

Sex differences in the association between parity and risk of preterm birth: A retrospective study from Vienna

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Abstract

Background Preterm births not only increase the immediate morbidity and mortality of newborns but also have long-term consequences. An analysis of the risk factors is therefore of great interest from a public health perspective.

Objectives The aim of this study was to analyze sex-specific differences in the association between parity and the risk of preterm birth in singleton births.

Methods 6,109 female and 6,505 male neonates born at the Donaustadt Clinic in Vienna between 2010 and 2020 were included in the study. The association between sex and preterm birth in the different parity groups was analyzed using binary logistic regressions, corrected for maternal parameters and the type of conception. Within each sex, the preterm birth rates for first, third and at least fourth births were compared with those for second births (reference group).

Results Only in first-born children biological sex appears to be a significant predictor of the risk of preterm birth, with biological males showing a 36.4% higher risk than biological females. When comparing within each sex, firstborn girls had a 1.844 times higher risk of preterm birth than second-born ones, and firstborn boys had a 1.740 times higher risk than second-born ones. Girls who were at least the fourth child had a 2.438 times higher risk than second-born girls.

Conclusion There are sex-specific differences in the association between preterm birth and parity.

Take-home message for students According to the male disadvantage hypothesis, the rate of preterm births is significantly higher among biologically male infants. Considering the association with parity, female and male first-borns have a significantly higher risk of preterm birth compared to second-born ones. This also applies to fourth and subsequent born girls compared to second-born ones.

Introduction

Globally, the preterm birth rate in 2020 ranged from 4 to 16%, with significant regional differences. As expected, the preterm birth rate is highest in the Global South, especially in developing countries and typical low-income regions, while it is very low in the Global North and in high-income countries (WHO 2023b). In Austria in 2020, the preterm birth rate was 7.3 per 100 live births (WHO 2023a). Preterm birth is defined as a birth before the 37th week of pregnancy (WHO 2023b). Preterm birth is associated with neonatal mortality and morbidity and is the leading cause of death in children under the age of five years (Perin et al. 2022). In addition, it can lead to long-term or lifelong health problems, developmental delays, or respiratory and cardiovascular problems (Mornioli et al. 2023). An analysis of possible risk factors is therefore of great importance from a public health perspective. The etiology of preterm birth is often unknown. In addition to genetic factors and maternal illness, however, biological sex appears to play a particular role. Several studies have observed an association between preterm birth and biological male sex (Liang et al. 2024; Peelen et al. 2016; Zhang et al. 2022). On the other hand, parity, which is also associated with low birth weight and neonatal mortality, was mentioned as a risk factor (Garces et al. 2020). However, the results of various studies on the significance of parity for preterm birth are inconclusive. While many studies described higher rates among first-time mothers (Delnord et al. 2018; Kashani-Ligumsky et al. 2024; Lin et al. 2021; Prunet et al. 2017; Tracy et al. 2007), others identified higher parity as a risk factor (Esan et al. 2026; Okui and Nakashima 2025; Rugumisa et al. 2021; Zhang et al. 2022). Furthermore, the possible underlying physiological mechanisms

of parity's relationship with preterm birth remain unclear.

To our knowledge, there are no studies on sex-specific differences in the relationship between parity and the risk of preterm birth, although it has been shown that maternal parameters such as suboptimal pre-pregnancy weight and low or advanced maternal age have a greater association with birth outcome and health of male newborns than on that of female newborns (Kirchengast and Hartmann 2009). Therefore, the aim of this study is to investigate sex-typical differences in the relationship between parity and the risk of preterm birth. Two hypotheses were tested:

1. The preterm birth rate is higher in the biological male sex than in the biological female sex.
2. The significance of parity for preterm birth is higher in the biological male sex than in the female sex.

Data set and methods

Data set

This single-center study based on medical records included data from 12,614 single births that took place at the Clinic Donaustadt in Vienna, Austria between 2010 and 2020. Strict inclusion criteria were a single pregnancy and a live birth. Exclusion criteria were genetic abnormalities, congenital diseases, maternal diseases such as diabetes mellitus or HIV infections, and planned caesarean sections, although it should be noted that planned caesarean sections are only performed at the Clinic Donaustadt if medically indicated, not at the mother's request. A total of 6,109 female and 6,505 male newborns met the inclusion criteria. The anonymized data

set was analyzed at the Department of Evolutionary Anthropology at the University of Vienna. The study was conducted in accordance with the Helsinki criteria and approved by a positive vote of the Ethics Commission of the City of Vienna (protocol number: EK 19-274-VK, 18 March 2020).

Maternal parameters

A detailed medical anamnesis of the pregnant women includes reproductive history, acute and chronic illnesses, nicotine consumption during pregnancy, and medication use. In addition, pre-pregnancy weight was reconstructed by measuring the mother's weight at the first prenatal examination, usually in the eighth gestational week, using digital scales accurate to 0.1kg. From this value and the mother's statement of her pre-pregnancy body weight, the mean value was calculated and defined as prepregnancy weight. The mother's height was also documented with a standard anthropometer during the first check-up. Body mass index (BMI) (kg/m²) was calculated to determine prepregnancy weight status. The mother's body weight was determined again before birth. The weight change during pregnancy was calculated by subtracting the prepregnancy weight from the end of pregnancy weight.

Newborn parameters

The biological sex of the newborns was determined immediately after birth. In addition, trained specialists determined the birth length of the newborns using a standard measurement board for infants and documented the birth weight using a digital infant scale.

Obstetric parameters

A birth before the 37th week of pregnancy was classified as preterm birth. The gestational age was calculated based on the first day of the last menstrual period and the results of ultrasound examinations in the first trimester. In addition, the type of conception (spontaneous or assisted) and previous pregnancies and births were documented.

Parity was divided into the following categories: parity of one (P1), parity of two (P2), parity of three (P3) and parity of four or more ($P \geq 4$). Since the parity group of two (P2) had the lowest preterm birth rate in the present sample, P2 was defined as the reference value against which the other parity values were compared, in accordance with the method by [Koullali et al. \(2020\)](#).

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics (version 29). Since, according to the results of the Kolmogorov-Smirnov test, no normal distribution could be assumed for maternal age, pre-pregnancy BMI, gestational weight gain, birth weight, birth length and the number of previous pregnancies, the sample parameters were given as median and semi-interquartile range. Group differences were tested for significance using the Mann-Whitney U test and Fisher's exact test.

To analyze the significance of biological sex for the association between parity and preterm birth, binary logistic regression models were created separately for each parity group with the dependent variable being the risk of preterm birth (0 corresponds to ≥ 37 weeks; 1 corresponds to < 37 weeks). We decided to perform the regression analyses for each parity group separately, because this study aimed to

answer the question in which parity group sex is a significant predictor of preterm risk. To include all parity groups in one model, we would need to code parity as a dummy variable because parity is a categorical variable. In this case, we would need to define a reference group. Our analysis strategy allowed to compare the effect sizes of sex between the individual parity groups.

Sex was a predictor variable, as were maternal age (in years), pre-pregnancy BMI (in kg/m²), gestational weight gain (in kg), nicotine consumption (no=0/yes=1) and type of conception (spontaneous=0/assisted=1). After Bonferroni correction, the new significance level here was $p < 0.0125$. For the comparison within the biological sex, a binary logistic regression model for each sex was performed with the dependent variable risk of preterm birth (0 corresponds to ≥ 37 weeks; 1 corresponds to < 37 weeks). Parity was coded as a dummy variable with a parity of two as the reference. Parities of 1, 3, and at least 4 – each compared to parity of 2 – were predictor variables, as well as maternal age, pre-pregnancy BMI, gestational weight gain, nicotine consumption and type of conception.

Results

Table 1 shows the maternal and neonatal parameters as well as the obstetric characteristics separated by sex. Significant differences between the two sexes existed only in birth weight and birth length, as well as in the preterm birth rate. Male newborns were significantly longer and heavier, but more likely to be born preterm. Their preterm birth rate (6.1%; $n=396$) was significantly higher than in female newborns (4.9%; $n=299$). The risk of being born preterm was 26% higher in the male sex ($\chi^2 = 8.615$, $p = 0.003$).

Figure 1 shows the percentages of preterm births in each parity group, separated by sex. Males showed an approximately U-shaped distribution, while female newborns showed a more J-shaped one.

Table 2 presents the associations between sex and risk of preterm birth within each parity group. All models, except that of $P \geq 4$, were statistically significant ($p(P1) < 0.001$; $p(P2) < 0.001$; $p(P3)=0.008$; $p(P \geq 4) = 0.136$), Nagelkerke R² was 0.030, 0.047, 0.033, and 0.031 respectively. Sex was significantly associated with preterm birth in first-borns. Male first-borns had a 36.4% higher risk of being born preterm than female first-borns. Second-born boys had a 40.9% higher risk of being born preterm than their female counterparts, but this association was no longer significant after Bonferroni correction. Other significant predictors of preterm birth are maternal weight gain in first-, second-, and third-borns as well as maternal age and nicotine consumption in first- and second-born children.

The association between parity and the risk of preterm birth for each sex is shown in Table 3. The models for both boys and girls were statistically significant ($p < 0.001$), Nagelkerke R² was 0.038 and 0.035 respectively. Compared to the second-born, the first-born child had a significantly increased risk of being preterm. First-born girls had a 1.844 times higher risk of being born preterm than second-born children of the same sex, and first-born boys had a 1.740 times higher risk. The risk of preterm birth did not differ significantly between third-born and second-born children. This applied to both biological sexes. The risk of preterm birth for at least fourth-born boys also did not differ significantly from that for second-born boys. Fourth-born girls, on the other hand, had a significantly 2.438 times higher risk of preterm birth. In both girls and boys other significant predictors for preterm birth were maternal

age, gestational weight gain and nicotine consumption.

In general, it should be noted, that statistical power especially in parity group $P \geq 4$ is limited due to small sample size, which is why results should be interpreted with caution.

Discussion

In our study, we found a marked impact of sex on preterm birth rate, but also on the association between parity and preterm birth. The first hypothesis, that preterm birth is more common in the biological

male sex than in the biological female sex, was verified in this study. It corresponds to the results of other studies (Liang et al. 2024; Peelen et al. 2016; Zhang et al. 2022) and can be interpreted in terms of the male disadvantage hypothesis. This hypothesis refers to sex differences in intrauterine as well as postnatal morbidity and mortality with a male disadvantage and the higher susceptibility of male fetuses to stress factors and suboptimal maternal conditions which is well reported by several studies (e.g., Elsmén et al. 2004; Kirchengast and Hartmann 2009; Mondal et al. 2014; Qiu et al. 2020). What causes this sex differences is yet unknown. In a review, Clifton (2010) suggested that differences in the structure and function of the placenta as

Table 1 Maternal, newborn and obstetrical characteristics according to sex

	females			males			p-value
	Median	SIQR	range	Median	SIQR	range	
n							
Maternal age (yrs)	31	3.5	14-55	30	3.5	15-54	0.412
PPBMI (kg/m ²)	22.86	2.85	13.30-58.09	22.86	2.86	14.13-57.30	0.957
Body height (cm)	165	5.0	141-188	165	4.5	140-193	0.753
Weight gain (kg)	14	3.5	-17 – 43	14	4.0	-17 – 41	0.120
Birth weight (g)	3340	295	470-5809	3500	320	700-5350	<0.001*
Birth length (cm)	50	1.5	28-60	51	1.5	33-58	<0.001*
Gestational week	39	0.5	26-42	39	1.0	26-42	0.243
Pregnancies	2	1.0	1-14	2	1.0	1-15	0.397
Previous births	2	0.5	1-9	2	0.5	1-10	0.175
	n	%		n	%		
Preterm birth	299	4.9%		396	6.1%		<0.001*
Parity 1 (P1)	2851	46.7%		2964	45.6%		0.594
Parity 2 (P2)	2191	35.9%		2361	36.3%		
Parity 3 (P3)	733	12.0%		818	12.6%		
Parity ≥ 4 ($P \geq 4$)	334	5.5%		362	5.6%		
ART	186	3.0%		169	2.6%		0.072
Nicotine	854	14%		857	13.2%		0.098

Legend: PPBMI = prepregnancy body mass index ; ART = Artificial reproductive technology

SIQR=semi-interquartile range, P1=primi-parity, P2=parity score of two, P3=parity score of three, $P \geq 4$ =parity score of at least four significance level= $p < 0.05$; significant results are asterisked (*)

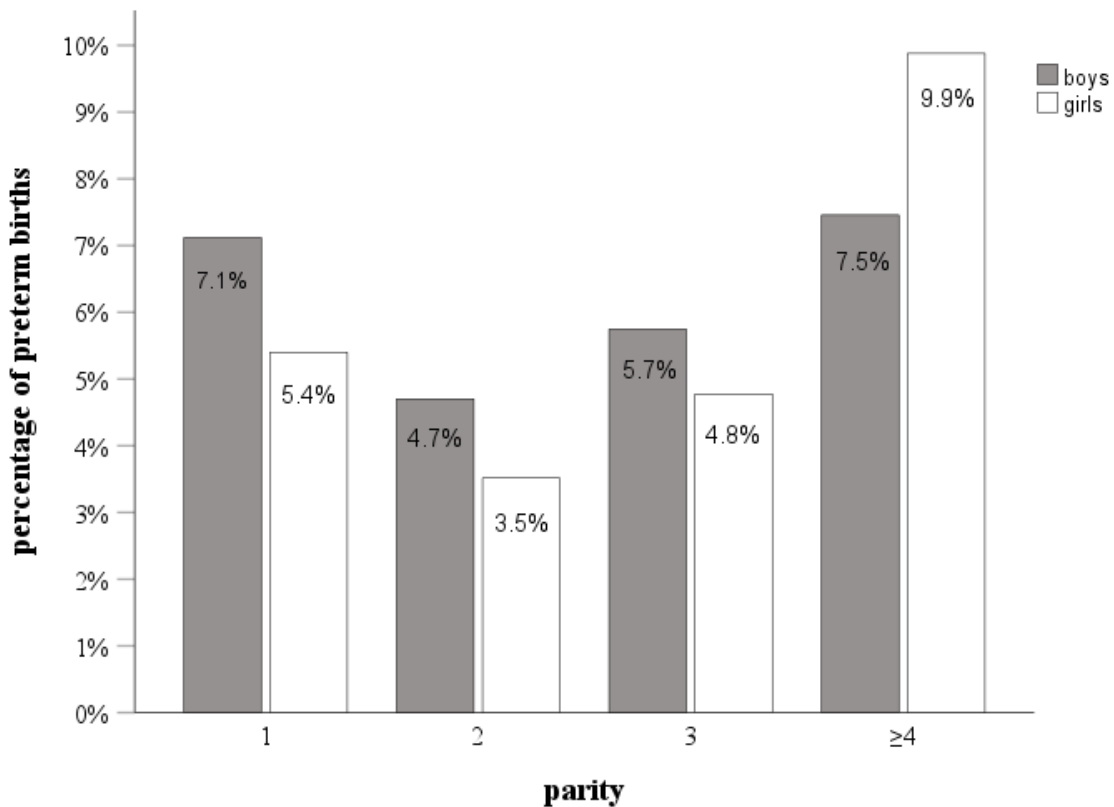


Figure 1 Percentage of preterm deliveries in each parity group separated by sex. Sample size in each parity group: parity 1: nboys=2964, ngirls=2851; parity 2: nboys=2361, ngirls=2191; parity 3: nboys=818, ngirls=733; parity ≥4: nboys=362, ngirls=334. Absolute frequencies of preterm birth: parity 1: nboys=211, ngirls=154; parity 2: nboys=111, ngirls=77; parity 3: nboys=47, ngirls=35; parity ≥4: nboys=27, ngirls=33

well as different fetal-placental patterns of gene and protein expression, immune function, steroid profile and growth factor pathway could play a role.

The second hypothesis presented in the introduction, that parity has a greater influence on preterm birth in the biological male sex, could not be clearly verified. First-born boys had a significantly higher risk of 36.4% of being born preterm than first-born girls, which represents a disadvantage for boys. Second-born boys also appeared to have a higher risk (approximately 40.9% higher) than second-born girls, although this was not significant after correction for multiple tests. So far, hypothesis 2 would be confirmed.

Being the first-born child was a significant risk factor for preterm birth for both bio-

logical sexes compared to the second-born ones of the corresponding sex. Apparently, there was a slightly stronger association in girls. Female first-borns had a 1.844 times higher risk of preterm birth, while male first-borns had a slightly lower risk (1.740 times higher risk). In addition, parity of at least four was a risk factor for preterm birth only in female newborns compared to parity of two.

As mentioned above, there are many studies that consider first birth to be a risk factor, but some studies have also found that higher parity is associated with an increased risk of preterm birth. [Hu et al. \(2018\)](#) observed an increased risk of preterm birth in women with a parity of ≥ 4 . [Koullali et al. \(2020\)](#) showed that women have an increased risk of

preterm birth during their first and fifth pregnancies, while Meis et al. (1995) report a U-shaped relationship between parity and the risk of preterm birth. In the present study, this applies to the biological male sex, while a more J-shaped association was observed in the biological female sex (Figure 1).

First births and a high number of births are risk factors in our study. This is not surprising: the first birth presents new challenges for the mother's body, while a high num-

ber of births places particular strain on the mother's body.

The direct mechanisms are not yet clear. Some parameters associated with the risk of preterm birth have also been found to be associated with parity. These include behavioral differences, such as increased fear of childbirth among first-time mothers (Rouhe et al. 2009) and women whose first birth was preterm, who are more likely to refrain from a second pregnancy (Miranda et al. 2011). The frequency of prenatal care

Table 2 Sex and risk of preterm birth within each parity group

Parity				95%-CI of Exp(B)		p
		B	Exp(B)	lower value	upper value	
P1	Sex	0.310	1.364	1.099	1.692	0.005*
	Maternal age (yrs)	0.026	1.026	1.006	1.047	0.009*
	PPBMI (kg/m ²)	0.003	1.003	0.982	1.025	0.759
	Weight gain (kg)	-0.060	0.942	0.924	0.961	<0.001*
	ART	0.415	1.514	0.982	2.334	0.060
	Nicotine	0.435	1.545	1.149	2.077	0.004*
P2	Sex	0.343	1.409	1.044	1.900	0.025
	Maternal age (yrs)	0.045	1.046	1.016	1.077	0.003*
	PPBMI (kg/m ²)	-0.021	0.979	0.949	1.009	0.166
	Weight gain (kg)	-0.091	0.913	0.887	0.941	<0.001*
	ART	-0.694	0.500	0.121	2.067	0.338
	Nicotine	0.837	2.310	1.579	3.380	<0.001*
P3	Sex	0.219	1.245	0.792	1.957	0.342
	Maternal age (yrs)	0.030	1.030	0.985	1.078	0.193
	PPBMI (kg/m ²)	-0.064	0.938	0.891	0.988	0.015
	Weight gain (kg)	-0.076	0.927	0.887	0.968	0.001*
	ART	-18.513	0.000	0.000	.	0.999
	Nicotine	-0.106	0.900	0.484	1.671	0.738
P _≥ 4	Sex	-0.313	0.731	0.427	1.250	0.252
	Maternal age (yrs)	-0.031	0.969	0.916	1.025	0.272
	PPBMI (kg/m ²)	0.008	1.008	0.959	1.059	0.751
	Weight gain (kg)	-0.043	0.958	0.914	1.005	0.080
	ART	-18.666	0.000	0.000	.	0.999
	Nicotine	0.516	1.675	0.915	3.067	0.094

Legend: PPBMI = prepregnancy body mass index ; ART = Artificial reproductive technology

B=regression coefficient, Exp(B)=odds ratio, CI=confidence interval

P1=primiparity, P2=parity score of two, P3=parity score of three, P_≥4=parity score of at least four

sex coded 0=female newborns, 1=male newborns

significance level=p<0.0125; significant results are asterisked (*)

visits among multiparous women (Otioku et al. 2021) could play an important role in the relationship between parity and the risk of preterm birth. In addition, some physiological phenomena have been postulated that are associated with both parity and preterm birth. Primiparity as a risk factor could, for example, be due to more sensitive membranes, leading to a higher incidence of premature membrane rupture (Robin et al. 2024), a smaller uterine cavity and reduced uteroplacental blood flow (Lin et al. 2021) or higher ferritin concentrations (Broekhuis et al. 2024). Higher parity could increase the risk of preterm birth due to lower hemoglobin concentrations (Ali et al. 2020), maternal anemia (Liabsuetrakul 2011; Kumari et al. 2019), a higher incidence of certain medical complications and placental pathologies (Aliyu

et al. 2005) and uterine changes due to previous pregnancies (Wagura et al. 2018). In general, the vaginal microbiome is altered by parity, which could be associated with adverse pregnancy outcomes (Kashani-Ligumsky et al. 2024).

In accordance with other studies reporting increased vulnerability in males in connection with suboptimal maternal conditions and parameters (Kirchengast and Hartmann 2009), this study also showed that male sex is a significant predictor of the risk of preterm birth in first-born children and possibly also in second-born children. However, when comparing within the same sex, newborns who were at least the fourth child had a significantly higher risk of preterm birth than second-born children only in girls.

Table 3 Parity and risk of preterm birth

		B	Exp(B)	95%-CI of Exp(B)		p
				lower value	upper value	
Preterm birth risk in boys	P1 vs. P2	0.554	1.740	1.363	2.221	<0.001*
	P3 vs. P2	0.119	1.126	0.789	1.608	0.514
	P _{≥4} vs. P2	0.298	1.347	0.858	2.115	0.195
	Maternal age (yrs)	0.022	1.022	1.002	1.043	0.028*
	PPBMI (kg/m ²)	-0.021	0.980	0.959	1.001	0.057
	Weight gain (kg)	-0.073	0.930	0.912	0.948	<0.001*
	ART	0.402	1.495	0.889	2.515	0.129
	Nicotine	0.591	1.805	1.380	2.361	<0.001*
Preterm birth risk in girls	P1 vs. P2	0.612	1.844	1.385	2.456	<0.001*
	P3 vs. P2	0.227	1.255	0.831	1.896	0.281
	P _{≥4} vs. P2	0.891	2.438	1.570	3.784	<0.001*
	Maternal age (yrs)	0.033	1.034	1.011	1.057	0.004*
	PPBMI (kg/m ²)	0.005	1.005	0.981	1.029	0.701
	Weight gain (kg)	-0.058	0.943	0.923	0.964	<0.001*
	ART	0.039	1.040	0.547	1.977	0.905
	Nicotine	0.366	1.442	1.050	1.980	0.024*

Legend: PPBMI = prepregnancy body mass index ; ART = Artificial reproductive technology

B=regression coefficient, Exp(B)=odds ratio, CI=confidence interval

P1=parity of one (coded 1) compared to parity of two (coded 0), P3=parity of three (coded 1)

compared to parity of two (coded 0), P_{≥4}=parity of at least 4 (coded 1) compared to parity of two (coded 0)

significant results are asterisked (*)

Two explanations are proposed for the different patterns of association between the risk of preterm birth and parity between and within sexes. Firstly, it is possible that in groups with higher parity, such as groups $P \geq 3$ and $P \geq 4$, the association of parity with the risk of preterm birth becomes even stronger in females. Accordingly, no significant sex difference could be observed in these parity groups. Furthermore, in the $P \geq 4$ group, there appears to be a tendency for girls to be at higher risk, although this is not statistically significant. This could possibly be due to the small sample size in this group. It could therefore even be the case that in groups with higher parity, such as $P \geq 4$, the risk in females exceeds that in males. Male newborns had a higher percentage of preterm births than females in every parity group, except in the $P \geq 4$ group. Here, the incidence was 7.5% for boys and 9.9% for girls. Furthermore, only in the $P \geq 4$ group was there a negative correlation between sex and the risk of preterm birth, albeit not a significant one – again, possibly due to the small sample size in this group. This initial explanation would suggest that in groups with low parity there is a disadvantage for males, but in groups with higher parity there is a disadvantage for females.

In contrast, the second explanation, would refer to a male disadvantage also in the higher parity groups resulting in a higher intrauterine mortality. Studies suggest that high parity is associated with a significantly increased risk of stillbirth (Awoleke and Adanikin 2016; Dasa et al. 2022). Accordingly, it is possible that an adverse impact of parity in first-born boys would result in an increased risk in preterm birth but in higher parity groups it would lead to higher intrauterine mortality. Thus, females would survive more likely but would show consequences not in form of higher intrauterine mortality but of increased preterm birth incidence.

This study has several limitations. It is a single-center study, so the results may not be transferable to other regions or population groups. As it was a retrospective study, it was not possible to control for other factors that influence the risk of preterm birth. No information was available on socioeconomic status or previous preterm births among siblings, which are known risk factors for preterm birth. In addition, the sample size in the groups with higher parity – especially $P \geq 4$ – was rather small, which may limit the possibilities for interpretation.

Conclusion

Future studies should focus not only on elucidating the mechanisms behind the relationship of parity with preterm birth, but also on the mechanisms behind the sex differences observed here. As this study is the first to examine sex differences in the association between preterm birth and parity, it needs to be replicated, particularly in countries with high fertility rates. This could be clinically significant not only for preventive measures, but also for the interpretation of data from countries where higher birth rates are more common and sex differences in neonatal mortality are reported.

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