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Association between antenatal care visit and preterm birth: a cohort study in rural Bangladesh

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ABSTRACT

Background Strengthening the antenatal care programme is suggested as one of the public health strategies to reduce preterm birth burden at a population level. However, the evidence so far available is inconclusive.

Objectives To evaluate the association between antenatal care (ANC) visit and preterm birth; and also to explore to what extent the increased usage of ANC after the initiation of the Maternal, Neonatal and Child Health (MNCH) project in Matlab, Bangladesh, contributed to the reduction of preterm birth.

Setting This population-based cohort study was conducted in Matlab, a subdistrict under Chandpur. The analysis was based on data collected from 2005 to 2009. In 2007, an MNCH project was initiated in the area that strengthened the ongoing ANC services.

Participants In total, 12 980 live births with their mothers during the study period were included in the analysis.

Analysis We performed logistic regression with generalised estimating equation models to evaluate the associations.

Outcome measures Preterm birth.

Results The number of ANC visits was associated with preterm birth in a dose-dependent way (p for linear trend <0.001). The adjusted odds of preterm birth were 2.4-times higher (OR 2.37, 95% CI 2.07 to 2.70) among women who received ≤1 ANC compared with women who received ≥3 ANC. We observed a significant reduction of preterm birth rates (OR 0.69, 95% CI 0.61 to 0.77) in the period after (2008 to 2009) MNCH project initiation in comparison to the period before (2005 to 2006). Controlling for ANC visits substantially attenuated this observed effect of the MNCH project on preterm birth (OR 0.88, 95% CI 0.77 to 0.99) (Sobel test of mediation p<0.001).

Conclusions ANC visits are associated with decreased occurrences of preterm births. Strengthening the ANC services should be prioritised in countries with high preterm birth rates to reduce the preterm birth burden at the population level.

Strengths and limitations of this study

► To our knowledge, this is the first study in Bangladesh that evaluated the association between antenatal care (ANC) and preterm birth occurrence.
► The study includes population-based prospectively collected data with a low number of missing information.
► Lack of information on the uptake of individual intervention prevented understanding of the role of each service included in the ANC package in the study area.
► Residual confounding may remain after sociodemographic variables adjustment due to the differential of important behavioural characteristics between groups based on the number of ANC visits.

15 million babies born preterm every year worldwide approximately one million dies within 28 days of birth due to complications from being born too soon.[2 3] Prevention of preterm birth and its associated adverse health outcomes remain one of the major public health issues all over the world. The pregnancy period is considered a critical window of opportunity for shaping the future health and well-being of mothers, fetuses and neonates.[4 5] Antenatal care (ANC) helps identify high-risk women to facilitate timely management of morbidities during pregnancy.[5] It also influences the change of harmful practices associated with adverse maternal and newborn health outcomes, including preterm birth incidence.[6–9] Strengthening the ANC programme is suggested as one of the public health strategies to reduce preterm birth burden at a population level. However, the evidence so far available is inconclusive.

Several studies have reported preterm birth associations with hypertensive disorder, vaginal bleeding and urogenital infections.[10–13] Lifestyle factors such as physical activities, stress and smoking during pregnancy are also found to be related to preterm

INTRODUCTION

Preterm birth is one of the adverse pregnancy outcomes responsible for significant morbidity and mortality among children less than 5 years of age.[1] Out of the estimated

birth.[14–17] An efficient ANC programme is expected to identify these maternal and social risk factors so that appropriate measures may be taken in time. Epidemiological studies have reported the associations between ANC uptake and preterm birth occurrence.[18–20] A population-based study among adolescent pregnancies reported a strong association between inadequate ANC coverage and preterm birth.[21] The risk increase in preterm birth is also correlated with the timing of care sought—the risk is higher in women who start ANC in late trimesters in comparison to women who started care in the early period of pregnancy.[7 22 23]

In contrast to the above findings, few studies did not observe any relationship between ANC uptake and preterm birth.[24 25] The evidence available so far is suggestive of an association between ANC and preterm birth occurrence. The earlier studies also had several limitations: the analyses mostly confined within a selected group of the population, the ANC package was not well described and the essential covariates were not available to adjust for potential confounding effects. Moreover, the number of studies from low-income countries is relatively low, with no report being available from Bangladesh thus far.

We initiated the Maternal, Neonatal and Child Health (MNCH) project in 2007 in rural Matlab, Bangladesh, that implemented evidence-based maternal and child health interventions along the continuum of pregnancy through postpartum periods. The MNCH project demonstrated that the intervention caused up to 36% reduction in perinatal mortality over the 2 years period of the study.[26] A substantial proportion of this mortality reduction was mediated by the increased usage of ANC.[27] Recently, we have demonstrated that the preterm birth rates decreased remarkably over the last 25 years in the same study area. About a quarter of this reduction was attributed to education and parity.[28] However, the influence of the area's ANC services on preterm birth occurrence remained unexplored. In this paper, we evaluated the associations between ANC and preterm birth. We also explored the extent to which the increased usage of ANC after the initiation of the MNCH project contributed to the reduction of preterm birth in rural Matlab, Bangladesh.

METHODS
Study setting, design and participants
The study site is located in Matlab upazila under Chandpur district. The International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) has been running a Health and Demographic Surveillance System (HDSS) over a population of about 220 000 in the area since 1966. In half of the HDSS area, icddr,b provides healthcare services to the women of childbearing ages and their children less than 5 years in age. This service area is divided into four administrative blocks. Each block serves a population of about 27 000 through a subcentre, staffed by

midwives, that provides 24 hours delivery care. Clinical services in the subcentres are supported by an icddr,b Hospital, located in Matlab Municipality, that offers basic obstetric care and is staffed by medical doctors and nurses. In the study area, icddr,b provides all services including ANC free-of-cost. It also ensures the availability of healthcare providers, and all logistics and supplies to facilitate the uptake of recommended services to all clients.

In this paper, we first analysed the prospectively collected data from 2005 to 2009 to evaluate the association between the number of ANC visits and preterm birth occurrences. We then used a before-after study design within the cohort to assess the effect of ANC coverage on preterm birth occurrences between the periods before (2005 to 2006) and after (2008 to 2009) implementation of the MNCH project. In total, 12 980 women who delivered live birth babies during the study period were included in the analysis.

The study participants in the MNCH Project provided the written informed consent.

Antenatal care services in the study area
According to the WHO's previous recommendation of four-visit focussed ANC for an uncomplicated pregnancy, we offer a minimum of four ANC services to all women in the icddr,b area. While the timing of ANC visits was flexible in the past, the schedule was fixed after the commencement of the MNCH project in 2007, with visits occurring 15 to 19, 24, 32 and 36 gestation weeks (GWs) of age. In the MNCH project period, we established an auto-generated ANC visit schedule based on the last menstrual period (LMP) dates of pregnant women to facilitate universal ANC coverage to all women in the study area. The ANC visit schedules were then sent to respective Community Health Workers (CHWs), subcentre clinics and icddr,b Hospital. The schedule was also recorded in the Take Action Card that contained educational materials to inform women of danger signs during pregnancy, delivery and postpartum periods.[27] This ANC schedule recording helped women to recapitulate the date of their upcoming ANC visit from the respective icddr,b facility.

We offered a package of ANC services that covered activities such as history taking, physical examination, risk identification and management and counselling, including birth preparedness. During the MNCH project period, we continued all the services mentioned above. However, the project also strengthened some of the existing services (mostly the counselling and behaviour change communication) and added new interventions in the ANC package. The new interventions were: (i) routine ultrasound for assessment of fetal growth, multiple pregnancies, congenital anomalies and malpresentation, (ii) anti-helminthic supplementation in the second trimester, (iii) antibiotic use for women with preterm premature rupture of the membranes, (iv) corticosteroid use for women with the risk of preterm birth and (iv) routine assessment and treatment of urinary tract infections (UTIs) in women attending the icddr,b Hospital. We also standardised the

existing counselling on nutrition, recognition of danger signs and birth preparedness by training all healthcare providers and introducing a checklist (online supplementary document S1) with periodic refresher training. The counselling was provided to women along with their support persons—the family members selected by the CHWs who agreed to be present during ANC visits and delivery. The details of ANC contents in the study area are described elsewhere (online supplementary document S2).[27] In the study area, women who visited icddr,b facilities for ANC received all the interventions included in the ANC package adopted for that particular period.

Data collection

The present paper used the prospectively collected data by the HDSS from 2005 to 2009 and also used the MNCH databases for additional information from the period of 2008 to 2009 (online supplementary document S3). In the study area, CHW identified pregnancy during routine home visits at every 2-month interval by urine pregnancy test of a woman who had missed her LMP, CHW then recorded the reported dates if the pregnancy was confirmed. Subsequently, identified women were then followed up prospectively to capture information on pregnancy outcome and ANC usage. Exposure was assessed by the number of ANC women received.

Miscarriage was defined as the loss of a fetus before 28 weeks of gestation. Stillbirth was defined as the birth of a dead fetus at or above 28 weeks of gestation. Live birth was defined as delivery of a fetus with any sign of viability.[26] Due to the unavailability of ultrasound assessment of gestation age during 2005 to 2006, we used reported LMP from the HDSS databases for the uniform assessment of gestational age during the study period. Gestational age was calculated by subtracting the LMP date from the date of delivery and was expressed in weeks. The outcome was preterm birth, which was defined as the delivery of a live-born baby before 37 completed GWs of age.

Detailed information on covariates such as women's age, parity, socioeconomic condition, education, mode of delivery, year of delivery, inter-pregnancy intervals, previous preterm birth and previous adverse pregnancy outcomes was extracted from the HDSS databases. Parity was defined as the number of live or dead children before the current pregnancy. The education level was determined by the number of years attended in schools. We assessed the socioeconomic condition by generating scores through principal component analysis based on the ownership of household assets such as selected consumer items (television, watch, and so on), dwelling characteristics (wall and roof materials) and type of drinking water and toilet facilities. The generated scores were then categorised into quintiles, where 1 represented the poorest and 5 the richest. The mode of delivery was assigned as a vaginal or caesarean section delivery. We calculated the inter-pregnancy interval by subtracting the LMP date of index pregnancy from the previous pregnancy outcome date and expressed in months. In addition,

we also calculated the gestational age of previous pregnancy, and categorised the live birth as previous preterm or term birth. Stillbirths or spontaneous abortions in the last pregnancy were considered as previous adverse pregnancy outcomes.

Due to data unavailability in the period before the MNCH project, we extracted some additional information from the MNCH databases to use in the analysis. We categorised ANC visits as timely or untimely for each visit window as per the protocol.[26] The visit was considered timely if the women had received ANC in the period 15 to 19 GWs, 23 to 25 GWs and 31 to 33 GWs for first, second and third ANC visits periods, respectively. Visits outside the range were considered untimely. Body mass index (BMI) was calculated by weight in kilograms divided by the square of the height in metres (kg/m^2). We diagnosed UTI if a woman had any symptoms (dysuria, frequency, urgency, lower abdominal or back pain and fever) of suspected UTI and if microscopic examination of urine revealed more than five pus cells per high power field. We also extracted the information if a woman was referred to a higher centre (from subcentre to icddr,b Hospital, or from icddr,b Hospital to subdistrict or district level facilities) for complications identified during ANC contact.

Statistical analysis

We analysed the data using descriptive and analytical approaches. In the analyses, live birth was categorised into preterm (GWs<37) and term (GWs≥37) births. Preterm birth was further categorised into very preterm (<32 GWs), moderate preterm (32 to 33 GWs) and late preterm births (34 to 36 GWs). We categorised the ANC visits into ≤1, 2 and ≥3 ANC visits due to a small number of women in 0 and >3 ANC visit groups. This categorisation of ANC visits is consistent with a previous publication with the same data set,[27] and also facilitated comparison of the period before and after the MNCH project due to small number of sample with >3 visits in the earlier period. Further, the timeliness of ANC usage was categorised into timely or untimely. Among the available covariates, we categorised age into <20, 20 to 24, 25 to 34 or ≥35 years, parity into 0, 1 to 2 or ≥3, education into 0, 1 to 5 or ≥6 years, and socioeconomic status by quintiles of asset scores. The number of birth was assigned as a singleton or twin birth. The inter-pregnancy interval was categorised into <6, 6 to 11, 12 to 17, 18 to 23, 24 to 47 and ≥48 m groups. Associations of covariates with ANC and preterm birth were determined by χ^2 tests. A covariate was assigned as a confounding factor if it was associated with both ANC and preterm birth. We performed the multiple logistic regression using generalised estimating equation models to estimate the odds of preterm birth adjusted for the confounding factors. This analytical model allowed us to adjust for multiple pregnancies in a single subject. We also assessed the effect of ANC usage on preterm birth odds after inclusion of stillbirths. Results of the regression were presented by ORs with their 95% CIs.

Table 1 The coverage of antenatal care visits by year in Matlab, Bangladesh

| | No. of antenatal care visits | | | | |
| | 0 | 1 | 2 | 3 | 4 or more |
	n (%)	n (%)	n (%)	n (%)	n (%)
2005	149 (5.7)	434 (16.6)	972 (37.3)	946 (36.3)	108 (4.1)
2006	86 (3.3)	323 (12.4)	1039 (40.0)	1036 (39.9)	112 (4.3)
2007	127 (4.9)	276 (10.7)	1015 (39.5)	792 (30.8)	358 (13.9)
2008	125 (4.7)	176 (6.6)	359 (13.4)	709 (26.5)	1311 (48.9)
2009	92 (3.6)	141 (5.6)	233 (9.2)	588 (23.3)	1473 (58.3)

To determine how ANC visits accounted for observed changes in preterm birth rates during the MNCH project period, we assessed the change in magnitude and significance of the pre–post intervention dummy variable (before=0; after=1) when adjusting for covariates, and ANC visits consecutively in different models. We conducted a Sobel test to assess whether ANC visits significantly mediated the effect of the MNCH intervention on the preterm birth rate.[29]

Patient and public involvement

Community residents or study participants were not involved in the elaboration of the research questions and study designs. There are no plans to disseminate the results of the research to study participants.

RESULTS

Out of 15 518 pregnancies recorded by the HDSS, 13 170 resulted in live births, 312 resulted in stillbirths and 2018 in miscarriages. Out of the total live birth deliveries, 190 had missing information on the sociodemographic variables, leaving 12 980 births (12 675 singletons and 305 twin birth) for analysis in the present paper.

During the MNCH study period, ANC usage was increased (table 1). The proportion of women with three or more ANC visits increased from 40% in 2005 to 82% in 2009. The median gestation age at the first ANC visit was 17 weeks for all groups of women who received 1 or 2 or ≥3 ANC. The median gestation age at the second ANC visit was also the same (27 weeks) for women who received 2 or ≥3 ANC. The median gestation age of preterm birth babies of women who received ≤1, 2 and ≥3 ANC was 35, 35 and 36 weeks, respectively. Among the total preterm births in the groups ≤1 ANC and 2 ANC, about 4% took place before 27 weeks.

There was a decreasing pattern of very, moderate and late preterm births during the study period; however, the decrease in late preterm birth was pronounced. Overall the preterm birth rate decreased from about 16.5% in 2005 to 11% in 2009 (table 2). We did not observe any changes in preterm birth proportions among the neonates born by caesarean section during the study period (table 2).

Table 3 presents the background characteristics of study women by year. Although we observed significant associations of the year of births with women's age, parity, attendance in school and socioeconomic condition by asset quintiles, the changes over the study periods were small. However, the caesarean section rates increased from 7% in 2005 to 18% in 2009 (table 3).

All the available covariates except inter-pregnancy interval and previous adverse pregnancy outcomes were found associated with ANC and preterm birth (table 4). Therefore, those factors were considered as potential confounders for adjustment in the regression model. Preterm births were more common in the older and higher birth order groups than in the younger and lower birth order groups, respectively. Higher school attendance and socioeconomic group women experienced less preterm birth occurrences in comparison to other groups. Women with previous preterm birth had a high proportion of preterm birth compared with women with previous term birth (table 4).

Additional information during the period of the MNCH project is presented in online supplementary table S1. The proportions of timely and untimely visits for first ANC visits were 68% and 32%, for second ANC visits were 25% and 75% and for third ANC visits were 69% and 31%, respectively. About 18% of women were underweight, 72% were normal weight and 10% were overweight. Among the women who attended ANC visits, about 3% had UTI and 10% were referred to a higher centre for complications (online supplementary table S1). We did not observe any association of preterm birth with prenatal BMI, UTI and referral to higher centres (data not shown).

In the logistic regression analysis, preterm birth was associated with the number of ANC visits in a dose-dependent way (p for linear trend <0.001). ORs of preterm birth were 2.37 (95% CI 2.07 to 2.70) and 1.73 (95% CI 1.54 to 1.94) for women who received ≤1 and 2 ANC visits, respectively, in comparison to the women who received ≥3 ANC visits (table 5).

When the analysis was stratified in different preterm birth categories, the ORs of very, moderate and late preterm births to the women who received ≤1 ANC were 5.80 (95% CI 4.20 to 8.07), 2.11 (95% CI 1.53 to 2.90) and 1.77 (95% CI 1.52

Table 2	The proportion of preterm birth by gestation age categories in 2005 to 2009 in Matlab, Bangladesh				
	2005	2006	2007	2008	2009
Very preterm (<32 GWs), % (95% CI)	2.0 (1.5 to 2.6)	2.0 (1.5 to 2.6)	3.1 (2.5 to 3.9)	1.6 (1.2 to 2.1)	1.6 (1.2 to 2,1)
Moderate preterm (32 to 33 GWs), % (95% CI)	2.6 (2.0 to 3.2)	2.4 (1.9 to 3.0)	2.7 (2.1 to 3.4)	1.8 (1.3 to 2.3)	1.4 (1.0 to 2.0)
Late preterm (33 to 36 GWs), % (95% CI)	12.0 (10.8 to 13.3)	11.7 (10.5 to 13.0)	10.4 (9.2 to 11.6)	8.8 (7.8 to 10.0)	8.0 (7.0 to 9.1)
All preterm births (<37 GWs), % (95% CI)	16.5 (15.1 to 17.9)	16.0 (15.0 to 17.4)	16.2 (14.7 to 17.6)	12.2 (10.9 to 13.4)	11.0 (9.8 to 12.3)
All preterm births (<37 GWs) in CS, % (95% CI)	10.7 (6.9 to 16.1)	11.4 (7.7 to 16.2)	14.2 (10.7 to 18.6)	13.5 (10.3 to 17.4)	8.5 (6.2 to 11.4)

CS, caesarean section; GWs, gestation weeks.

to 2.06), respectively, compared with the women with ≥3 ANC. The corresponding ORs for women with 2 ANC were 3.04 (95% CI 2.19 to 4.23), 2.26 (95% CI 1.72 to 2.97) and 1.40 (95% CI 1.22 to 1.59), respectively, compared with the women who received ≥3 ANC visits.

Furthermore, we observed that the odds of preterm birth increased for women with untimely visits compared with the women with timely visits after adjusting the available covariates. However, when the numbers of ANC visit categories were introduced in the model, the associations were no more observed (online supplementary table S2). We observed similar preterm birth odds when stillbirths were included in the analysis (online supplementary table S3).

We observed a 30% decrease in preterm birth odds (OR 0.70, 95% CI 0.63 to 0.78) in the base model (no factor was adjusted for) among the women delivered in the study area after the intervention period. Consecutive adjustment of covariates in model 2 (maternal age, parity, education in year and asset quintile) and model 3 (the mode of delivery, previous preterm birth and multiple births), we observed almost no change in effect estimates with 31% decrease in preterm birth odds (OR 0.69, 95% CI 0.61 to 0.77). In the final model (model 4), when we added ANC visits for adjustment, we observed substantial attenuation of the odds during the MNCH intervention period (OR 0.88, 95% CI 0.77 to 0.99) (table 6). A Sobel test indicated that the reduction of effect when adjusting for ANC visit was statistically significant (p<0.001). This finding suggests increasing ANC coverage accounted for the significant portion of the reduction of odds of preterm birth due to the MNCH programme.

DISCUSSION

Preterm birth remains one of the important public health problems worldwide. In the present study, we observed that the number of ANC visits was associated with preterm birth in a dose-dependent way. The women who attended more ANC visits had fewer probabilities of having preterm births. For the first time, we have demonstrated that high usage of ANC service appears to mediate a large proportion of the observed 31% decreased odds of preterm birth burden after the initiation of the MNCH project which helped in strengthening ANC services in the area (online supplementary document S1 and S2). The reduction in preterm was the probable direct effect of increased usage of ANC rather than the sociodemographic or selected reproductive health factors included in the analyses. The study findings underscore that ANC services might play a substantial role in the reduction of preterm birth at population level.

There is a scarcity of studies evaluating the association between usage of ANC and preterm birth occurrence. The study finding is consistent with a few studies that reported that women with inadequate ANC care had a higher risk of preterm birth.[18 19 30 31] However, these studies are mostly from high-income countries. Therefore the effect

Table 3 Characteristics of pregnant women in the study in Matlab, Bangladesh

Variable name	2005 n (%)	2006 n (%)	2007 n (%)	2008 n (%)	2009 n (%)	P value*
Age in year						<0.001
<20	266 (10.2)	296 (11.4)	269 (10.5)	299 (11.2)	279 (11.0)	
20–24	826 (31.7)	858 (33.1)	678 (26.4)	887 (33.1)	845 (33.4)	
25–34	1186 (45.5)	1152 (44.4)	1373 (53.5)	1237 (46.2)	1144 (45.3)	
≥35	331 (12.7)	290 (11.2)	248 (9.7)	257 (9.6)	259 (10.2)	
Parity						<0.001
0	904 (34.6)	995 (38.3)	965 (37.6)	1002 (37.4)	1000 (39.6)	
1–2	1282 (49.1)	1206 (46.5)	1259 (49.0)	1348 (50.3)	1235 (48.9)	
≥3	423 (16.2)	395 (15.2)	344 (13.4)	330 (12.3)	292 (11.6)	
Education in year						<0.001
0	484 (18.6)	546 (21.0)	307 (12.0)	581 (21.7)	400 (15.8)	
1–5	708 (27.1)	639 (24.6)	550 (21.4)	796 (29.7)	619 (24.5)	
≥6	1417 (54.3)	1411 (54.4)	1711 (66.6)	1303 (48.6)	1508 (59.7)	
Asset quintiles						0.013
1-poorest	409 (15.7)	408 (15.7)	363 (14.1)	428 (16.0)	374 (14.8)	
2	467 (17.9)	436 (16,8)	442 (17.2)	453 (16.9)	429 (17.0)	
3	504 (19.3)	570 (22.0)	523 (20.4)	577 (21.5)	474 (18.8)	
4	623 (23.9)	568 (21.9)	594 (23.1)	594 (22.2)	557 (22.0)	
5-richest	606 (23.2)	614 (23.7)	646 (25.2)	628 (23.4)	693 (27.4)	
Mode of delivery						<0.001
Vaginal	2431 (93.2)	2373 (91.5)	2255 (87.9)	2310 (86.2)	2066 (81.8)	
Caesarean	178 (6.8)	221 (8.5)	309 (12.1)	370 (13.8)	461 (18.2)	
Pregnancy type						
Twin	69 (2.6)	42 (1.6)	22 (2.1)	60 (2.2)	79 (3.1)	0.006
Singleton	2540 (97.4)	2554 (98.4)	2513 (97.9)	2620 (97.8)	2448 (96.9)	
Inter-pregnancy interval in month						
<6	132 (8.1)	86 (5.6)	108 (7.1)	120 (8.2)	91 (6.8)	0.001
6–11	94 (5.8)	67 (4.4)	77 (5.1)	81 (5.6)	78 (5.9)	
12–17	110 (6.8)	113 (7.4)	98 (6.5)	71 (4.9)	73 (5.5)	
18–23	133 (8.2)	112 (7.3)	106 (7.0)	90 (6.2)	91 (6.8)	
24–47	598 (36.7)	555 (36.2)	547 (36.2)	512 (35.1)	430 (32.4)	
≥48	562 (34.5)	601 (39.2)	575 (38.1)	585 (40.1)	566 (42.6)	
Previous preterm birth						
<37 gestation weeks	237 (17.8)	243 (19.0)	189 (15.0)	194 (16.3)	146 (13.7)	0.003
≥37 gestation weeks	1098 (82.2)	1033 (81.0)	1075 (85.0)	999 (83.7)	918 (86.3)	
Previous pregnancy outcomes						
Induced miscarriage	46 (2.8)	25 (1.6)	26 (1.7)	29 (2.0)	30 (2.3)	0.35
Spontaneous miscarriage	165 (10.1)	142 (9.3)	145 (9.6)	167 (11.4)	172 (12.9)	
Stillbirth	42 (2.6)	49 (3.2)	47 (3.1)	42 (2.9)	38 (2.9)	
Live birth	1376 (84.5)	1318 (85.9)	1293 (85.6)	1221 (83.7)	1089 (81.9)	

*By χ² tests.

estimates may not be easily comparable due to differences in ANC contents and service delivery systems in low-income country settings. While two studies from USA and China and few systematic reviews showed a similar increased risk of preterm births with prenatal cares, they are not comparable to our findings due to dissimilarities

Table 4 Association of background characteristics with antenatal care visits and gestational age at birth in Matlab, Bangladesh, 2005 to 2009

| | No. of antenatal care visits | | | | No. of births by gestational age | | |
| | 0–1 | 2 | ≥3 | | <37 weeks | ≥37 weeks | |
	n (%)	n (%)	n (%)	P value*	n (%)	n (%)	P value*
Age in year				<0.001			<0.001
<20	199 (14.1)	407 (28.9)	803 (57.0)		182 (12.9)	1227 (87.1)	
20–24	559 (13.7)	1141 (27.9)	2394 (58.5)		524 (12.8)	3570 (87.2)	
25–34	894 (14.7)	1676 (27.5)	3522 (57.8)		841 (13.8)	5251 (86.2)	
≥35	277 (20.0)	394 (28.4)	714 (51.6)		320 (23.1)	1065 (76.9)	
Education in year				<0.001			<0.001
0	435 (18.8)	659 (28.4)	1224 (52.8)		424 (18.3)	1894 (81.7)	
1–5	508 (15.3)	912 (27.5)	1892 (57.1)		550 (16.6)	2762 (83.4)	
≥6	986 (13.4)	2047 (27.9)	4317 (58.7)		893 (12.1)	6457 (87.9)	
Parity				<0.001			<0.001
0	610 (12.5)	1399 (28.8)	2857 (58.7)		565 (11.6)	4301 (88.4)	
1–2	939 (14.8)	1707 (27.0)	3684 (58.2)		909 (14.4)	5421 (85.6)	
≥3	380 (21.3)	512 (28.7)	892 (50.0)		393 (22.0)	1391 (78.0)	
Asset quintiles				<0.001			<0.001
1-poorest	365 (18.4)	558 (28.2)	1059 (53.4)		395 (19.9)	1587 (80.1)	
2	336 (15.1)	659 (29.6)	1232 (55.3)		345 (15.5)	1882 (84.5)	
3	435 (16.4)	754 (28.5)	1459 (55.1)		386 (14.6)	2262 (85.4)	
4	382 (13.0)	798 (27.2)	1756 (59.8)		375 (12.8)	2561 (87.2)	
5-richest	411 (12.9)	849 (26.6)	1927 (60.5)		366 (11.5)	2821 (88.5)	
Mode of delivery				<0.001			0.001
Vaginal	1727 (15.1)	3257 (28.5)	6451 (56.4)		1688 (14.8)	9747 (85.2)	
Caesarean section	202 (13.1)	357 (23.2)	980 (63.7)		177 (11.5)	1362 (88.5)	
Inter-pregnancy interval in month							
<6	92 (17.1)	154 (28.7)	291 (54.2)	<0.001	93 (17.3)	444 (82.7)	0.096
6–11	69 (17.4)	96 (24.2)	232 (58.4)		49 (12.3)	348 (87.7)	
12–17	82 (17.6)	131 (28.2)	252 (54.2)		81 (17.4)	384 (82.6)	
18–23	104 (19.5)	130 (24.4)	298 (56.0)		84 (15.8)	448 (84.2)	
24–47	425 (16.1)	708 (26.8)	1509 (57.1)		383 (14.5)	2259 (85.5)	
>=48	369 (12.8)	819 (28.3)	1701 (58.9)		473 (16.4)	2416 (83.6)	
Previous birth							
<37 gestation weeks	197 (19.5)	297 (29.4)	515 (51.0)	<0.001	294 (29.1)	715 (70.9)	<0.001
≥37 gestation weeks	741 (14.5)	1383 (27.0)	2999 (58.5)		658 (12.8)	4465 (87.2)	
Previous adverse pregnancy outcomes							
Yes	133 (13.2)	264 (26.2)	612 (60.7)	0.047	148 (14.7)	861 (85.3)	0.789
No	1008 (15.6)	1774 (27.5)	3671 (56.9)		1015 (15.7)	5438 (84.3)	

*By χ² tests.

in population, model selection or the way the prenatal care usage was measured.[20 21 32] On the other hand, a few studies did not find any association, and a discrepancy with our study findings may be due to the selected population group and different inclusion criteria in those studies.[25 33]

The possible role of ANC on the attenuation of the odds of preterm birth during the MNCH project period

Table 5 Association between antenatal care and preterm birth among pregnant women in Matlab, Bangladesh, 2005 to 2009

No. of antenatal care visit	Crude		Adjusted*	
	OR	95% CIs	OR	95% CIs
≤1	2.63	2.32 to 2.99	2.37	2.07 to 2.70
2	1.75	1.57 to 1.96	1.73	1.54 to 1.94
≥3†	1	1	1	1

*Adjusted for women's age, parity, education in years, asset quintiles, mode of delivery, previous preterm birth and multiple births.
†Reference category

may not be fully explained; however, a few potential factors may be mentioned. Strengthening the existing prenatal care services and adding new interventions in the programme probably facilitated early detection and management of risk factors such as preterm birth in the previous pregnancy, multiple births, anaemia, diabetes, hypertensive disorders and UTIs, and thus influence preterm birth rate reduction (online supplementary document S1 and S2). The high usage of ANC services observed in our study signifies that the pregnant population was exposed to favourable preventive and curative services for preterm birth occurrence. Although inconclusive, the pronounced rate reduction in late preterm birth categories might be further construed as favouring the decline due to ANC. However, the lack of detail morbidity and nutrition information from the previous period of the MNCH project limited our ability to understand the causal pathway between the ANC service usage and preterm birth. Additionally, the possible causes of 12% decrease of preterm birth odds (OR 0.88, 95% CI 0.77 to 0.99) during the MNCH intervention periods even after adjustment of ANC visits remain unexplained.

The strengths of our population-based study are the large sample size with information on dependent and independent variables collected prospectively, and also the inclusion of almost all pregnant population from a defined geographical area. Important sociodemographic and reproductive health factors were available to analyse and adjust for potential confounding effect. However, the study findings should be interpreted cautiously due to the inherent bias related to observation studies, as randomising the participants was not possible due to the universal acceptance of beneficial effect of ANC service provision on maternal and newborn health. Besides, the probability of ANC uptake directly depends on the duration of gestation before the occurrence of outcomes. However, the similar distributions of median gestation ages of preterm births and the significant difference of ORs between the women of ≤1 ANC and 2 ANC usage groups, support the results of the present study. Exclusion of stillbirth from the analysis may lead to underestimation of preterm birth rates.[34] However, it is commonly excluded from the calculation when reporting preterm birth and also for international comparison.[34] Several studies in Bangladesh excluded stillbirths that reported the rates and risk factors of preterm births,[35 36] including the one reported using the data from the same study area.[28] The observed similar effect estimates when stillbirths were included underscore that bias was unlikely due to measurement of preterm birth among live births only (online supplementary table S3).

Although the study has included several important covariates in the analyses, the observed results might be influenced by other unmeasured factors such as smoking, alcohol consumption and infections including, syphilis, HIV and malaria. However, the prevalence of these factors in pregnant women population in rural Bangladesh is extremely low, and therefore probably had no roles in the observed effect estimates.[37–40] Other factors such as stress, physical activity, indoor air pollution and exposure to toxic metals that were reported to increase the risk of preterm births remain unmeasured in the study.[41] Future studies should consider these factors to assess comprehensively the impact of ANC usage on preterm births.

The WHO recommended eight ANC contacts instead of four focussed ANC visits for an uncomplicated pregnancy in 2016.[5] However, most of the low-income countries,

Table 6 Antenatal care and preterm birth before and after Maternal, Neonatal and Child Health (MNCH) project in icddr,b area Matlab, Bangladesh

	ORs (95% CIs)*			
	Model 1†	Model 2‡	Model 3§	Model 4¶
Intervention period				
Before **	1	1	1	1
After	0.70 (0.63 to 0.78)	0.68 (0.60 to 0.76)	0.69 (0.61 to 0.77)	0.88 (0.77 to 0.99)

*Consecutive adjustment of covariates in the model and changes of ORs on preterm birth before (2005 to 2006) and after (2008 to 2009).
†Base model-crude OR.
‡Adjusted for maternal age, parity, education and asset scores.
§Adjusted for covariates in the model 2 + mode of delivery, previous preterm birth and multiple births.
¶Adjusted for the covariates in model 3 + number of antenatal care visits.
**Reference category.
icddr,b, International Centre for Diarrhoeal Disease Research, Bangladesh.

including Bangladesh, have not adopted the new recommendation yet. Further, the coverage of four ANC visits is still low in those countries. The recent report from Bangladesh Health and Demographic Survey in 2018 presented data for the last 3 years. It showed that the precentage of 3+ ANC visits was about 58%.[42] In the study area, we already achieved about 82% 3+ ANC visits in 2009. In the present paper, we emphasise that the programme that achieves high ANC usage and ensures universal coverage of interventions in the ANC package (Document S2) for all clients may facilitate the reduction of preterm birth at the population level. Although the results emanated from 10+ years old data, the finding is still relevant from public health points of view in Bangladesh and most of the low-income countries.

In conclusion, we have reported the associations between ANC uptake and preterm birth incidence. Preterm birth remains one of the major causes of under 5 year mortality globally.[1] Understanding the biology related to preterm birth incidence is still limited. To date, there is a lack of intervention that could reduce the preterm birth burden at a population level. An efficient ANC programme may address many of the socio-behavioural and reproductive factors linked to biological mediators such as infection, inflammation, stressors and nutritional factors causing preterm birth.[43] Pending the availability of a new intervention to address the biological factors associated with preterm birth, the country with high preterm birth rates should prioritise strengthening the ANC services with increased coverage at a population level.

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