

# Preterm birth determinants among newborns at six public hospitals in Northeast Amhara, Ethiopia: unmatched case-control study

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## Research

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# Abstract

## Background

Preterm birth is a global public health problem. Worldwide, every year about 15 million newborns are born preterm and about 1.1 million of them die due to complications related to prematurity. More than 81% of preterm births were in Asia and Sub-Saharan Africa. Nowadays, preterm birth is the first leading cause of under-five mortality and is one of the limiting factors for achieving a reduction in under-five mortality rate. Therefore, the aim of this study was to identify the determinants of preterm birth at public hospitals in the Northeast Amhara, Ethiopia, 2019.

## Method

Hospital-based unmatched case-control study was conducted at public hospitals in Northeast Amhara, Ethiopia from March 15 th to April 25 th , 2019. Data were collected using interviewer-administered structured pre-tested tool and document review for cases and controls. Data were entered in to Epi Info version 7.2.2.6 and exported to SPSS version 23 software for data analysis. Bi-variable and multivariable binary logistic regression were used to measure the association between preterm birth and risk factors. Adjusted Odds ratio (AOR) at 95% confidence interval (CI) was calculated and P value  $\leq 0.05$  declared statistically significant.

## Result

The study identified that ANC follow up less than four visits [AOR 2.267, CI (1.205, 4.264)], pregnancy-induced hypertension [AOR 4.453, CI (1.276, 15.536)], no iron/folic acid supplementation during pregnancy [AOR 4.175, CI (1.632, 10.680)], anemia during pregnancy [AOR 4.776, CI (1.492, 15.285)], and birth defect [AOR 6.160, CI (1.896, 20.013)] were significantly associated determinants of preterm birth.

## Conclusion

Antenatal care follow up fewer than four visits, pregnancy induced hypertension, no iron/folic acid supplementation during pregnancy, being anemic during pregnancy, and birth defect were important determinants of preterm birth.

## Background

Preterm birth (PTB), commonly defined as births before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last normal menstrual period (LNMP) (1).

The magnitude of PTB shows variation among different parts of the world and is growing through time. Globally, it is estimated that 15 million babies are born too soon each year and the majority of PTBs were in Asia and Sub-Saharan Africa where health systems are weak in access and minimum health services utilization. Additionally, preterm complications account for more than one million neonatal deaths each year(2,3). From 11 countries which have greater than 15% prevalence of prematurity, all countries are

found in Sub-Saharan African except Pakistan and Indonesia. Besides, poor countries have a higher prevalence of preterm births than rich countries (4). In Ethiopia, the overall PTB rate is 12% and the prevalence of PTB in different parts of the country ranges from 4.4–25.9% (2,5,6)

For the first time in history, PTB is the leading cause of death in children younger than 5 years worldwide covering 17% of under-five and 35% of neonatal deaths(7–9). Premature infants are particularly vulnerable to complications due to impaired respiration, difficulty in feeding, poor body temperature regulation and high risk of infection. Babies who are born before they are physically ready to face the world encounter greater risks of serious health problems, including cerebral palsy, intellectual impairment, chronic lung disease, and vision and hearing loss(4,10).

Premature babies also face drastically different odds of death depending on where they are born. From those extremely preterm babies (< 28 weeks) born in developing countries, greater than 90% of them die, while greater than 90% of extremely preterm babies in developed countries survive(4).

Among the 10 countries with the highest numbers of babies dying from PTB complications, India is the first followed by Nigeria. Ethiopia takes the 8th place with 24,400 child deaths per year (9). Different interventions have been implemented to prevent and improve the survival of PTB which demands huge financial capacity imposing a huge economic burden for the family, the community and the nation at large (4,11).

Every Women Every Child initiative set a target for 50% reduction in PTB deaths by 2025 which needs governments and the global community to take direct action to address deaths due to preterm birth, otherwise, the global total of preterm deaths will not reduce significantly, with around 900,000 premature babies continuing to die every year by 2025(12).

Several risk factors for PTB have been identified across the world. The potential risk factors for PTB includes, but not limited, maternal risk factors like past adverse birth outcomes(PTB, stillbirth, LBW), obstetric complications(PIH, PROM), maternal infections(HIV, malaria, UTI) and no ANC follow up while having  $\geq 4$  ANC checkup, IPI 24–36 months, maternal age 20–35 were found to be protective for PTB (13–15). However, risk factors for PTB are not always global; risk assessment should be carried out progressively at local, regional, and then global levels(16).

In poorer countries, like Ethiopia, where fewer resources are destined for healthcare, the direct, indirect, immediate and later repercussions of prematurity constitute a relevant public health issue. However, the great majority of scientific evidence accumulated on this subject is generated in developed countries. Besides, the potential risk factors are varied in different locations. Therefore, this study will have its own contribution to avert PTB and its consequences by identifying risk factors.

## **Method**

### **Study design and period**

A facility-based unmatched case-control study was conducted at public hospitals in Northeast Amhara, Ethiopia from March 15th to April 25th, 2019.

## Study Area

The study was conducted in Northeast part of Amhara region, Ethiopia. The study was employed in six randomly selected governmental hospitals (Debre Birhan Referral hospital, Tarmaber Primary Hospital, Kemisie General Hospital, Dessie Referral Hospital, Borumeda Hospital, and Woldia general Hospital).

## Source Population

All newborns who were born in public hospitals of Northeast Amhara, Ethiopia.

## Study Population

All newborns who were born in selected public hospitals of Northeast Amhara, during data collection time.

## Inclusion And Exclusion Criteria

### Inclusion criteria

#### Cases

All alive singleton preterm newborns (< 37 completed weeks of gestation) who was born in study hospitals of northeast Amhara.

#### Controls

All alive singleton term newborns (37 completed weeks to 42 weeks) at the same hospitals.

### Exclusion Criteria

- Newborns whose mothers did not remember their LMP.
- Newborns whose mothers had a serious illness or with difficulty of communication during the study period.

## Sample Size Determination

Sample size was determined by using EPI info version 7.2.2.6 by a double-population proportion difference formula. Different variables that have a high contribution for PTB was used and the variable that yields the

highest sample size was selected. The sample size was calculated considering the following assumptions:  $r = 3$  (ratio of controls to cases), 80% power and 95% confidence level. ANC < 4 with P Control = 42%, P Case = 60.7% was selected. Based on this, the sample size was 323. By considering a 10% non-response rate, the final sample size was 356 with 89 cases and 267 controls.

## Sampling Technique

The total sample size was allocated proportionately according to their caseloads for selected hospitals. Cases were preterm newborns (gestational age < 37 completed weeks) and controls were term newborns (gestational age of  $\geq 37$  weeks to 42 weeks). Systematic sampling technique was employed to select controls and cases every fifth intervals and every two intervals respectively. The first participant was selected by lottery method.

## Study Variables

### Dependent variable

Preterm birth (Yes/No)

### Independent Variables

Socioeconomic factors (including paternal age & education), obstetric history related factors, history of adverse birth outcomes, Obstetric complications, maternal medical conditions, behavioral factors, maternal anthropometrics, and infant characteristics.

## Operational Definition

Preterm birth

Newborns born before 37 completed weeks of gestation  
underweight

Mothers with MUAC less than 23 cm (17,18)

Alcohol drinking  
(19,20)

A unit of alcohol

It is equivalent to 17.7 ml or 14 g of pure strength alcohol

Binge drinkers

mothers who drink  $\geq 3$  drinks at a time/per seat

Drinkers: mothers who use at least one unit of any alcohol during their pregnancy categorized into three levels:

Passive smoking

living with someone who smoked during the mother's pregnancy

## Data Collection Tools And Procedures

Data was collected using interviewer-administered, structured pretested questionnaires and record review. The questionnaires include data on socio-demographic characteristics, obstetrics characteristics, infant characteristics, maternal anthropometrics, medical disorders, maternal infections, and behavioral factors. The questionnaires were prepared by reviewing different kinds of literature from related studies and EDHS 2016, (14,15,21–23). Confirmation of Gestational age was taken from documentation and for non-recorded data, information was taken from mother's report of LNMP. The data was collected by six trained midwifery graduates and supervised by MSc nurses.

MUAC was measured by using flexible non-stretched tape taken at mid-point of left upper arm at relaxed position, without any clothing and with optimal tape tension between acromion process on shoulder blade and tip of olecranon process of ulna. Height was also measured using height Stadiometer with sliding head bar without shoes, standing erect, with shoulder blades, buttocks and heels touching the measuring board, looking straight ahead, shoulders relaxed, arms at sides, legs straight and knees together, feet flat and with heels together. Two height measurements were taken and average was used if readings are within 1 cm each other and record to the nearest 1 cm.

## Data Quality Control

Data collectors and supervisor were trained for half a day on objective and methods of the study, study tools, how to approach the patient, and take anthropometric measures. In order to assess the validity and reliability of the tool and clarity of the variable, pre-test was done on 5% of the sample size newborns who were delivered out of the study hospitals two weeks ahead of data collection. During the data collection process, regular monitoring and supervision of the overall activity was done by the supervisors and principal investigator to check for completeness and ensure the quality of data. Besides, data cleaning and coding was carried out before analysis. The measurement tool was prepared in English and translated into local language (Amharic).

## Data Processing And Analysis

The collected data were checked for completeness and entered into EPI info version 7.2.2.6 and exported to SPSS version 23 for analysis. Data were summarized using text, tables, and graphs. Model goodness of fit test was checked by Hosmer-Lemeshow test (P-value = 0.224) and fitted. Multicollinearity between independent variables was assessed by using VIF (1.1–1.27) and no problem detected. Binary logistic regression model was used to measure the association between preterm birth and risk factors. Variables that had P-value  $\leq 0.2$  on bi-variable regression analysis and had association with preterm birth in

previous studies were fitted into the multivariable logistic regression model to assess their association with the outcome variable. Adjusted Odds ratio (AOR) with 95% confidence interval (CI) was calculated and P value  $\leq 0.05$  declared statistically significant.

## Results

### Socio-demographic characteristics of respondents

In this study, 356 participants were included. From these participants, 89 were preterm newborns (cases) and 267 were term newborns as controls with 100% response rate. The median age of mothers was  $25 \pm 8$  (IQR) years in case group and  $26 \pm 7$  (IQR) years in control group with a minimum of 17 and a maximum of 45 years. The paternal median age was  $31 \pm 7$  (IQR) years ranges from 20 to 60 years. Regarding religion, 50 (56.2%) cases and 129 (48.3%) controls were Orthodox Christian. Majority of the respondents, 69 (77.5%) cases and 220 (82.4%) controls were married and living together. Concerning the educational level of parents, 34 (38.2%) mothers and 27 (30.4%) fathers in the case group had no formal education while 108 (44.4%) mothers and 89 (41.1%) fathers in the control group. About occupation, 46 (51.7%) cases and 132 (49.4%) controls were housewives. Forty-eight (53.9%) newborns in case-group and 148 (55.4%) newborns in control-group were male in sex. (Table 1)

**Table 1: Distribution of socio-demographic characteristics among mothers who gave birth at public hospitals of Northeast Amhara, Ethiopia, 2019**

Variable	Category	Cases (%)	Controls (%)	Total
Residence	Rural	42 (47.2%)	98 (36.7%)	140 (39.3%)
	Urban	47 (52.8%)	169 (63.3%)	216 (60.7%)
Age of mother	<20	6 (6.7%)	10 (3.7%)	16 (4.5%)
	20-34	68 (76.4%)	226 (84.6%)	294 (82.6%)
	≥35	15 (16.9%)	31 (11.6%)	46 (12.9%)
Educational status	Not able to read and write	20 (22.5%)	58 (21.7%)	78 (21.9%)
	Able to read and write	14 (15.7%)	50 (18.7%)	64 (18.0%)
	Primary education	19 (21.3%)	58 (21.7%)	77 (21.6%)
	Secondary education	23 (25.8%)	60 (22.5%)	83 (23.3%)
	Higher education	13 (14.6%)	41 (15.4%)	54 (15.2%)
Marital status	Married	69 (77.5%)	220 (82.4%)	289 (81.2%)
	Separated	16 (18.0%)	30 (11.2%)	46 (12.9%)
	Single/Divorced/Widowed	4 (4.5%)	17 (6.4%)	21 (5.9%)
Religion	Orthodox	50 (56.2%)	129 (48.3%)	179 (50.3%)
	Muslim	33 (37.1%)	120 (44.9%)	153 (43.0%)
	Protestant	5 (5.6%)	13 (4.9%)	18 (5.1%)
	Catholic	1 (1.1%)	5 (1.9%)	6 (1.7%)
Occupational status	Housewife	46 (51.7%)	132 (49.4%)	178 (50.0%)
	Farmer	10 (11.2%)	30 (11.2%)	40 (11.2%)
	Merchant	14 (15.7%)	40 (15.0%)	54 (15.2%)
	Government/NOGs employee	19 (21.3%)	65 (24.3%)	84 (23.6%)
Educational status of father	Not able to read and write	11 (12.4%)	45 (16.9%)	56 (15.7%)
	Able to read and write	16 (18.0%)	54 (20.2%)	70 (19.7%)
	Primary education	21 (23.6%)	49 (18.4%)	70 (19.7%)
	Secondary education	25 (28.1%)	62 (23.2%)	87 (24.4%)
	Higher education	16 (18.0%)	57 (21.3%)	73 (20.5%)
Age of father	<25	5 (5.6%)	10 (3.7%)	15 (4.2%)
	25-29	30 (33.7%)	63 (23.6%)	93 (26.1%)
	30-34	25 (28.1%)	95 (35.6%)	120 (33.7%)

	35-39	16 (18.0%)	49 (18.4%)	65 (18.3%)
	≥40	13 (14.6%)	50 (18.7%)	63 (17.7%)
Income (monthly)	<3000 Birr	52 (58.4%)	130 (48.7%)	182 (51.1%)
	≥3000 Birr	37 (41.6%)	137 (51.3%)	174 (48.9%)
Infant sex	Male	48 (53.9%)	148 (55.4%)	196 (55.1%)
	Female	41 (46.1%)	119 (44.6%)	1. (44.9%)

## Maternal Obstetric Related Factors

In this study, 66 (74.2%) cases and 113 (42.3%) controls had fewer than four ANC visits. Among these, 25 (28.1%) cases and 13 (4.9%) controls had no ANC follow up. Regarding Iron/folic acid supplementation, 44 (49.4%) cases and 45 (16.9%) controls had used no Iron/folic acid. About 13 (14.6%) cases and 7 (2.6%) controls had experienced anemia during pregnancy. The majority, 66 (74.2%) newborns in case-group and 217 (81.3%) newborns in control-group were born through spontaneous vaginal delivery. Concerning, past adverse birth outcome, 8 (25%) cases and 18 (17.3%) controls had one or more past adverse birth outcomes. Past adverse birth outcomes encountered were LBW 5 (15.6%), Stillbirth 3 (9.4%), and Abortion 3 (9.4%) among cases and 6 (5.8%), 9 (8.7%), and 7 (6.7%) among controls respectively. (Table 2)

Table 2

Maternal obstetric related factors among mothers who gave birth at public hospitals of Northeast Amhara, Ethiopia, 2019

Variable	Category	Cases (%)	Controls (%)	Total
ANC Follow up	No	25 (28.1%)	13 (4.9%)	38 (10.7%)
	< 4	41 (46.1%)	100 (37.5%)	141 (39.6%)
	≥ 4	23 (25.8%)	154 (57.7%)	177 (49.7%)
Time of ANC initiation	First trimester	23 (35.9%)	97 (38.2%)	120 (37.7%)
	Second trimester	40 (62.5%)	150 (59.1%)	190 (59.7%)
	Third trimester	1 (1.6%)	7 (2.8%)	8 (2.5%)
Birth interval	No previous birth	57 (64.0%)	163 (61.0%)	220 (61.8%)
	< 24 months	5 (5.6%)	19 (7.1%)	24 (6.7%)
	24–36 months	20 (22.5%)	68 (25.5%)	88 (24.7%)
	≥ 37 months	7 (7.9%)	17 (6.4%)	24 (6.7%)
Parity	Primipara	57 (64.0%)	163 (61.0%)	220 (61.8%)
	Multipara	32 (36.0%)	104 (39.0%)	136 (38.2%)
Iron/folic acid supplementation	No	44 (49.4%)	45 (16.9%)	89 (25.0%)
	30–60 tabs	36 (40.4%)	144 (53.9%)	180 (50.6%)
	> 60 tabs	9 (10.1%)	78 (29.2%)	87 (24.4%)
Anemia	No	76 (85.4%)	260 (97.4%)	336 (94.4%)
	Yes	13 (14.6%)	7 (2.6%)	20 (5.6%)
Hemoglobin Level	< 11 g/dl	25 (28.1%)	35 (13.1%)	60 (16.9%)
	≥ 11 g/dl	64 (71.9%)	232 (86.9%)	296 (83.1%)
Mode of delivery	Spontaneous	66 (74.2%)	217 (81.3%)	283 (79.5%)
	Induction	18 (20.2%)	16 (6.0%)	34 (9.6%)
	C-section	5 (5.6%)	34 (12.7%)	39 (11.0%)
Pregnancy status	Unplanned	22 (24.7%)	33 (12.4%)	55 (15.4%)
	Planned	67 (75.3%)	234 (87.6%)	301 (84.6%)
Maternal Rh factor	Positive	59 (66.3%)	187 (70.0%)	246 (69.1%)
	Negative	25 (28.1%)	72 (27.0%)	97 (27.2%)

Variable	Category	Cases (%)	Controls (%)	Total
	Unknown	5 (5.6%)	8 (3.0%)	13 (3.7%)
Maternal height	< 150	20 (22.5%)	35 (13.1%)	55 (15.4%)
	≥ 150	69 (77.5%)	232 (86.9%)	301 (84.6%)
Maternal MUAC	< 23	44 (49.4%)	88 (33.0%)	132 (37.1%)
	≥ 23	45 (50.6%)	179 (67.0%)	224 (62.9%)
History of adverse birth outcome	No	24 (75.0%)	86 (82.7%)	110 (80.9%)
	Yes	8 (25.0%)	18 (17.3%)	26 (19.1%)
Type of adverse birth outcome	LBW	5 (15.6%)	6 (5.8%)	11 (8.1%)
	Stillbirth	3 (9.4%)	9 (8.7%)	12 (8.8%)
	Abortion	3 (9.4%)	7 (6.7%)	10 (7.4%)

Table 3

Maternal infection and chronic disease related factors among mothers who gave birth at public hospitals of Northeast Amhara, Ethiopia, 2019

Variable	Category	Cases (%)	Controls (%)	Total
Chronic medical illness	No	83 (93.3%)	253 (94.8%)	336 (94.4%)
	Yes	6 (6.7%)	14 (5.2%)	20 (5.6%)
Type of medical illness	HPN	3 (3.4%)	4 (1.5%)	7 (2.0%)
	DM/KD/LD?TD/	4 (4.49%)	10 (3.74%)	14 (3.93%)
Maternal infection	UTI	10 (11.2%)	24 (9.0%)	34 (9.6%)
	Malaria	1 (1.1%)	4 (1.5%)	5 (1.4%)
	TB	1 (1.1%)	5 (1.9%)	6 (1.7%)
	HIV/AIDS	0 (0%)	8 (3.0%)	8 (2.2%)

Key: DM = diabetes mellitus, KD = kidney disease, LD = liver disease, TD = thyroid disorder

Table 4

Behavioral factors among mothers who gave birth at public hospitals of Northeast Amhara, Ethiopia, 2019

Variable	Category	Cases (%)	Controls (%)	Total
Alcohol drinking during pregnancy	No	62 (69.7%)	199 (74.5%)	261 (73.3%)
	Yes	27 (30.3%)	68 (25.5%)	95 (26.7%)
Type of alcohol drunk	Tella	19 (21.3%)	56 (21.0%)	75 (21.1%)
	Areke	6 (6.7%)	7 (2.6%)	13 (3.7%)
	Beer	8 (9.0%)	24 (9.0%)	32 (9.0%)
	Wine/Tej	7 (7.9%)	7 (2.6%)	14 (3.9%)
Frequency of drinking	Daily/Weekly	9 (33.3%)	13 (19.1%)	22 (23.2%)
	Fortnightly/Monthly	7 (25.9%)	13 (19.1%)	20 (21.0%)
	Occasionally	11 (40.7%)	42 (61.8%)	53 (55.8%)
Unit of alcohol per week (recent month)	No alcohol	65 (73.0%)	223 (83.5%)	288 (80.9%)
	1–3 unit	21 (23.6%)	40 (15.0%)	61 (17.1%)
	≥ 4 unit	3 (3.4%)	4 (1.5%)	7 (2.0%)
Khat chewing during pregnancy	No	84 (94.4%)	248 (92.9%)	332 (93.3%)
	Yes	5 (5.6%)	19 (7.1%)	24 (6.7%)
Frequency of khat chewing	Daily/Weekly	1 (20%)	4 (21.1%)	5 (20.8%)
	Fortnightly	0 (0%)	5 (26.3%)	5 (20.8%)
	Monthly	0 (0%)	1 (5.3%)	1 (4.2%)
	Occasionally	4 (80%)	9 (47.4%)	13 (54.2%)
Passive Smoking	No	87 (97.8%)	261 (97.8%)	348 (97.8%)
	Yes	2 (2.2%)	6 (2.2%)	8 (2.2%)
Any medication during pregnancy	No	74 (83.1%)	227 (85.0%)	301 (84.6%)

Variable	Category	Cases (%)	Controls (%)	Total
	Yes	15 (16.9%)	40 (15.0%)	55 (15.4%)
Frequency of medication use	Daily	12 (80.0%)	34 (85.0%)	46 (83.6%)
	Weekly	0 (0%)	1 (2.5%)	1 (1.8%)
	Occasionally	3 (20.0%)	5 (12.5%)	8 (14.5%)

Table 5

Bi-variable and Multi-variable analysis of determinants associated with preterm birth among mothers who gave birth at public hospitals of Northeast Amhara, Ethiopia, 2019

Variables	Category	Cases (%)	Controls (%)	COR (95% CI)	AOR (95% CI)
Residence	Rural	42 (47.2%)	98 (36.7%)	1.541 (0.949, 2.503)	0.998(0.521,1.912)
	Urban	47 (52.8%)	169 (63.3%)	1	1
Pregnancy status	Unplanned	22 (24.7%)	33 (12.4%)	2.328 (1.273, 4.259)	0.995(0.442,2.242)
	Planned	67 (75.3%)	234 (87.6%)	1	1
ANC follow up	< 4 ANC visit	66 (74.2%)	113 (42.3%)	3.911 (2.295, 6.665)	2.267(1.205,4.264)**
	≥ 4 ANC visit	23 (25.8%)	154 (57.7%)	1	1
Age of mother in years	< 19	6 (6.7%)	10 (3.7%)	1.240(0.379, 4.056)	1.326(0.290,6.060)
	20–34	68 (76.4%)	226 (84.6%)	0.622(0.317, 1.219)	1.009(0.419,2.431)
	≥ 35	15 (16.9%)	31 (11.6%)	1	1
PIH	No	75 (84.3%)	261 (97.8%)	1	1
	Yes	14 (15.7%)	6 (2.2%)	8.120 (3.016, 21.858)	4.453(1.276,15.536)**
PROM	No	77 (86.5%)	259 (97%)	1	1
	Yes	12 (13.5%)	8 (3.0%)	5.045 (1.991, 12.789)	3.159(0.938,10.638)
Congenital malformation	No	74 (83.1%)	262 (98.1%)	1	1
	Yes	15 (16.9%)	5 (1.9%)	10.622 (3.737, 30.186)	6.160(1.896,20.013)*

Key: COR = crude odds ratio, AOR = adjusted odds ratio, CI = confidence interval, \*=P-value < 0.01, \*\*=p-value ≤ 0.05

Variables	Category	Cases (%)	Controls (%)	COR (95% CI)	AOR (95% CI)
Iron/folic acid supplementation	No iron use	44 (49.4%)	45 (16.9%)	8.474(3.78718.962)	4.175(1.632,10.680)*
	30–60 tabs	36 (40.4%)	144 (53.9%)	2.167(0.9934.730)	1.838(0.765,4.418)
	≥ 60 tabs	9 (10.1%)	78 (29.2%)	1	1
Anemia during current pregnancy	No	76 (85.4%)	260 (97.4%)	1	1
	Yes	13 (14.6%)	7 (2.6%)	6.353 (2.448, 16.489)	4.776 (1.492, 15.285)*
Hemoglobin level	< 11 mg/dl	25 (28.1%)	35 (13.1%)	2.589 (1.445, 4.639)	1.880(0.925,3.821)
	≥ 11 mg/dl	64 (71.9%)	232 (86.9%)	1	1
Height of Mothers	< 150 cm	20 (22.5%)	35 (13.1%)	1.921 (1.042, 3.542)	1.112(0.513, 2.411)
	≥ 150 cm	69 (77.5%)	232 (86.9%)	1	1
MUAC	< 23 cm	44 (49.4%)	88 (33.0%)	1.989 (1.221, 3.239)	1.481(0.812,2.699)
	≥ 23 cm	45 (50.6%)	179 (67.0%)	1	1
Income (monthly)	< 3000 EBR	52 (58.4%)	130 (48.7%)	1.481 (0.912, 2.406)	1.388(0.738,2.608)
	≥ 3000 EBR	37 (41.6%)	137 (51.3%)	1	1

Key: COR = crude odds ratio, AOR = adjusted odds ratio, CI = confidence interval, \*=P-value < 0.01, \*\*=p-value ≤ 0.05

## Fetal Related Factors

The mean gestational age among PTBs and term births were  $34 \pm 1.94$  weeks and  $39.02 \pm 1.27$  weeks, respectively. In the case group, 17 (19.1%) newborns were small for gestational age whereas 12 (4.5%) newborns in control group were low birth weight. Concerning fetal distress, 5 (5.6%) cases and 15 (5.6%) controls had fetal distress. On the other hand, 15 (16.9%) preterm newborns and 5 (1.9%) term newborns had a visible congenital/birth defect.

## Current Obstetric Complications

During current pregnancy, about 23 (25.8%) cases and 27 (10.1%) controls had one or more of pregnancy-related complications. Pregnancy-related complications occurred among cases were APH 3 (3.4%), Pre-eclampsia 2 (2.2%), PROM 12 (13.5%), PIH 14 (15.7%), and Hyperemesis gravidarum 4 (4.5%) whereas 1 (0.4%), 3 (1.1%), 8 (3.0%), 6 (2.2%), and 11 (4.1%) controls had the same obstetric complications in the same order.

## Maternal Infection And Chronic Disease Related Factors

About 6 (6.7%) cases and 14 (5.2%) controls had a chronic medical illness. Chronic hypertension was observed in 3 (3.4%) cases and 4 (1.5%) controls. Concerning maternal infections, UTI among 10 (11.2%) cases and 24 (9%) controls, and HIV/AIDS 8 (3.0%) among controls were found. Table-3

## Behavioral And Lifestyle Related Factors

Twenty-seven (30.3%) cases and 68 (25.5%) controls were drunk alcohol. The alcoholic beverage drunk comprised of "Tella", "Tej", "Areke", Beer, and Wine. The majority, 19 (21.3%) cases and 56 (21.0%) controls drunk "Tella". Regarding Khat chewing during pregnancy, 5 (5.6%) cases and 19 (7.1%) controls were chewed khat. About 15 (16.9%) cases and 40 (15.0%) of their counterparts were used medication other than minerals, vitamins, and iron/folic acid prescribed or from the counter. (Table-4)

## Determinants Associated With Preterm Birth

In bi-variable logistic regression analysis at 95% level of confidence, ANC follow up, pregnancy status, PIH, PROM, Congenital malformation, Iron/folic acid supplementation, Anemia and hemoglobin level during current pregnancy, Height of mothers, and MUAC were statistically significant with PTB. In multivariable logistic regression analysis at  $P\text{-value} \leq 0.05$ , ANC follow up, PIH, Congenital malformation, Iron/folic acid consumption, and Anemia during current pregnancy remained significantly associated determinants of PTB.

The chance of being preterm among newborns whose mothers had had fewer than four ANC follow up was about 2 times more than newborns whose mothers had had four or more ANC follow up [AOR 2.267, CI (1.205, 4.264)]. Newborns of mothers with PIH were four and half folds higher to be preterm [AOR 4.453 CI (1.276, 15.536)] compared to newborns born from mothers with no PIH. Similarly, newborns whose mothers had not used iron/folic acid supplementation during current pregnancy were 4 times increased the risk to be born preterm [AOR 4.175, (1.632, 10.680)] compared to their counterparts. The odds of being preterm in newborns with a birth defect were 6 times higher [AOR 6.160, CI (1.896, 20.013)] compared to newborns without a birth defect. Additionally, those newborns that born from mothers who had had

anemia during current pregnancy were about 5 times higher to be born preterm [AOR 4.776 (1.492, 15.285)] than newborns whose mothers had no anemia. (Table-5)

## Discussion

This study was intended to identify determinants for PTB in order to tackle the burden of the disease and its associated problems. The study has tried to look at the determinants of PTB by incorporating numerous risk factors as possible.

This study revealed that newborns whose mothers followed ANC less than four times were about two times more likely to be preterm as compared to their counterparts. This finding is consistent with facility-based case-control studies done in Ethiopia; Jimma (AOR: 4.8), and Central Tigray (AOR: 2.15), North-Eastern Tanzania (AOR 3.25), and Nigeria (AOR 6.13). This might be due to that lack of/ inadequate ANC follow up decreases the chance of identifying risks of PTB and providing appropriate interventions for its prevention(14,21).

In this study, current PIH showed statically significant association with PTB. PIH increased the odds of PTB by four and half folds in newborns of mothers having PIH than newborns of mothers without PIH. Similarly, significant associations have been reported from studies done in Ethiopia, Gondar (AOR = 5.36), Jimma (AOR 6), and Central Tigray (AOR 3.24), and other studies from Kenya (7.81), and Iran (AOR 7.30). This might be due to hypertension increases the resistance of blood to uterine vessels reducing the utero-placental blood flow that may affect the exchange of nutrients and oxygen between mother and fetus which in turn results intrauterine growth restriction that causes PTB. Additionally, complications of PIH may cause vascular damage to the placenta, which induces the oxytocin receptors, leads to preterm labor and delivery(14,24–26). Even though this may not be causal in nature, PIH is a common reason for indicated preterm deliveries and this may explain its association with PTB.

This study also showed that anemia during current pregnancy were another independent determinant for PTB. Newborns whose mothers had anemia during current pregnancy were at increased risk to be born preterm compared to those newborns of mothers without anemia. This finding is in line with the studies conducted in Ethiopia, Jimma (AOR 2.7), Systematic review and meta-analysis in low- and middle-income countries (RR: 1.63) and Korea (AOR 1.53). This might be due to that anemia and iron deficiency by causing hypoxia and maternal infections induce maternal and fetal stress which leads to the formation of corticotrophin-releasing hormone. Excess corticotrophin-releasing hormone is the major risk factor for preterm labor, PIH, PROM and inhibits fetal growth by stimulating cortisol production. Another possible explanation is that iron deficiency may cause oxidative damage to the erythrocytes and the fetoplacental unit affecting placental function(27,28).

The present study revealed that the chance of being preterm among neonates having birth defect was about six times more significant compared to those neonates without any visible birth defect. This finding agrees with the studies done in Tigray, Ethiopia (AOR 3.20) and Missouri U. S. A (AOR 3.20). There are plausible but need to be proven explanations that birth defects may result PTB. Among these, certain birth

defects associated with abnormal connective tissue may increase the risk of preterm delivery, PTB and birth defects may have shared a common risk factors, and even not observed in our case, prenatal diagnosis of birth defect may lead to deliberately planned delivery through induction or cesarean section before 37 weeks of gestation(29,30). As stated by the study done in Ethiopia, this might be due to the interaction of environmental and genetic risk factors that contribute to PTB(15). As observed in this study, it may be due to that most mothers with birth defect newborns had no iron/folic acid supplementation during current pregnancy.

Lack of iron/folic acid supplementation during current pregnancy also another significant factor for PTB. It increases the chance of PTB by four folds. A study from Kenya also showed 80% protective effect of prescribed iron/folic acid during pregnancy with PTB (AOR OR = 0.20). Another study from Sudan reported that folic acid level was associated with a lower risk of PTB (OR = 0.64) and there was a significant positive correlation between gestational age and folic acid level. This finding also supported by findings from China. The reason, in part, may be due to iron/folic acid supplementation prevents anemia and its effect. However, this finding contradicts the report from Bangladesh that iron/folic acid supplementation was a risk factor for PTB. We cannot definitively elucidate the disagreements between the studies in the association between maternal iron/folic acid supplementation and PTB, but it has been reported that the effects of hemoglobin concentration on birth outcomes could differ by ethnicity (31). It needs further interventional study.

## Conclusion

The study indicated that ANC follow up fewer than four visits, PIH, no iron/folic acid supplementation during current pregnancy, being anemic and birth defect were significantly associated determinants of preterm birth.

Health education and awareness creation about the benefit of adequate ANC follow, iron/folic acid consumption, and early prevention of pregnancy-related complications are very important during pregnancy. It is also advisable to prevent and treat maternal anemia during pregnancy.

Strengthening patient tracing mechanism through phone call or home visit when mothers interrupt their follow up is advisable. Monitoring and evaluation of the effectiveness of maternal and child health/MCH services is also better.

## Abbreviations

ANC: antenatal care; AOR: adjusted odd ratio; CI: confidence interval; COR: crudes odd ratio; EDHS: Ethiopian demographic and heath survey ; HIV/AIDS: Human Immunodeficiency virus/ Acquired immunodeficiency syndrome; IQR: interquartile range ; LBW: low birth weight; LMP: last menstrual period; LNMP: Last normal menstrual period; MSc: Master of science; MUAC: mid upper arm circumference; PIH: pregnancy induced hypertension; PROM: premature rupture of membrane; PTB: preterm birth; SPSS: Statistical Package for Social Sciences; UTI: urinary tract infection; VIF: variance inflation factor

# Declarations

## Ethics approval and consent to participate

The Ethical clearance was obtained from the Ethical Review Committee of School of Nursing on behalf of University of Gondar Ethical Review Board. A permission letter was also obtained from the study Hospitals' quality control office. After explanation had given about the purpose of the study, written consent was obtained from parent or legal guardian of the children. For parents or legal guardian who could not read and write, a thumbprint was used in place of the participant's signature. Anonymous questioner was used to protect the identity and confidentiality of the information obtained. Besides, once the information was gathered from the patient, it was put under a locked cupboard and in a password protected computer.

**Consent to publish:** Not applicable.

**Availability of data and material:** all relevant data are available in the main document.

## Competing interest

The authors declared that we have no any competing interests.

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## Authors' contribution

**MS** wrote the proposal, participated in data collection, analyzed the data and drafted the manuscript. **NBT** and **HSM** approved the proposal with revisions, participated in data collection, data analysis and revised subsequent drafts of the manuscript. All authors read and approved the final manuscript.

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