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Maternal correlates of spontaneous preterm birth in Kazakhstan: a matched case-control study

Zhibek Oralkhan[1], Lazzat Sarsenova[1], Maira Kopbayeva[5], Kuanysh Tastambek[1], Andrej M. Grjibovski[1, 3–5], Akzhenis Berdalinova[1, 2], Aru Balmagambetova[2], Gulmira Zhurabekova[1, 2]

[1] Al-Farabi Kazakh National University, Almaty, Kazakhstan;
[2] West Kazakhstan Marat Ospanov State Medical University, Aktobe, Kazakhstan;
[3] Northern State Medical University, Arkhangelsk, Russia;
[4] Northern (Arctic) Federal University, Arkhangelsk, Russia;
[5] Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan

ABSTRACT

BACKGROUND: Preterm birth (PTB) continues to be a persistent health issue that significantly impacts neonatal morbidity and mortality worldwide. In Kazakhstan, the prevalence of PTB is 7% making a substantial contribution to adverse health outcomes among infants. However, there is a lack of comprehensive research on the factors contributing to PTB in Kazakhstan.

AIM: To study maternal factors associated with spontaneous PTB among Kazakh women.

MATERIAL AND METHODS: A case control study was conducted in three major reproductive hospitals in Atyrau, Aktobe and Kyzylorda from October 2022 to January 2023. The sample consisted of 90 cases with singleton live spontaneous PTB and 180 controls with spontaneous full-term delivery. Bivariate associations between categorical variables were assessed by chi-squared tests. Independent variables with p <0.1 in the bivariate analysis were entered into a conditional logistic regression model. Odds ratios (OR) with 95% confidence intervals (CI) were calculated.

RESULTS: Maternal education, periodontitis, body mass index and a history of PTB in previous pregnancies were associated with PTB in bivariate analysis. In multivariable models, only prior PTB (OR=38.10; 95% CI: 8.34–142.00) and periodontal disease (OR=2.09; 95% CI: 1.15–3.80) were associated with an increased risk of extremely and very preterm births while higher education (OR=0.44; 95% CI: 0.19–0.98) and a history of PTB (OR=27.20; 95% CI: 5.38–137.00) were associated with moderate to late PTB.

CONCLUSION: Our results are in line with the international evidence on prior PTB being the most important determinant of PTB in the index pregnancy. Moreover, our findings on the associations with periodontal disease underline the importance of a targeted, individualized and interdisciplinary antenatal care to the reduction in the prevalence of PTB.

Keywords: preterm birth; risk factors; pregnancy; periodontal disease; Kazakhstan.

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Факторы риска спонтанных преждевременных родов в Казахстане: исследование случай-контроль методом подобранных пар

Ж. Оралхан[1], Л. Сарсенова[1], М. Копбаева[5], К. Тастамбек[1], А.М. Гржибовский[1, 3, 4, 5], А. Бердалинова[1, 2], А. Балмагамбетова[2], Г. Журабекова[1, 2]

[1] Казахский национальный университет имени аль-Фараби, Алматы, Казахстан;
[2] Западно-Казахстанский государственный медицинский университет имени Марата Оспанова, Актобе, Казахстан;
[3] Северный государственный медицинский университет, Архангельск, Россия;
[4] Северный (Арктический) федеральный университет, Архангельск, Россия;
[5] Казахский национальный медицинский университет имени Асфендиярова, Алматы, Казахстан

АННОТАЦИЯ

Обоснование. Преждевременные роды (ПР) остаются актуальной проблемой здравоохранения, оказывающей значительное влияние на неонатальную заболеваемость и смертность во всем мире. В Казахстане распространённость ПР составляет 7%, что вносит существенный вклад в неблагоприятные исходы в младенческом периоде. Тем не менее в Казахстане отсутствуют комплексные исследования факторов риска ПР .

Цель. Изучить факторы риска спонтанных ПР у казахских женщин.

Материал и методы. Исследование методом случай-контроль проводили в трёх крупных учреждениях родовспоможения в городов Атырау, Актобе и Кызылорда с октября 2022 по январь 2023 г. Выборка состояла из 90 женщин со спонтанными ПР и 180 — со срочными родами. В исследование включали только одноплодные беременности. Бивариантные связи между категориальными переменными оценивали с помощью критерия хи-квадрат Пирсона. Независимые переменные, связанные с исходом на уровне значимости менее 0,1 в бивариантном анализе были введены в условную логистическую регрессионную модель. Силу связи определяли с помощью отношения шансов (ОШ) с 95% доверительными интервалами (ДИ).

Результаты. Образование матери, пародонтит, индекс массы тела и наличие ПР в анамнезе были значимо связаны с ПР при проведении бивариантного анализа. В многомерных моделях только ПР в анамнезе (ОШ=38,10; 95% ДИ: 8,34–142,00) и заболевания пародонта (ОШ=2,09; 95% ДИ: 1,15–3,80) были связаны с повышенным риском ПР в срок до 32 недель. Более высокий уровень образования (ОШ=0,44; 95% ДИ: 0,19–0,98) и наличие ПР в анамнезе (ОР=27,20; 95% ДИ: 5,38–137,00) были связаны с ПР в срок от 32 до 36 недель.

Заключение. Результаты исследования не противоречат международным данным о том, что ПР в анамнезе являются наиболее сильным прогностическим фактором для ПР. Кроме того, полученные данные о сильной связи с заболеваниями пародонта подчёркивают важность целенаправленной, индивидуализированной и междисциплинарной дородовой помощи для снижения распространенности ПР.

Ключевые слова: преждевременные роды; факторы риска; беременность; заболевания пародонта; Казахстан.

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INTRODUCTION

Preterm birth (PTB) is a complex syndrome with significant long-term health implications. It refers to the delivery of a live baby before 37 completed weeks of gestation [1]. Clinically, approximately half of all PTB are idiopathic, characterized by spontaneous onset of labor. The other half can be attributed to preterm premature rupture of membranes (PPROM) or medically indicated reasons [2]. Globally, more than one in ten babies is born preterm, and these PTB account for about 75% of perinatal deaths [3]. PTB affects both developed and developing countries regardless of social vulnerability [3, 4].

PTB presents numerous challenges for both maternal and fetal outcomes. Preterm babies are more susceptible to a range of health problems, including mental retardation, vision impairment, and cerebral palsy, when compared to full-term babies [5]. Furthermore, prematurity has been linked to the development of cardiovascular disease, diabetes, and cancer in adulthood [6]. Additionally, a history of PTB increases the risk of subsequent preterm deliveries for mothers [7].

As other pregnancy outcomes, the probability of PTB is influenced by both the external environment and maternal factors. Interestingly, the risk factors for PTB vary among different countries and even within neighborhoods of the same country [8, 9]. Some commonly reported maternal risk factors for PTB include socio-economic characteristics, a history of PTB [7, 10], smoking during pregnancy [11], a short cervical length [12], periodontal diseases [13], multiple pregnancies [14], maternal overweight, chronic somatic diseases, and pregnancy complications [15–17]. Furthermore, genetic factors have been identified that predispose individuals to preterm labor [18]. Inadequate prenatal care services may also contribute to the disparities in PTB rates [19].

In Kazakhstan, pregnant women are entitled to receive free antenatal care through the public health system, regardless of their socioeconomic status or geographic location. This service model has successfully achieved a remarkable 99.2% coverage of antenatal care [20]. Gaining a comprehensive understanding of the factors influencing the current population is essential for implementing effective preventive strategies, particularly in the case of PTB. The prevalence of PTB in Kazakhstan is around 7% with an increasing trend over the recent decades. Given that PTB are responsible for a substantial proportion of infant deaths, identification of their determinants or associated factors may have an important contribution to reduction of infant mortality.

The aim of this study was to identify predictors of spontaneous PTB among Kazakh women.

MATERIAL AND METHODS

This hospital-based case-control study was conducted on a sample of 270 Kazakh women, including 90 cases of singleton live spontaneous PTB and 180 controls. Minimal required sample size was calculated at the planning phase of the study. The abovementioned sample size ensures a statistical power of 87% for the level of alpha error of 5% for two-tailed tests for the odds ratios of 2.0 or above. All data were collected in the Atyrau and Aktobe regions in Western Kazakhstan, and in Kyzylorda region in Southern Kazakhstan. Data collection took place from October 2022 to January 2023 in reproductive and perinatal centers. During this period, 90 women who delivered before 37 gestational weeks were considered for this study. Exclusion criteria were twin- or triplet pregnancies, pre-eclampsia, pregnancy-induced hypertension, gestational diabetes, induced labor, and Caesarean section, were excluded from the study. Women with term babies weighing over 2500 g without any pregnancy complications comprised a control group. Controls were selected in a 2:1 ratio and matched to cases according to infant sex and delivery date. More than 99% of pregnant women in Kazakhstan receive their maternal care from these local health centers, therefore the risk of selection bias was considered as low [18]. All of the health care centers provided free maternal and child care for their target groups under the same conditions.

Potential participants were provided with an information sheet that explained the aims and procedures of the study, their responsibilities, possible risks and side effects, potential benefits, alternatives to participation, the confidentiality of data, and the voluntary nature of participation. Those who were willing to participate provided signed consent to take part in the study. They were then given a questionnaire, which took approximately 5 minutes to complete. The questionnaire was pre-tested for clarity prior to the study initiation. A trained researcher who was fluent in both Kazakh and Russian conducted a pilot survey among 30 pregnant visitors at the Aktobe reproductive and perinatal center.

A structured self-administered questionnaire with cross-verify the responses from medical report was used to explore the risk factors related to spontaneous PTB, including the mother's age, educational level, marital status, employment, income, current smoking status, exposure to secondhand smoke, alcohol intake habits, number of pregnancies, pre-gestational weight and height, complications during pregnancy, previous obstetric history, gestational week at labor, and type of delivery. Data on maternal weight, placental weight, weight and length of the baby as well as infant sex were obtained from the medical documentation. A normal pre-pregnancy weight was defined as having a BMI of 18.0–24.99 kg/m^2. Pre-pregnancy overweight was defined as having a BMI between 25.0 and 29.99 kg/m^2, while pre-pregnancy obesity was defined as having a BMI ⩾30.0 kg/m^2 [22].

The periodontal health condition was assessed shortly after filling out the questionnaire by a dentist who measured bleeding on probing, probing depth, and clinical attachment loss. This assessment was conducted at six different sites using a periodontal probe and dental mirror. Periodontitis was diagnosed in cases of the presence of pocket depth

⩾4 mm on one or more sites of more than four teeth, as well as the presence of clinical attachment loss of 3 mm or above [21]. Births that occurred prior to the 28th week of gestation were classified as extremely preterm births (EPTB) while births between the 28th and the 32nd weeks were termed as very preterm births (VPTB). The final groups of PTB after the completed 32nd week were classified as moderate to late preterm births (MLPTB).

Independent associations between PTB and potential predictors were studied using a multivariable conditional logistic regression model. Crude and adjusted odds ratios (OR) were calculated with 95% confidence intervals (CI). Multivariable analysis was performed only on variables associated with the outcome in crude analysis at the level of significance below 0.1. The analyses were repeated separately for MLPTB and EPTB+VPTB. All analyses were performed using Stata software, version 18.0 (Stata Corp., TX).

The study was approved by the al-Farabi Kazakh National University Ethical Committee (Protocol IRB-A308). Written consent was obtained from all the participants. Permissions for the use of medical records were obtained from the concerned hospital authorities. Surveys were administered by the medical personnel. The authors analyzed the dataset with no personal information, and they did not have access to personal data.

RESULTS

Among the 90 singleton PTB included in the study, 17 were extremely preterm, 37 were very preterm and 36 were moderate to late preterm. The mean age of the pregnant women was 28.7 (SD=6.1) years with no difference between cases and controls (p=0,921). The mean BMI of the participants was 24.0 (SD=4.2) kg/m^2. No differences between cases and controls were observed when age (p=0.921) and pre-gestational BMI (p=0.094) were treated as continuous variables. Only 7% of the women had duration of education below 12 years. At the same time, 36% of women were out of work. All the women were ethnic Kazakhs. None reported smoking and consuming alcohol. However, 20% of the participating women were reported being exposed to smoking because of having a smoking family member. Statistically significant differences between cases and controls were observed by mothers' education, BMI, periodontal diseases, and history of PTB in previous pregnancies in the bivariate analysis (Table 1).

In multivariable analysis, women with a history of previous PTB were more likely to have PTB compared to women with no PTB. Moreover, women who had periodontitis during pregnancy had twice as high odds of PTB compared to women with who did not). Restriction of the analysis to EPTB and VPTB yielded similar findings. At the same time, MLPTB were associated with a history of PTB and maternal education while associations with periodontitis reduced to non-significant level (Table 2).

Table 1. Distribution of socio-demographic, anthropometric characteristics, periodontitis, and a history of preterm birth across cases and controls in four cities in Kazakhstan

Variables	Controls (n=180)	Cases (n=90)	p
Age, years			
<25	50 (27.8)	31 (34.4)	0.566
25–29	58 (32.2)	25 (27.8)	
30–34	38 (21.1)	15 (16.7)	
35+	34 (18.9)	19 (21.1)	
Education			
Secondary	70 (38.9)	48 (53.3)	0.024
Higher	110 (61.1)	42 (46.7)	
Employment			
Out of work	63 (35.0)	36 (40.0)	0.422
Employed	117 (65.0)	54 (60.0)	
Income			
⩽2 minimum wages	30 (16.7)	20 (22.2)	0.533
2–5 minimum wages	101 (56.1)	48 (53.3)	
⩾6 minimum wages	49 (27.2)	22 (24.4)	
Gravidity			
1	45 (25.0)	24 (26.7)	0.251
2–4	101 (56.1)	42 (46.7)	
⩾5	34 (18.9)	24 (26.7)	
Pre-pregnancy weight			
Obese/overweight	53 (29.4)	38 (42.2)	0.040
Normal weight	127 (70.6)	52 (57.8)	
Periodontitis			
Yes	45 (25.0)	39 (43.3)	0.002
No	135 (75.0)	51 (56.7)	
History of preterm birth			
Yes	2 (1.1)	26 (28.9)	<0.001
No	178 (98.9)	64 (71.1)	

DISCUSSION

Our study is among the first multicenter studies in Kazakhstan exploring factors associated spontaneous PTB in Kazakhstan. Our findings are in line with the international evidence regarding a history of PTB being the most important predictor of PTB in the index pregnancy. Moreover, our findings corroborate the evidence on the associations between periodontitis and PTB. Interestingly, education was a predictor of MLPTB, but not VPTB and EPTB.

Table 2. Associations between preterm birth and socio-demographic, anthropometric characteristics, periodontitis, and a history of preterm birth in four cities in Kazakhstan

Parameters	All preterm births			Very- and extremely preterm births			Moderate to late preterm births		
Variables	Adjusted OR	95% CI	*p*	Adjusted OR	95% CI	*p*	Adjusted OR	95% CI	*p*
Education									
Secondary	1.00	Reference	0.201	1.00	Reference	0.697	1.00	Reference	0.047
Higher	0.69	0.39–1.22		0.87	–		0.44	0.19–0.98	
Pre-pregnancy weight									
Obese / overweight	1.56	0.86–2.82	0.123	1.32	0.63–2.73	0.462	1.90	0.84–4.29	0.122
Normal weight	1.00	Reference		1.00	Reference		1.00	Reference	
Periodontitis									
Yes	2.09	1.15–3.80	0.016	2.08	1.01–4.29	0.048	1.89	0.83–4.31	0.131
No	1.00	Reference		1.00	Reference		1.00	Reference	
History of preterm birth									
Yes	32.5	7.43–142	<0.001	38.1	8.34–174	<0.001	27.2	5.38–137	<0.001
No	1.00	Reference		1.00	Reference		1.00	Reference	

Prediction of PTB remains a challenge for practicing obstetricians due to its multifactorial etiology. PTB may result from a constellation of environmental, psychological, social, and genetic risk factors [2, 11]. The conflicting results of the different studies point to the complexity of the association between possible risk factors and spontaneous PTB [8, 11, 14, 15]. Ethnicity and behavioral habits such as smoking and alcohol consumption are part of highlighted factors in other studies [11, 23, 24]. However, only ethnic Kazakh women took part in this study and none of them reported smoking or drinking alcohol. The mean age of the participants in our study was similar to what has been reported from other countries [11, 23].

In literature, the most studied socio-economic factors include age, education, household income and employment status of the mother [8–11]. However, the results remain controversial. The contribution of inequalities in maternal educational level to the outcome of PTB found in our study is generally in line with other studies, which highlighted educational level is more clearly related to inequalities in PTB than occupation and household income [25]. Moreover, it appeared that education was more important predictor of MLPTB than for VPTB and EPTB. Contrary to the results of large Canadian and Danish studies who reported an advanced or younger maternal age is one of the risk contributors, we failed to observe associations between PTV and maternal age [26, 27].

Unlike other studies [14, 28], the number of pregnancies prior to the index pregnancy was not associated with PTB that might be a result of a small sample size that cannot detect small effects.

Greater odds for PTB were observed among women who were overweight or obese before pregnancy and women with periodontitis which is in line with results of the studies conducted in other countries [13, 15, 16]. Physiological changes during pregnancy may influence the onset and development of gingivitis and can also worsen the clinical course of already existing periodontitis [29–31]. Periodontal diseases affecting oral health during pregnancy are highly prevalent, and have consequences not only for physical well-being, but also impair quality of life [32, 33]. Our results highlight the importance of the effect of BMI and periodontal diseases on spontaneous PTB and may assist in risk assessment and counseling during even before pregnancy.

Our findings of association between prior and subsequent PTB is consistent with most of the similar studies which support that history of preterm first birth was a major risk factor for subsequent PTB [7, 34–39]. In a prior study with risk estimates reported more than one in six women with preterm history had a preterm second birth [7]. Genetics, susceptible to inflammation and placental disorders including placental insufficiency may be pronounced for the common pathways of the recurrence of the adverse pregnancy outcome [7, 40]. Our study, consistent with the similar studies confirms the importance of a targeted, individualized, and interdisciplinary antenatal care while the nature of the PTB is multifactorial [7, 21].

The current study was one of the few epidemiological studies on pregnant women in Kazakhstan and provides a snapshot of factors associated with PTB among Kazakh women [41]. The sample size was sufficient to detect the odds of 2.0 or greater limiting the possibility to study the factors that have not so strong effects on the outcome. Moreover, the use of three settings for data collection and participation of only ethnic Kazakh women limits the generalizability

of the findings to the national level. However, it covers a representative sample in Atyrau, Aktobe and Kyzylorda which are the areas predominantly populated by ethnic Kazakhs. Additionally, the regional reproductive and prenatal hospitals in our study cover more than 90% of PTB in the regions reducing the probability of selection bias. Nevertheless, this study demonstrates that studies in the field of perinatal epidemiology are feasible in Kazakhstan outside large cities and that the main findings are in line with the international evidence. Large cohort studies or nation-wide studies using medical information systems are required for better understanding of the factors involved in the etiology of PTB in Kazakhstan.

CONCLUSIONS

The findings suggest that a history of PTB and periodontal disease are important predictors of spontaneous PTB, particularly EPTB and VPTB. Maternal education was found significant predictor for MLPTB only. More research is warranted with the further going aim to provide targeted, individualized and interdisciplinary approach to prevent PTB.

ADDITIONAL INFORMATION

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AUTHORS' INFO

***Gulmira Zhurabekova,** MD, PhD; Associated Professor;
address: 71 al-Farabi Ave., Almaty, Republic of Kazakhstan, 050040
ORCID: 0000-0002-2166-3095;
e-mail: zhurabekova.gulmira@kaznu.kz

Zhibek Oralkhan, MD;
ORCID: 0000-0002-8884-6523;
e-mail: september_becca@hotmail.com

Lazzat Sarsenova, PhD;
ORCID: 0000-0001-8643-0703;
email: lazzat.sarsenova@kaznu.kz

Maira Kopbayeva, MD, PhD; Professor;
ORCID: 0000-0002-7439-5573;
e-mail: m_kopbay@mail.ru

Kuanysh Tastambek, PhD;
ORCID: 0000-0002-2338-8816;
e-mail: tastambeku@gmail.com

Andrej M. Grjibovski, MD, MPhil, PhD;
ORCID: 0000-0002-5464-0498;
eLibrary SPIN: 5118-0081;
e-mail: a.grjibovski@yandex.ru

Akzhenis Berdalinova;
ORCID: 0000-0002-5735-9538;
e-mail: berdalinova77@mail.ru

Aru Balmagambetova, MD, PhD;
ORCID: 0000-0003-1151-5651;
e-mail: aru.b.84@mail.ru

*Corresponding author / Автор для корреспонденции

ОБ АВТОРАХ

***Журабекова Гульмира,** PhD; доцент;
адрес: Проспект Аль-Фараби, 71, Алматы, Республика Казахстан, 050040;
ORCID: 0000-0002-2166-3095;
e-mail: zhurabekova.gulmira@kaznu.kz

Оралхан Жибек;
ORCID: 0000-0002-8884-6523;
e-mail: september_becca@hotmail.com

Сарсенова Лаззат, PhD;
ORCID: 0000-0001-8643-0703;
e-mail: lazzat.sarsenova@kaznu.kz

Копбаева Маира, PhD, профессор;
ORCID: 0000-0002-7439-5573;
e-mail: m_kopbay@mail.ru

Тастамбек Куануш, PhD;
ORCID: 0000-0002-2338-8816;
e-mail: tastambeku@gmail.com

Гржибовский Андрей Мечиславович, д.м.н., профессор;
ORCID: 0000-0002-5464-0498;
eLibrary SPIN: 5118-0081;
e-mail: a.grjibovski@yandex.ru

Бердалинова Акженис;
ORCID: 0000-0002-5735-9538;
e-mail: berdalinova77@mail.ru

Балмагамбетова Ару, PhD;
ORCID: 0000-0003-1151-5651;
e-mail: aru.b.84@mail.ru