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Trends and risk of recurrent preterm birth in pregnancy cohorts in rural Bangladesh, 1990–2019

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ABSTRACT

Introduction A history of preterm birth reportedly increases the risk of subsequent preterm birth. This association has primarily been studied in high-income countries and not in low-income settings in transition with rapidly descending preterm birth figures. We evaluated the population-based trends of preterm births and recurrent preterm births and the risk of preterm birth recurrence in the second pregnancy based on prospectively studied pregnancy cohorts over three decades in Matlab, Bangladesh.

Methods A population-based cohort included 72 160 live births from 1990 to 2019. We calculated preterm birth and recurrent preterm birth trends. We assessed the odds of preterm birth recurrence based on a subsample of 14 567 women with live-born singletons in their first and second pregnancies. We used logistic regression and presented the associations by OR with a 95% CI.

Results The proportion of preterm births decreased from 25% in 1990 to 13% in 2019. The recurrent preterm births had a similar, falling pattern from 7.4% to 3.1% across the same period, contributing 27% of the total number of preterm births in the population. The odds of second pregnancy preterm birth were doubled (OR 2.18; 95% CI 1.96 to 2.43) in women with preterm birth compared with the women with term birth in their first pregnancies, remaining similar over the study period. The lower the gestational age at the first birth, the higher the odds of preterm birth in the subsequent pregnancy (test for trend p<0.001).

Conclusion In this rural Bangladeshi setting, recurrent preterm births contributed a sizeable proportion of the total number of preterm births at the population level. The increased risk of recurrence remained similar across three decades when the total proportion of preterm births was reduced from 25% to 13%.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Studies mainly performed in high-income countries show that a history of preterm birth has been associated with subsequent preterm birth recurrence.

WHAT THIS STUDY ADDS

⇒ In a transitional society with preterm births decreasing from very high to moderate levels, the increased risk of preterm birth recurrence remained constant, contributing to one-fourth of the total number of preterm births.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings underline the importance of identifying women at risk of preterm birth and ensuring appropriate perinatal management of mothers and neonates in low-income settings.

INTRODUCTION

Preterm birth is defined as any birth occurring before the completion of 37 weeks of gestation. Worldwide, it is a significant public health problem.[1] It affects about 10% of all pregnancies globally, with an estimated 13.4 million babies born preterm each year.[2] About 70%–80% of global preterm births occur in Southern Asia and sub-Saharan Africa.[2 3] Bangladesh is ranked seventh in contributing to the global preterm birth burden.[4] Previous studies indicated decreasing trends of preterm births, with proportions varying from 22% to 11% between 2007 and 2014 in Bangladesh.[5 6] Preterm birth is a leading cause of under-5 child mortality.[7] It is also associated with severe morbidity, including cerebral palsy, blindness and deafness in early life.[8 9] Furthermore, preterm birth is associated with respiratory illness, metabolic disorder and neurological impairment in later life.[10 11] These short-term and long-term consequences imply high costs to the health systems. The families also experience considerable psychological and financial burdens.[12] Understanding the epidemiology and determinants of preterm births is essential for prevention, management of the consequences and policy formation.

Sociodemographic, behavioural, nutritional, biological and environmental factors have been associated with preterm

births.[5 6 13] Researchers have tried to predict women at risk of preterm births. However, these models have not been suitable as public health tools.[14 15] In studies mainly performed in high-income countries, earlier preterm births have consistently been identified as a risk factor for subsequent preterm births.[16–18] Recurrent preterm births are defined as two or more deliveries taking place before 37 completed gestational weeks,[19] contributing a considerable proportion of the overall preterm birth burden. The magnitude of recurrent preterm birth risks has varied by gestational age at first birth, spontaneous and induced, and singleton and multiple births.[18–20] Systematic reviews have confirmed increased risks of recurrent preterm birth in women with prior singleton spontaneous preterm births.[16 18 21 22] The overall risk of preterm births has been reported to be between 4 and 6 times for women with preterm births compared with term birth in the previous pregnancy.[23] A few studies also have reported an increased risk of preterm births in second pregnancy when the first pregnancy ended with an induced preterm birth.[19 24]

The above findings emphasise the importance of obtaining histories of previous pregnancies and births to identify those at risk for subsequent preterm birth. However, current evidence emanates primarily from high-income countries. Many studies were hospital based, therefore, not reflecting the risks of recurrent preterm births at the population level.[18 25] Furthermore, no studies have evaluated recurrent preterm births in populations transitioning from higher to lower preterm birth rates. Using the Health and Demographic Surveillance System (HDSS) databases in Matlab, Bangladesh, we reported a remarkable decrease in preterm birth over 25 years. About one-fourth of this reduction was attributed to increased maternal education and reduced parity.[5] However, little has been documented on the recurrence of preterm birth in low-resource settings such as Bangladesh. Therefore, we evaluated the population-based trends of preterm births and recurrent preterm births and the risk of preterm birth recurrence in the second pregnancy based on prospectively studied pregnancy cohorts from 1990 to 2019 in Matlab, Bangladesh. We also assessed the recurrence risks by spontaneous or induced birth in the first pregnancy.

METHODS

Study setting, design and sample

The study site was Matlab Upazila (subdistrict) under the Chandpur district in Bangladesh. Since 1966, the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) has run an internationally recognised and unique HDSS in 142 villages with a population of about 220 000.[26] The HDSS area is divided into two parts based on service provision: the icddr,b, and government service areas. In the icddr,b service area, women of childbearing age and their children under 5 years receive healthcare through icddr,b recruited medical staff. In the government service area, the population receives care at government health facilities like in other parts of the country. The icddr,b service area is divided into four administrative blocks. Each block has a population of about 27 000 and is served by a subcentre operated by midwives. These facilities provide 24-hour maternal and child health services. The icddr,b hospital in Matlab municipality provides free maternal and child healthcare and serves as a referral facility. This population-based cohort study included 72 160 live births recorded by the icddr,b service area of HDSS from 1990 to 2019.

Data collection

In this paper, we included all live births in the icddr,b service area from 1 January 1990 to 31 December 2019 to assess population-based proportions of preterm and recurrent preterm births. For the risk assessment of recurrent preterm birth, we restricted the analysis to the subsample of women who had their first and second live births during the study period.

In the Matlab HDSS, vital events, including birth, death, marriage, and in-migration and out-migration, are recorded by Community Health Research Workers during routine household visits. The visit schedule changed during the study period; it was every 2 weeks up to 2000, monthly from 2001 to 2007, and after that, every second month. The Community Health Research Workers asked all married women of reproductive age about their menstruation since the last visit to identify pregnancies. In 2007, icddr,b introduced urine pregnancy tests to strengthen the identification process. Women with missing periods for more than 14 days or positive urine pregnancy tests were recorded as pregnant, and the last menstrual period (LMP) dates were registered. We assessed the validity of the reported LMP date in this setting using ultrasound-based gestational age available from studies conducted in the same area that showed a high agreement between LMP and ultrasound-based gestational age (Cronbach's alpha=0.89).[5 27]

Pregnant women were followed up prospectively to record pregnancy outcomes, including delivery date and type. Early fetal loss was defined as the loss of a fetus before 28 gestational weeks. Late fetal loss or stillbirth was defined as the loss of a fetus at or after 28 gestational weeks. Live birth was defined as the birth of a baby with signs of viability. We calculated gestational age at birth by subtracting the LMP date from the delivery date, expressed in weeks.

Preterm birth was any live birth before 37 completed weeks of gestation. Live births in the first pregnancy were further categorised into very (<32 weeks), moderate (32–33 weeks), late (34–36 weeks) preterm births and term births (≥37 weeks). The term births were further divided into early-term (37–38 weeks) and full-term (≥39 weeks) births. The recurrent preterm birth was defined as a live birth before 37 completed weeks in the second pregnancy to a woman who delivered a preterm live birth in her first pregnancy.

We also divided preterm births according to clinical subtype, that is, spontaneous or induced preterm birth in the first pregnancy. A spontaneous preterm birth is defined as labour initiation with intact or premature rupture of membranes and birth before 37 weeks of gestation. Induced preterm birth was a medically induced birth or birth by caesarean section before 37 weeks. However, due to a lack of detailed clinical information, we used vaginal delivery and caesarean section as spontaneous or induced preterm birth indicators. We limited the analysis stratified for clinical delivery subtypes to the period from 2005 to 2019 due to the earlier unavailability of caesarean section information.

We extracted data on women's age, educational level, birth interval and household socioeconomic status (wealth quintiles) from the HDSS databases. Women's age at first pregnancy was categorised into <20, 20–24 and ≥25 years. Women's education was defined as the number of years completed at school and grouped into 0, 1–5 and ≥6 years of school attendance. Birth intervals were computed by subtracting the pregnancy outcome date of the previous pregnancy from the pregnancy outcome date of the subsequent pregnancy and expressed in months. Birth intervals were categorised into <18, 18–23, 24–47 and ≥48 months. Asset scores were generated through principal component analysis based on household asset ownership, including land possession and housing structure, and divided into quintiles, where one represented the poorest and five the wealthiest group.[28]

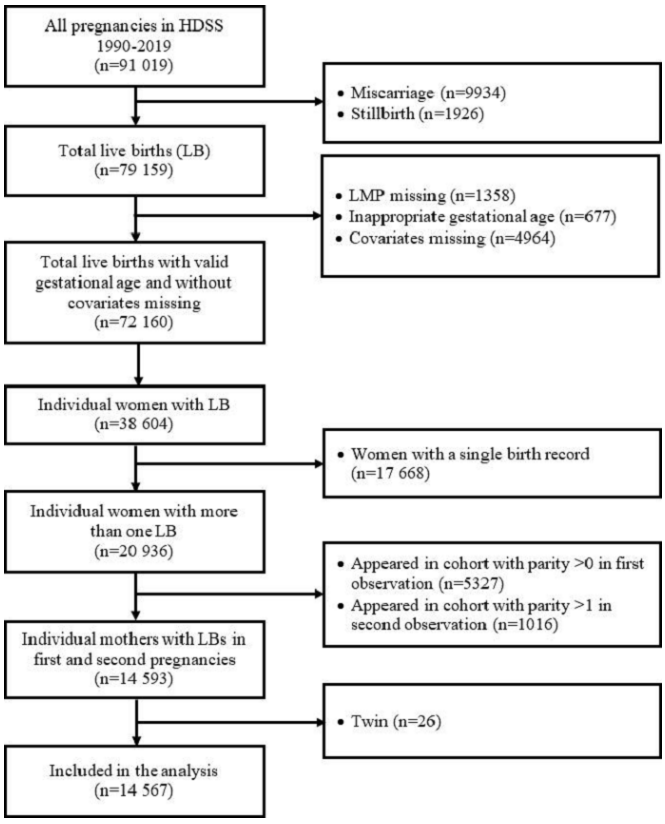

Figure 1 Study flow chart. HDSS, Health and Demographic Surveillance System; LMP, last menstrual period.

Data analysis

We used proportions, means or medians to characterise study participants. The proportions of the overall preterm births and the recurrent preterm births by year were presented graphically. In the risk analysis, we used logistic regression to obtain OR of preterm birth in the subsequent pregnancy. First, we assessed the risks by dividing the gestation age into preterm (<37 weeks) and term births (≥37 weeks). After that, we categorised the gestational age at birth into <32, 32–33, 34–36, 37–38 and ≥39 weeks to assess the risk patterns by exposure levels. We then evaluated the associations of sociodemographic and reproductive factors with preterm birth recurrence restricting the analysis to women who had preterm births in their first pregnancies. We checked multicollinearity between the explanatory variables by applying the correlation coefficient (Spearman's r) (online supplemental table 1). We then used the directed acyclic graph (https://dagitty.net/dags.html) to ascertain the potential confounders and mediators and included them in the model accordingly (online supplemental figures 1 and 2). Furthermore, the fitness of the models in the logistic regression was evaluated by the Hosmer-Lemeshow goodness-of-fit tests. To determine the robustness of associations, we presented the risks by the three cohort periods: 1990–1999, 2000–2009 and 2010–2019. Finally, we explored if spontaneous and induced preterm births influenced preterm birth recurrence by stratifying the subsample into three groups: <37 gestation weeks, spontaneous; <37 gestation weeks, induced and ≥37 gestation weeks. The results were expressed as adjusted ORs with 95% CIs. The linear trends of associations by gestational age at birth were tested by Wald statistics. We considered a p<0.05 as statistically significant.

Furthermore, we used the Cox proportional hazards model to assess the likelihood of having another preterm birth of a woman who had a preterm birth in the first pregnancy. We included all women with singleton birth in the first delivery regardless of whether they had a second delivery or not. In this analysis, the birth date in the first pregnancy was set as time=0. Follow-up was censored if an outcome event (preterm birth) did not happen at the end of follow-up or the mother migrated out of the area. We evaluated the assumptions of proportional hazards by assessing the hazards plot and by testing if the Schoenfeld residuals were independent of time. The results were presented by adjusted HR (aHR) with 95% CI. All analyses were performed using Stata V.16 (StataCorp).

RESULTS

In total, there were 91 019 pregnancies in the HDSS databases from 1990 to 2019. After excluding stillbirths, induced and spontaneous miscarriages, and those missing LMP dates and covariates, 72 160 live births were available to determine population-based preterm birth and recurrent preterm birth proportions (figure 1). A total

Table 1 Characteristics of all women with live births and the subsample of women with live births in their first pregnancy included in the analysis of recurrent preterm births in Matlab, Bangladesh from 1990 to 2019

	All live births (n=72 160)			Sub-sample of women with live births in first pregnancy (n=14 567)		
Characteristics	**Preterm**	**Term**	**Total**	**Preterm**	**Term**	**Total**
Maternal age (year)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
<20	2401 (18.2)	11 485 (19.5)	13 886 (19.2)	1329 (52.8)	5763 (47.8)	7092 (48.7)
20–24	4050 (30.7)	19 496 (33.0)	23 546 (32.6)	988 (39.3)	5133 (42.6)	6121 (42.0)
≥25	6741 (51.1)	27 987 (47.5)	34 728 (48.2)	198 (7.9)	1156 (9.6)	1354 (9.3)
Education (year)						
0	5004 (37.9)	14 757 (25.0)	19 761 (27.4)	775 (30.8)	2231 (18.5)	3006 (20.6)
1–5	3664 (27.8)	14 301 (24.3)	17 965 (24.9)	727 (28.9)	2896 (24.0)	3623 (24.9)
≥6	4524 (34.3)	29 910 (50.7)	34 434 (47.7)	1013 (40.3)	6925 (57.5)	7938 (54.5)
Wealth quintiles						
1-poorest	2685 (20.4)	10 258 (17.4)	12 943 (17.9)	425 (16.9)	1645 (13.6)	2070 (14.2)
2	2499 (18.9)	10 194 (17.3)	12 693 (17.6)	464 (18.4)	1924 (16.0)	2388 (16.4)
3	2633 (20.0)	11 575 (19.6)	14 208 (19.7)	525 (20.9)	2468 (20.5)	2993 (20.5)
4	2722 (20.6)	12 892 (21.9)	15 614 (21.6)	544 (21.7)	2820 (23.4)	3364 (23.1)
5-wealthiest	2653 (20.1)	14 049 (23.8)	16 702 (23.2)	557 (22.1)	3195 (26.5)	3752 (25.8)
Delivery type*						
Normal vaginal delivery	3143 (68.5)	21 918 (69.2)	25 061 (69.1)	494 (82.2)	3969 (75.4)	4463 (76.1)
Caesarean section	1443 (31.5)	9764 (30.8)	11 207 (30.9)	107 (17.8)	1294 (24.6)	1401 (23.9)

*Information available from 2005.

of 38 604 women contributed to these live births. Women with only one delivery (n=17 668), women entered into the cohort with parity more than zero at the first observed delivery (n=5327), and women more than one on the second observed delivery (n=1016) and twin pregnancies (n=26) were excluded. Finally, 14 567 women who had their first and second consecutive live births within the study period were included in the analysis for recurrent preterm birth risks (figure 1).

Table 1 presents the characteristics of the participants for all live birth and for the subset of live births at their first delivery that were included in the risk analysis. The mean (SD) ages of all women and the subsample of women were 25.5 (5.8) and 20.6 (3.2) years, respectively. At the first delivery, about half of the women who delivered were less than 20 years, one-fifth had no education and one-quarter had been delivered by caesarean section (table 1).

Across the study period, the average proportion of preterm births was 18.3%. The overall proportion of preterm births decreased consistently from 24.7% in 1990 to 13.1% in 2019. From 2008 onwards, it remained at around 12% (figure 2). The recurrent preterm birth proportions followed a similar decreasing pattern and reduced from 7.4% in 1990 to 3.1% in 2019 (figure 2). However, the contribution of recurrent preterm births to the total preterm births was relatively constant, with a reduction from 30% in 1990 to 24% in 2019, an average of 27% across the study period (figure 2).

Figure 3 illustrates the preterm birth proportion in first and second births. It was 17.3% in the first birth and 14.6% in the second, remaining relatively constant across the study period. The proportion of caesarean sections increased from 6.8% in 2005 to 57% in 2019. The high proportions towards the end of the study period were not linked to any increase in the occurrence of preterm births (figure 2, table 1).

Online supplemental figure 3 presents the proportion of preterm birth in the second pregnancy by gestation age in weeks at delivery in the first pregnancy. The proportion of preterm birth in the second pregnancy was about 26% among women with preterm birth (<37 gestation weeks) in the first pregnancy. The proportion of preterm birth in the second pregnancy was highest when the first pregnancy was very preterm (35%) and lowest when full term (10.2%) (online supplemental figure 3).

The overall odds of a recurrent preterm birth (spontaneous or induced) was about two times higher (OR 2.18, 95% CI 1.96 to 2.43) in women with a history of preterm birth compared with women without a history of preterm birth. The lower the gestational age was at the first birth, the higher the OR of preterm birth in the subsequent pregnancy (test for trend p<0.001) (table 2). The odds of recurrent preterm birth in the second pregnancy were

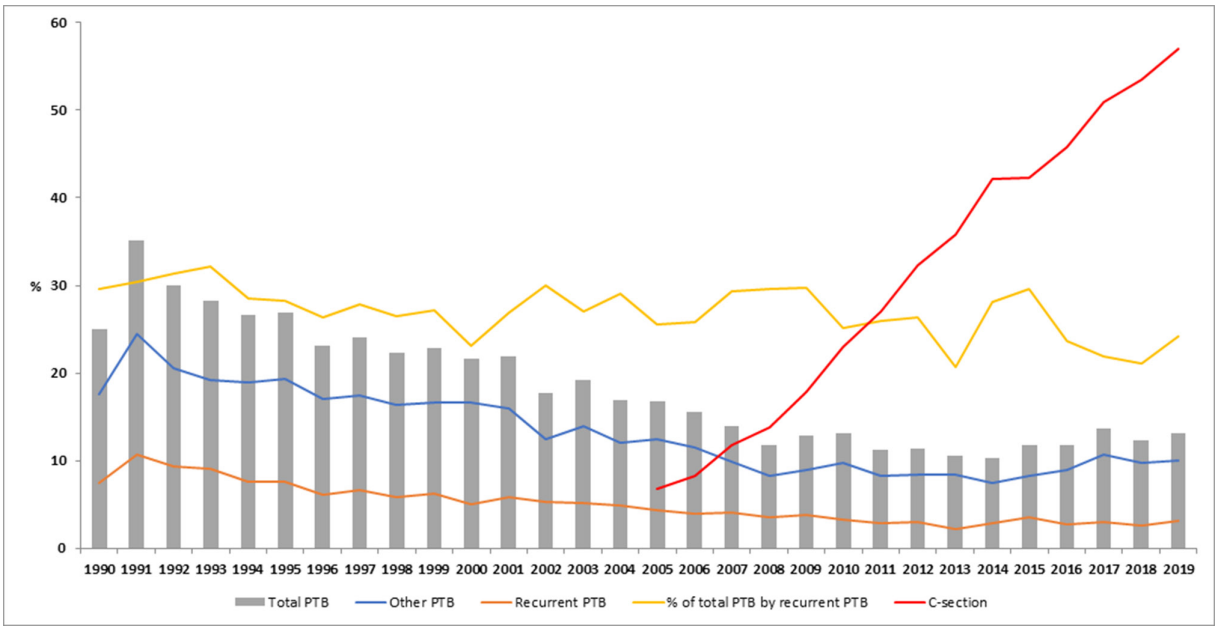

Figure 2 Prevalence of total preterm births, recurrent preterm (including proportion of total preterm birth), and caesarean sections in Matlab, Bangladesh, 1990 to 2019. PTB = preterm birth. C-section = caesarean section.

highest when the first pregnancy had ended with very preterm birth (<32 gestational weeks, OR 4.06, 95% CI 2.95 to 5.58) (table 2). We observed increased odds at 37–38 weeks of gestation at first pregnancy compared with women with ≥39 weeks (OR 1.72; 95% CI 1.54 to 1.93) (table 2).

Further, in a time-to-event analysis, we included all women with a singleton first birth, disregarding whether they had a second birth or not. The likelihood of having another preterm birth of a woman in a subsequent pregnancy was about 1.7 times higher (aHR 1.67, 95% CI 1.52 to 1.85) compared with women who had term birth in the first pregnancy (online supplemental table 2).

Out of the available covariates, socioeconomic conditions by household wealth quintiles (OR 1.53, 95% CI 1.12 to 2.10), and birth interval (OR 1.81, 95% CI 1.27 to 2.58) were associated with recurrent preterm birth odds in second pregnancy (table 3).

We also observed similar preterm birth recurrence risks when the analyses were stratified by three 10-year periods of the study cohort (online supplemental table 3). A similar risk estimates of preterm birth recurrence in spontaneous and induced deliveries in second pregnancy were also observed in women with spontaneous or induced deliveries during their first pregnancy (online supplemental tables 4 and 5).

DISCUSSION

In this population-based pregnancy cohort study across three decades in rural Bangladesh, the proportion of preterm births declined from 25% in 1990 to 13% in 2019. Recurrent preterm births followed a similar decrease, contributing 27% of the total preterm births in the population. Compared with women who had a term birth in their first pregnancy, the risk of second pregnancy preterm birth recurrence was two times higher.

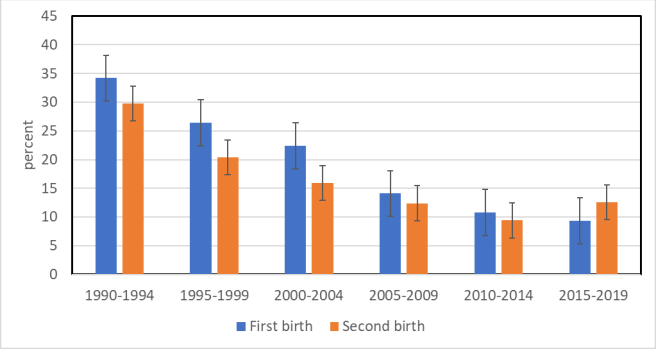

Figure 3 Proportion of preterm birth in the first and second pregnancies in Matlab, Bangladesh, 1990 to 2019. Error bars represent 95% confidence intervals of proportions.

The lower the gestational age at first birth, the higher the risk of recurrence of preterm birth. Even births weeks 37 and 38, compared with week 39 or more, had an increased risk of preterm birth in a subsequent pregnancy. We observed a similar risk increase of recurrent preterm birth whether the first delivery was by caesarean or vaginal delivery.

There need to be more studies evaluating the proportion of recurrent preterm birth and its contribution to the total number of preterm births at the population level. Few studies from low-income and middle-income countries have evaluated the proportions and risks of recurrent preterm birth. No previous studies have assessed recurrent preterm births in a setting with sharply declining total proportions of preterm birth. Studies

Table 2 Association between preterm birth in first pregnancy and preterm birth in the second pregnancy within gestational age categories at first birth. Matlab, Bangladesh, 1990 to 2019 (n=14,567)

Gestation age at first birth (weeks)	Second pregnancy					
			Preterm birth odds			
			Crude		Adjusted*	
	Term birth (n=12442)	Preterm birth (n=2125)	OR	95% CI	Adjusted OR†‡	95% CI
<32	117	63	4.74	3.46 to 6.48	4.06	2.95 to 5.58
32–33	288	141	4.31	3.48 to 5.33	3.59	2.89 to 4.46
34–36	1455	451	2.73	2.40 to 3.09	2.34	2.06 to 2.66
37–38	2910	598	1.81	1.61 to 2.02	1.72	1.54 to 1.93
≥39§	7672	872	1	1	1	1

*Hosmer and Lemeshow goodness-of-fit test p=0.106.
†Adjusted for maternal education, socioeconomic status by wealth quintiles and calendar year of second birth.
‡$P_{\text{-linear trend}} = 0.001$ by Wald χ^2 test.
§Reference category.

from Tanzania and India reported recurrent preterm birth rates of 24% and 32%, respectively, in second pregnancies,[25 29] figures similar to the proportion observed in our study. The level of recurrence found in our study was on the same level as those reported from high-income countries, where the recurrence ranged from 16% to 32%.[30–33]

Our study confirms the increased recurrence risks in second pregnancies already reported in earlier studies.[25 31–34] The dose–response relationship between

Table 3 Association of sociodemographic factors with recurrent preterm birth in subsequent births in Matlab, Bangladesh, 1990–2019 (n=2515)

	No of birth in second pregnancy		Recurrent preterm birth odds	
	Live birth	Preterm birth	Model 1* OR (95% CI)	Model 2†‡ OR (95% CI)
Maternal age in years				
<20	195	69	1.90 (1.36 to 2.64)	1.38 (0.95 to 2.01)
20–24	1347	368	1.30 (1.17 to 1.58)	1.18 (0.96 to 1.45)
≥25§	973	218	1	1
Education in years				
0	764	233	1.57 (1.27 to 1.94)	1.20 (0.93 to 1.54)
1–5	722	194	1.29 (1.03 to 1.61)	1.09 (0.86 to 1.39)
≥6§	1029	228	1	1
Wealth quintiles				
1-poorest	519	155	1.67 (1.25 to 2.25)	1.53 (1.12 to 2.10)
2	475	129	1.93 (1.45 to 2.56)	1.78 (1.32 to 2.41)
3	509	128	1.37 (1.03 to 1.82)	1.30 (0.97 to 1.75)
4	551	146	1.48 (1.12 to 1.96)	1.49 (1.12 to 1.99)
5-wealthiest§	461	97	1	1
Birth interval in months				
<18	180	75	2.23 (1.62 to 3.08)	1.81 (1.27 to 2.58)
18–23	152	48	1.44 (1.00 to 2.08)	1.13 (0.77 to 1.68)
24–47	851	209	1.02 (0.83 to 1.24)	0.89 (0.72 to 1.10)
≥48§	1332	323	1	1
Calendar year of second birth				
1990–1999	912	279	1.64 (1.29 to 2 .09)	1.38 (1.04 to 1.82)
2000–2009	1009	250	1.22 (0.96 to 1 .56)	1.16 (0.90 to 1.50)
2010–2019§	594	126	1	1

*Model 1: crude OR.
†Model 2: adjusted for maternal age, education, socioeconomic status by wealth quintiles, birth interval and calendar year of second birth.
‡Hosmer and Lemeshow goodness-of-fit test p=0.343.
§Reference category.

gestational age in index pregnancies and subsequent recurrent preterm birth risks has been shown.[35–38] However, the categorisation of gestational age in the index pregnancies differs from earlier studies where the early preterm birth included births before 34 weeks of gestation.[37] A multicountry study from high-income countries concluded that the risk of recurrent preterm birth in subsequent pregnancies was 4–6 times higher in women of prior preterm delivery.[23] We also observed that birth weeks 37–38, compared with week 39 or more, increased the risk of subsequent preterm birth. A study conducted in California found a similar risk increase.[18] A significant proportion of births occur at that gestational age.[39]

We observed that women from the low-wealth quintiles had a higher risk of recurrent preterm birth. Several studies have observed an increased risk associated with unfavourable socioeconomic characteristics in high-resource and low-resource settings.[40–42] We also observed the associations between birth intervals and preterm birth recurrence consistent with studies conducted in high-income countries.[43 44]

The mechanisms behind the occurrence of recurrent preterm birth are not fully elucidated. Earlier studies reported several factors associated with the risk of recurrent preterm births. These factors include intrauterine infection,[45] maternal undernutrition,[46] hypertensive disorders,[47] placental abnormalities,[48] elevated cervicovaginal fetal fibronectin concentrations[49] and short cervix.[50] Due to a lack of clinical data in our population-based surveillance system, we could not analyse the influence of such factors in our cohort. Furthermore, multiple aetiologies are involved for preterm birth, and genetic predisposition has been suggested as one of these pathways.[51 52] More research is needed to fully understand the mechanisms behind the occurrence of preterm birth recurrence.

We prospectively collected all information in this population-based pregnancy cohort study. Data included all deliveries to analyse total and recurrent preterm births and all first and second deliveries of women for risk analysis in a well-defined rural population. The large sample size of the study allowed risk stratification. The validity of the study results was supported by the observed dose–response relationship of preterm birth recurrence by gestational age and similar risk estimates observed between three periods of the study cohort (1990–1999, 2000–2009 and 2010–2019) and between spontaneous and indicated preterm birth categories (2005–2019). We used the prospectively collected LMP-based gestational age and delivery date, which is unique in a low-resource rural setting. Smoking is a risk factor for preterm birth recurrence,[53] but women in the study area practically never smoke, and this factor was therefore not included in the analysis.[54] Finally, 6999 participants were not included in the analysis due to a lack of valid gestational age and covariate information. This number of omissions was only 8.8% of the participants, unlikely to influence the study's risk estimates.

We used vaginal and caesarean deliveries to represent spontaneous and induced delivery. These proxy measurements may cause misclassification of clinical type of delivery and, therefore, may influence the present study's observed risk estimates for women with vaginal and caesarean deliveries. Further, the caesarean section data from 2005 and onwards did not include information on the elective caesarean section, particularly at the 37 and 38 weeks of delivery. We need more information to explore the mechanisms of how the subsequent recurrence of preterm birth was affected by caesarean deliveries. We only included live births in the first and second pregnancies. Therefore, the study could not assess the risks at higher birth orders.

CONCLUSION

In the present study, we have provided unique information on recurrent preterm births in a society that moved from a very high to a much lower total preterm birth burden. Even after adjusting for relevant sociodemographic factors, the study showed an increased risk of preterm birth recurrence in second pregnancies that remained at similar levels across the three-decade study period. These findings underline the importance of identifying women at risk of preterm birth and ensuring appropriate perinatal management of mothers and neonates in low-income settings. However, more research is needed to understand the role of modifiable social and reproductive factors on recurrent preterm birth reduction.

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Contributors SA and AR designed the study. SA, UTN, MR and JP prepared the dataset and were involved in the preliminary analysis. LÅP and AR were involved in the final analysis. SA and AR prepared the first draft of the manuscript. All authors participated in editing the manuscript and approved the final version for submission. The corresponding author had full access to all data and had the final responsibility for the decision to submit for publication. AR is responsible for the overal content as a guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The present study used routine prospectively collected data by the HDSS. HDSS periodically receives consent from the household heads for routine household visits and data collection and receives approval from the Institutional Review Board (IRB) of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). The present study was approved by IRB, the Research and Ethical Review committees of icddr,b (PR- 14069).

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Data availability statement Data are available on reasonable request.

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Supplementary tables and figures

Table S1. Spearman correlation coefficient matrix of maternal characteristics

	Maternal age in years	**Education in years**	**Wealth quintiles**	**Birth interval in months**	**Calendar year of second birth**
Maternal age in years	1	0.103*	0.063*	0.372*	0.133*
Education in years	0.103*	1	0.311*	0.051*	0.392*
Wealth quintiles	0.063*	0.311*	1	0.009	0.028*
Birth interval in months	0.372*	0.051*	0.009	1	0.223*
Calendar year of second birth	0.133*	0.392*	0.028*	0.223*	1

*P<0.05

Table S2. Risk of recurrent preterm birth when all women in the first delivery were included regardless of whether they had a second delivery or not. Cox proportional hazards analysis (n=25,140, events=2118, censored=23,022).

Gestational age at first birth (weeks)	No. of women followed-up	Events*		Unadjusted Hazards Ratio (95% confidence interval)	Adjusted Hazards Ratio (95% confidence interval)†‡
		No.	%		
<37	3848	633	16.4	2.26 (2.06-2.48)	1.67 (1.52-1.85)
≥37	21292	1485	7.0	1	1

*Preterm birth in second pregnancy
†Adjusted for socioeconomic status by asset quintiles, maternal education, and year follow-up ended.
‡Schoenfeld residuals proportional hazard assumption *P*=0.086

Table S3. Recurrent preterm birth risks stratified by study period in Matlab, Bangladesh, 1990 to 2019.

	1990-1999			2000-2009			2010-2019		
Gestational age at birth (weeks)	n (%)	Crude OR (95% CI)	Adjusted OR (95% CI) †	n (%)	Crude OR (95% CI)	Adjusted OR (95% CI) †	n (%)	Crude OR (95% CI)	Adjusted OR (95% CI) †
<32	65 (2.0)	3.72 (2.24 – 6.19)	3.64 (2.18 – 6.07)	72 (1.3)	5.47 (3.33 – 8.96)	5.29 (3.21 – 8.73)	43 (0.8)	2.95 (1.40 – 6.19)	2.92 (1.39 – 6.15)
32-33	172 (5.3)	3.06 (2.19 – 4.28)	3.02 (2.15 – 4.22)	170 (3.0)	4.50 (3.19 – 6.35)	4.12 (2.91 – 5.83)	87 (1.5)	3.54 (2.14 – 5.86)	3.54 (2.14 – 5.88)
34-36	675 (21.0)	1.86 (1.50 – 2.30)	1.84 (1.48 – 2.28)	767 (13.7)	2.75 (2.24 – 3.39)	2.55 (2.07 – 3.15)	464 (7.9)	2.90 (2.26 – 3.74)	2.89 (2.24 – 3.72)
37-38	791 (24.6)	1.57 (1.27 – 1.93)	1.55 (1.26 – 1.92)	1367 (24.4)	1.92 (1.59 – 2.31)	1.8 (1.53 – 2.22)	1350 (23.7)	1.72 (1.41 – 2.09)	1.72 (1.41 – 2.08)
≥39*	1515 (47.1)	1	1	3233 (57.6)	1	1	3796 (66.1)	1	1

†Adjusted for maternal education, socioeconomic status by wealth quintiles, and calendar year of second birth
*Reference category

Table S4. Recurrent spontaneous preterm birth odds in second pregnancy by spontaneous and indicated preterm birth in first pregnancy in Matlab, Bangladesh, 2005 to 2019.

	Spontaneous preterm birth odds in second pregnancy			
Gestational age at birth (weeks) in first pregnancy	<37 Gestational weeks (n)	≥37 Gestational weeks (n)	Crude odds ratio (95% confidence intervals)	Adjusted odds ratio (95% confidence interval) [†]
<37, spontaneous (n)	87	322	2.81 (2.18 – 3.63)	3.13 (2.40 – 4.07)
<37, induced (n)	1	4	2.60 (0.29 – 23.34)	3.00 (0.33 – 27.04)
≥37[*] (n)	464	4831	1	1

[†]adjusted for maternal education, socioeconomic status by wealth quintiles, and calendar year of second birth
[*]reference category

Table S5. Recurrent indicated preterm birth odds in second pregnancy by spontaneous and indicated preterm birth in first pregnancy in Matlab, Bangladesh, 2005 to 2019.

	Indicated preterm birth odds in second pregnancy			
Gestational age at birth (weeks) in first pregnancy	<37 Gestational weeks (n)	≥37 Gestational weeks (n)	Crude odds ratio (95% confidence intervals)	Adjusted odds ratio (95% confidence interval) [†]
<37, spontaneous (n)	13	72	1.28 (0.70 – 2.34)	1.23 (0.67 – 2.26)
<37, induced (n)	29	73	2.82 (1.80 – 4.41)	2.73 (1.75 – 4.29)
≥37[*] (n)	287	2035	1	1

[†]adjusted for maternal education, socioeconomic status by wealth quintiles, and calendar year of second birth
[*]reference category

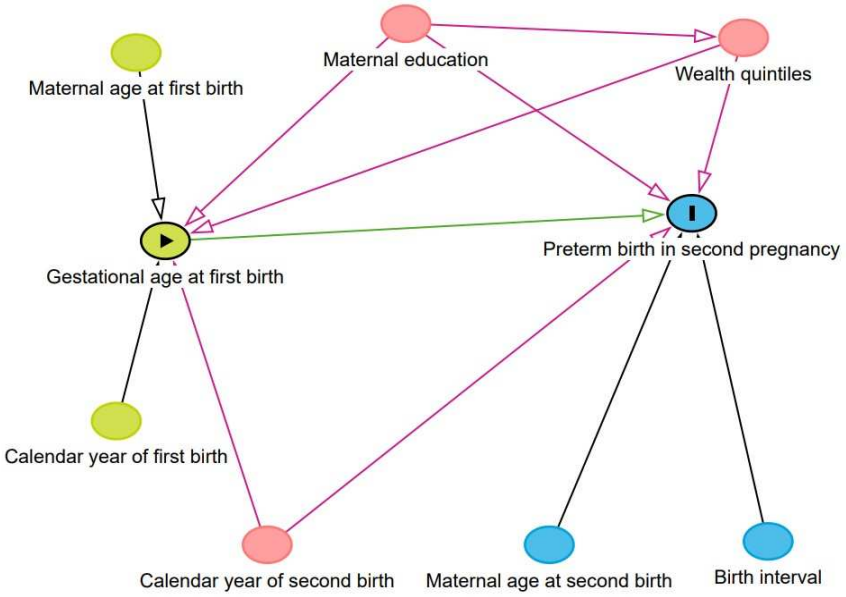

Figure S1: Directed acyclic graph showing exposure, outcome and other observed covariates. The exposure is marked green with an arrow; the outcome is marked blue with a vertical line; the ancestors of the outcome are marked blue; the ancestors of outcome and exposure are marked red.

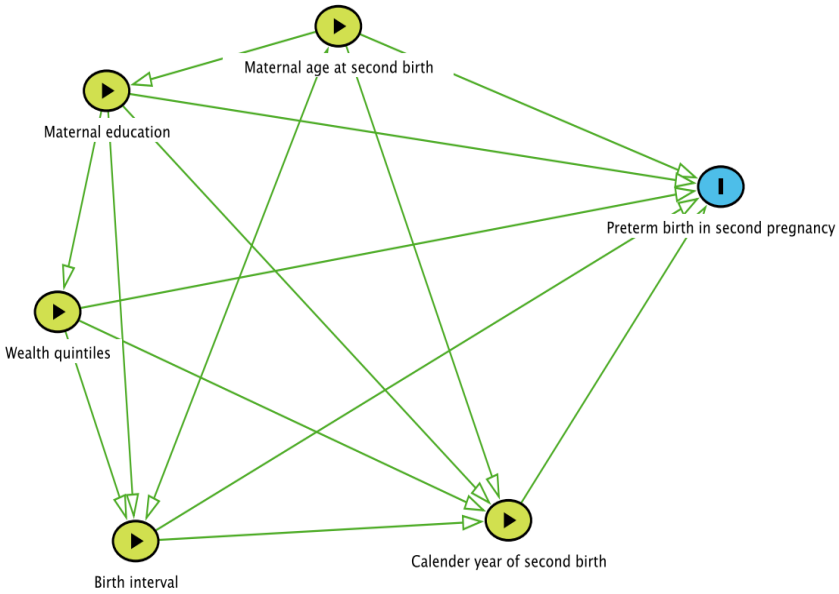

Figure S2: Directed acyclic graph showing exposures and outcome. Exposures are marked green with an arrow, and the outcome is marked as blue with a vertical line.

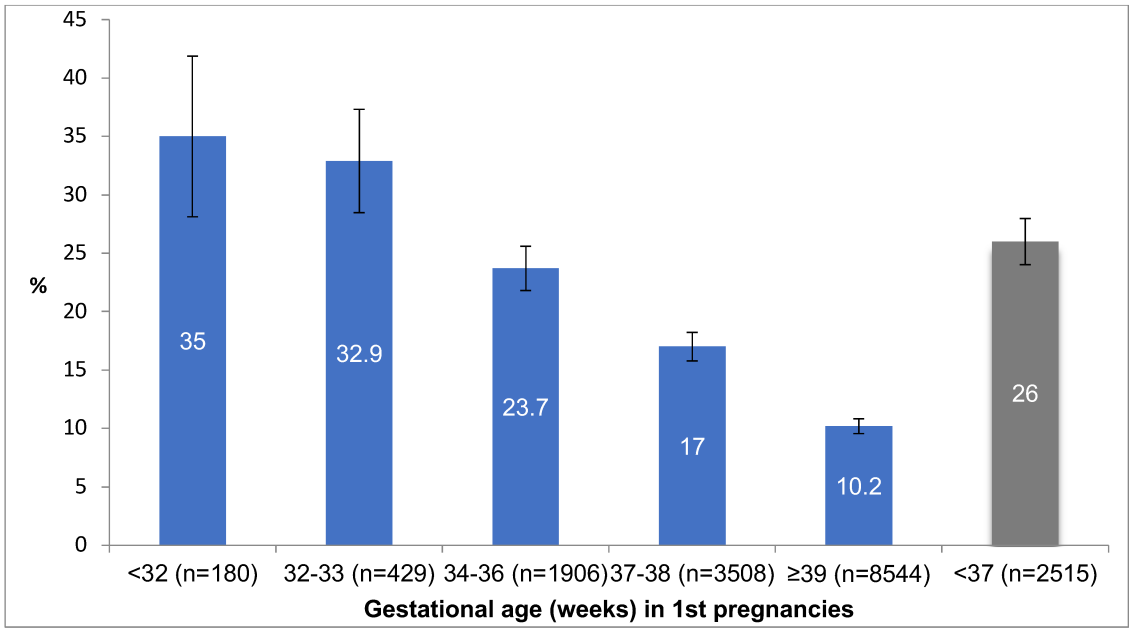

Figure S3. Proportion of preterm birth in second pregnancy based on the gestational age at delivery in first pregnancy in Matlab, Bangladesh, 1990 to 2019