8	135	4.4	28	9.0	8	5.9	

N, number of cases.
*Significant *P*-values indicate that differences in proportion exist between the term and preterm birth groups for the indicated characteristics.

Post factum we examined more closely our findings for mothers who first attended outpatient clinics late in pregnancy (GA > 30 weeks). They had a higher proportion of missing GA values (20.1%) compared to those with known GAs (1%; $P < 0.001$). The vital status of singleton infants with known and missing GA were also compared. Infants with missing GA values had a higher proportion of stillbirths (4.3% vs. 0.4%, respectively, $P < 0.001$); totally for 23 stillbirths GA was unknown. Among stillbirths in general, there was a higher proportion of mothers with late visits to outpatient clinics, smokers, unmarried women, mothers with previous preterm births ($P < 0.001$), less educated, overweight women, and women aged ≥35 years ($P < 0.01$).

Comments

Prevalence of PTB

The prevalence of PTB of 6.9% in our study is comparable with data on live PTB from European countries.[4] However, it differs from previously published studies based on the MCBR. In a 2011 preliminary report for 2006 and 2007,[6] the prevalence for overall PTB was estimated at 8.7%. This higher prevalence may be influenced by study design, such as less stringent exclusion criteria for twins and errors in GA estimates. A more recent study based on the MCBR reported a prevalence of 5.5% of spontaneous PTB in Murmansk County.[23] Compared to the present study with 4.8% of spontaneous PTB, the former used LMP-based estimation of GA and did not exclude infants with high BW who were misclassified as preterm.

There were 23 stillborn babies among births with missing GA. If all of them had been preterm, the real PTB rate would be 7.0% instead of the 6.9% estimated. Similarly, the overall proportion of preterm stillbirths would have been 3.9% as opposed to the 3.2% reported in the present study.

The respective distribution between the extremely, very, and moderate-to-late PTB categories in our study was 4.6, 9.1 and 86.3%, and is generally in line with the results of a meta-analysis of data from 41 countries (specifically, 5.2, 10.4, and 84.3%).[2] The

© 2016 John Wiley & Sons Ltd

Table 3. Adjusted OR values and 95% CIs calculated by multinomial logistic regression analysis for the potential risk factors itemised in Table 1

Characteristic	Moderate-to-late birth vs. term birth Adjusted OR (95% CI)[a]	Very preterm birth vs. term birth Adjusted OR (95% CI)[a]	Extremely preterm birth vs. term birth Adjusted OR (95% CI)[a]
Age, years			
<18	1.37 (1.05, 1.79)	1.03 (0.40, 2.64)	1.22 (0.36, 4.23)
18–34	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
≥35 years	1.30 (1.14, 1.48)	1.43 (0.99, 2.08)	1.07 (0.60, 1.91)
Education			
None or primary (class 1–9)	1.51 (1.22, 1.85)	1.65 (0.88, 3.08)	2.92 (1.39, 6.10)
Secondary (class 10–11)	1.33 (1.20, 1.48)	1.41 (1.02, 1.95)	1.03 (0.64, 1.66)
Vocational school	1.19 (1.08, 1.32)	1.27 (0.92, 1.75)	0.82 (0.51, 1.34)
Higher	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Marital status			
Single	1.47 (1.30, 1.66)	2.0 (1.42, 2.81)	1.82 (1.04, 3.19)
Married	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Cohabitant	1.39 (1.26, 1.54)	1.32 (0.97, 1.79)	2.01 (1.31, 3.08)
BMI, kg/m^2			
Underweight (<18.5)	1.26 (1.08, 1.46)	0.94 (0.56, 1.61)	0.30 (0.07, 1.24)
Normal weight (18.5–24.9)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Overweight and obese (≥25.0)	1.14 (1.04, 1.24)	0.86 (0.65, 1.13)	1.07 (0.60, 1.91)
Smoking during pregnancy			
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes	1.13 (1.02, 1.24)	1.25 (0.94, 1.67)	0.93 (0.59, 1.46)
Alcohol abuse			
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes	2.78 (1.82, 4.24)	4.16 (1.74, 9.93)	1.91 (0.25, 14.34)
Parity			
Primipara	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Multipara	1.03 (0.94, 1.12)	1.11 (0.85, 1.46)	0.81 (0.53, 1.23)
Prior preterm birth			
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes	2.49 (2.06, 3.00)	3.48 (2.19, 5.23)	6.65 (3.77, 11.75)
Prior spontaneous abortions (0–22 weeks)			
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes	1.24 (1.11, 1.38)	1.65 (1.21, 2.23)	3.06 (2.05, 4.56)
Prior induced abortions			
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes	1.10 (1.01, 1.19)	1.36 (1.06, 1.76)	1.96 (1.32, 2.91)
Diabetes mellitus or gestational diabetes			
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes	5.52 (3.57, 8.53)	12.16 (5.44, 27.21)	3.72 (0.50, 27.48)
Birth defects			
No	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Yes	1.63 (1.35, 1.97)	3.55 (2.36, 5.33)	2.13 (0.98, 4.60)

OR, odds ratio; CI, confidence interval.
[a]Adjusted for all other variables in the column.

decreasing trend of PTB rates from 2006 to 2011 suggests a change in risk factor impact on PTB rate over time. The introduction of regionalised perinatal care in 2008, which aimed to improve both antenatal and postnatal care, could partly explain the observed trend. Our study is based on a large sample of births, provides new, recent information about PTB risk in Russia, and adds to the very sparse literature on risk factors for PTB in Russia or the former Soviet Union.

© 2016 John Wiley & Sons Ltd

Risk factors of PTB

Our findings demonstrate that maternal factors which enhance the PTB risk were similar for all three groups, and this is consistent with other studies.[5,14] More specifically, we observed a strong association between unmarried status and increased risk of PTB at any GA as others have.[22,31] Social disadvantage, higher rates of unemployment and smoking, as well as lack of social support and financial resources, constitute likely reasons.[31] Our observation that the prevalence of being single or cohabiting was the lowest for term births coincides with a Finnish study[31]. Similarly, our findings regarding the effect of maternal smoking agree with earlier studies.[14,21,22] Smoking as a risk is not surprising since, in addition to nicotine and carbon monoxide, cigarette smoke contains many potentially organic toxic substances (e.g. tars and other organic compounds) in addition to toxic metals, hydrogen cyanide, and nitrogen oxides.[32] Causal relationships between tobacco smoke and PTBs are complex and remain unclear. Impacts could include restricted placental blood flow due to nicotine-induced vasoconstriction; increased risk of membrane rupture; altered cell signalling; prostaglandin synthesis disorder; carbon monoxide-induced fetal hypoxia, among others.[33] Furthermore, tobacco smoking may have a preterm prelabour effect on fetal membranes.[21] We found an increased risk of moderate-to-late PTB in smokers. By contrast, previously published data show a significant association between smoking and PTB at 27–33 weeks.[21]

We observed only a small increase in the risk of moderate-to-late PTB in overweight or obese women. The role of obesity in PTB is controversial because of disparities between studies. For instance, Hendler *et al.*[34] report that the cervix is longer in obese women. Since a short cervical length is one of the strongest predictors of spontaneous PTB, a longer cervix might partly explain the lower risk of spontaneous PTB in obese women. However, white adipose tissue is known to play a role in inflammation and immunity by producing and releasing pro- and anti-inflammatory factors.[35] Obesity contributes to a higher risk of urinary and genital tract infections,[36] as well as to postpartum urinary tract infections.[37] An association between overweight and obesity and acute chorioamnionitis in PTB has been established.[36] Compared to women with normal weight, obese mothers have a twofold higher rate of this infection, which may lead to PTB at 24–30 weeks of gestation.[38] We found no evidence of increased risk of very and extremely PTB in underweight women, and only a small increase in the risk of moderate-to-late PTB. Nevertheless, many studies demonstrate an association between low maternal weight and spontaneous PTB.[23,39]

The near six and twelve-fold increases in the risk of moderate-to-late and very PTB for women with diabetes mellitus or gestational diabetes, respectively, compared to those without was not unexpected. For example, Lepercq *et al.*[40] demonstrate a prevalence of 9% among women with Type I diabetes mellitus. Furthermore, and relative to women with normal BMI, gestational diabetes is more common in obese pregnant women,[36] which our findings support.

Our finding of increasing OR of PTB with decreasing GA in women with prior PTBs is consistent with the conclusion of Mercer *et al.*[17] They report that spontaneous PTBs are associated with subsequent PTB at <28 weeks gestation. Interestingly, McManemy *et al.*[18] indicate that the recurrence risk of PTBs is affected by the frequency, order, and severity of prior occurrences. Prior induced and spontaneous abortions also increase this risk.[41] Several predisposing factors have been suggested for this, including persistent or recurrent intrauterine infections,[42] abnormal placentation,[17] and short cervix.[39]

The risk of moderate-to-late PTB in our cohort was 1.6-fold higher among infants with birth defects compared to those without; for very PTB it was near 4-times higher. There is indeed evidence for a link between birth defects and PTB.[43,44] Rasmussen *et al.*[43] found that, compared to infants without birth defects, the risk of PTB in infants with birth defects was two-fold higher; it was the highest for those born at 29–32 weeks of gestation. Causal pathways for this occurrence are not well understood, although it has been speculated that there are some common sociodemographic factors involved.[43] Among 51 156 births eligible for this study birth defects were recorded as an indication for surgery and/or induction of labour in 23 specific cases. As we studied both induced and spontaneous PTB, we did not exclude them from the study.

Strengths and limitations

The relatively large population size of our study provided the possibility of investigating multiple risk factors involved in PTB. It allowed adjustment for a large

© 2016 John Wiley & Sons Ltd

number of risk factors that included not only maternal sociodemographic, life style and medical characteristics, but also fetal birth defects. Additionally, the registry-based design minimises the risk of selection bias. The MCBR covers 98.9% of all births in Murmansk County[25] during the study period, and thereby enhances the external validity and generalisability of our results.

We treated spontaneous and induced PTB as one group. By contrast, other studies suggest that risk factors for spontaneous PTB may differ from those of induced PTB.[20,21] Since the data on labour induction in MCBR were limited, we included both.

Estimating GA on the basis of the combination of early ultrasound biometry and LMP helped us minimise missing and implausible GA values. A comparison of the medians of GA detected by both methods yielded comparable results with 279 and 278 days in the LMP-based and ultrasound-based approaches, respectively. Those with missing GA information likely had higher risk of PTB as the proportion of some risk factors in this group was higher. Perhaps for some of these cases, the birth involved some type of emergency. In such situations, entry of detailed medical history might be omitted or forgotten. Consequently, no data on ultrasound examination and LMP were available and thereby circumvented the estimation of GA. In general, the prevalence of PTB is slightly underestimated in our study population, although the degree of underestimation is likely to be small.

Unfortunately, maternal prepregnancy BMI was not recorded in the MCBR. However, since maternal BMI does not change much during the first 14 weeks of gestation,[45] an early pregnancy assessment was employed. Under-reporting of alcohol abuse may have occurred, since the MCBR recorded information was based on reports by health care professionals on 'evidence of alcohol abuse.' Another limitation is that smoking may have been under estimated as it involved self-reporting.

Conclusions

The overall prevalence of PTB in Murmansk County was 6.9%, while those of extremely, very, and moderate-to-late PTB were 0.3, 0.6, and 6.0% respectively. Maternal low educational level, unmarried status, alcohol abuse, diabetes mellitus/gestational diabetes, as well as adverse prior pregnancy outcomes, were common risk factors for two or all three PTB groups. Young (<18), older (≥35) and women who smoked, were underweight or overweight/obese, all were at higher risk of moderate-to-late PTB. Preventive strategies to reduce PTB should focus on smoking and alcohol cessation and improved management of maternal obesity (as well as insufficient weight), diabetes mellitus, and gestational diabetes.

Acknowledgements

The authors thank the MCBR staff for providing data for this study.

References

1 WHO: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. *Acta Obstetricia et Gynecologica Scandinavica*. 1977; 56:247–253.
2 Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, *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* 2012; 379:2162–2172.
3 Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, *et al*. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bulletin of the World Health Organization* 2010; 88:31–38.
4 Euro-Peristat project with SCPE and Eurocat. European Perinatal health report. The health of pregnant women and babies in Europe in 2010. 2013. http://www.europeristat.com/ [last accessed 25 June 2015].
5 Grjibovski AM, Bygren LO, Yngve A, Sjostrom M. Large social disparities in spontaneous preterm birth rates in transitional Russia. *Public Health* 2005; 119:77–86.
6 Anda EE, Nieboer E, Wilsgaard T, Kovalenko AA, Odland JO. Perinatal mortality in relation to birthweight and gestational age: a registry-based comparison of Northern Norway and Murmansk County, Russia. *Paediatric and Perinatal Epidemiology* 2011; 25:218–227.
7 Kozlovskaya A, Bojko E, Odland JO, Grjibovski AM. Secular trends in pregnancy outcomes in 1980–1999 in the Komi Republic, Russia. *International Journal of Circumpolar Health* 2007; 66:437–448.
8 Ancel PY, Goffinet F, Kuhn P, Langer B, Matis J, Hernandorena X, *et al*. Survival and morbidity of preterm children born at 22 through 34 weeks' gestation in France in 2011: results of the EPIPAGE-2 cohort study. *JAMA Pediatrics* 2015; 169:230–238.
9 Locksmith G, Duff P. Infection, antibiotics, and preterm delivery. *Seminars in Perinatology* 2001; 25:295–309.
10 Mazor-Dray E, Levy A, Schlaeffer F, Sheiner E. Maternal urinary tract infection: is it independently associated with adverse pregnancy outcome? *The Journal of Maternal-Fetal & Neonatal Medicine* 2009; 22:124–128.

© 2016 John Wiley & Sons Ltd

11 Fraser AM, Brockert JE, Ward RH. Association of young maternal age with adverse reproductive outcomes. *New England Journal of Medicine* 1995; 332:1113–1117.

12 Nelson K, Lohsoonthorn V, Williams MA. Preterm delivery risk in relation to maternal occupational and leisure time physical activity among Thai women. *Asian Biomedicine: Research, Reviews and News* 2009; 3:267–277.

13 Albertsen K, Andersen A-MN, Olsen J, Grønbæk M. Alcohol consumption during pregnancy and the risk of preterm delivery. *American Journal of Epidemiology* 2004;159:155–161.

14 Grillo E, Freitas PF. Smoking and other pre-gestational risk factors for spontaneous preterm birth. *Revista Brasileira de Saúde Materno Infantil* 2011; 11:397–403.

15 Han Z, Mulla S, Beyene J, Liao G, McDonald SD. Maternal underweight and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. *International Journal of Epidemiology* 2011; 40:65–101.

16 Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikstrom AK, *et al*. Maternal obesity and risk of preterm delivery. *Journal of the American Medical Association* 2013; 309:2362–2370.

17 Mercer BM, Goldenberg RL, Moawad AH, Meis PJ, Iams JD, Das AF, *et al.* The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. *American Journal of Obstetrics and Gynecology* 1999; 181:1216–1221.

18 McManemy J, Cooke E, Amon E, Leet T. Recurrence risk for preterm delivery. *American Journal of Obstetrics and Gynecology* 2007;196:576. e571-576; discussion 576. e576-577.

19 Raisanen S, Gissler M, Saari J, Kramer M, Heinonen S. Contribution of risk factors to extremely, very and moderately preterm births – register-based analysis of 1,390,742 singleton births. *PLoS ONE* 2013; 8:e60660.

20 Auger N, Le TU, Park AL, Luo ZC. Association between maternal comorbidity and preterm birth by severity and clinical subtype: retrospective cohort study. *BMC Pregnancy and Childbirth* 2011; 11:67.

21 Henderson JJ, McWilliam OA, Newnham JP, Pennell CE. Preterm birth aetiology 2004-2008. Maternal factors associated with three phenotypes: spontaneous preterm labour, preterm pre-labour rupture of membranes and medically indicated preterm birth. *The Journal of Maternal-Fetal and Neonatal Medicine* 2012; 25:642–647.

22 Kozlovskaya A, Odland JØ, Grjibovski AM. Maternal occupation and marital status are associated with birth weight and risk of preterm birth in Monchegorsk (Murmansk Region) during a 30-year period. *Human Ecology* 2014; 8:3–12. (in Russian).

23 Sharashova EE, Anda EE, Grjibovski AM. Early pregnancy body mass index and spontaneous preterm birth in Northwest Russia: a registry-based study. *BMC Pregnancy Childbirth* 2014; 14:303.

24 Baranov E, Bugakova N, Gelvanovsky M, Gokhberg L, Dianov M, Elizarov V, *et al. The Demographic Yearbook of Russia, 2013: Statistical Handbook*. Moscow: Rosstat, 2014.

25 Anda EE, Nieboer E, Voitov AV, Kovalenko AA, Lapina YM, Voitova EA, *et al.* Implementation, quality control and selected pregnancy outcomes of the Murmansk County Birth Registry in Russia. *International Journal of Circumpolar Health* 2008; 67:318–334.

26 Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. *Obstetrics and Gynecology* 1996; 87:163–168.

27 Platt RW, Abrahamowicz M, Kramer MS, Joseph KS, Mery L, Blondel B, *et al.* Detecting and eliminating erroneous gestational ages: a normal mixture model. *Statistics in Medicine* 2001; 20:3491–3503.

28 Tukey J. *Exploratory Data Analysis*. Menlo Park, Cal., London, Amsterdam, Don Mills, Ontario, Sydney: Addison-Wesley, 1977.

29 Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. *BMC Pediatrics* 2013; 13:59.

30 BMI Classification. Global Database on Body Mass Index. World Health Organization. 2006. Retrieved July 27, 2012.

31 Raatikainen K, Heiskanen N, Heinonen S. Marriage still protects pregnancy. *BJOG* 2005; 112:1411–1416.

32 Counts ME, Morton MJ, Laffoon SW, Cox RH, Lipowicz PJ. Smoke composition and predicting relationships for international commercial cigarettes smoked with three machine-smoking conditions. *Regulatory Toxicology and Pharmacology* 2005; 41:185–227.

33 Ion R, Bernal AL. Smoking and preterm birth. *Reproductive Sciences* 2015; 22:918–926.

34 Hendler I, Goldenberg RL, Mercer BM, Iams JD, Meis PJ, Moawad AH, *et al.* The Preterm Prediction study: association between maternal body mass index and spontaneous and indicated preterm birth. *American Journal of Obstetrics and Gynecology* 2005; 192:882–886.

35 Fantuzzi G. Adipose tissue, adipokines, and inflammation. *Journal of Allergy and Clinical Immunology* 2005; 115:911–919; quiz 920.

36 Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, *et al.* Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. *International Journal of Obesity and Related Metabolic Disorders* 2001; 25:1175–1182.

37 Usha Kiran TS, Hemmadi S, Bethel J, Evans J. Outcome of pregnancy in a woman with an increased body mass index. *BJOG* 2005; 112:768–772.

38 Naeye RL. Maternal body weight and pregnancy outcome. *The American Journal of Clinical Nutrition* 1990; 52:273–279.

39 Goldenberg RL, Iams JD, Mercer BM, Meis PJ, Moawad AH, Copper RL, *et al.* The preterm prediction study: the value of new vs standard risk factors in predicting early and all spontaneous preterm births. *American Journal of Public Health* 1998; 88:233–238.

40 Lepercq J, Coste J, Theau A, Dubois-Laforgue D, Timsit J. Factors associated with preterm delivery in women with type 1 diabetes: a cohort study. *Diabetes Care* 2004; 27:2824–2828.

41 Swingle HM, Colaizy TT, Zimmerman MB, Morriss FH Jr. Abortion and the risk of subsequent preterm birth: a systematic review with meta-analyses. *Journal of Reproductive Medicine* 2009; 54:95–108.

© 2016 John Wiley & Sons Ltd

42 Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *New England Journal of Medicine* 2000; 342:1500–1507.

43 Rasmussen SA, Moore CA, Paulozzi LJ, Rhodenhiser EP. Risk for birth defects among premature infants: a population-based study. *Journal of Pediatrics* 2001; 138:668–673.

44 Honein MA, Kirby RS, Meyer RE, Xing J, Skerrette NI, Yuskiv N, *et al.* The association between major birth defects and preterm birth. *Maternal and Child Health Journal* 2009; 13:164–175.

45 Fattah C, Farah N, Barry SC, O'Connor N, Stuart B, Turner MJ. Maternal weight and body composition in the first trimester of pregnancy. *Acta Obstetricia et Gynecologica Scandinavica* 2010; 89:952–955.

© 2016 John Wiley & Sons Ltd