Maternal Risk Factors Associated with Preterm Birth: A Case Control Study

Sonam Gyamtsho,[1] Karma Tenzin,[2] Tshering Choeda[3]

[1]Department of Obstetrics and Gynecology. Jigme Dorji Wangchuck National Referral Hospital. Thimphu,

[2,3] Faculty of Postgraduate medicine, Khesar Gyalpo University of Medical Sciences of Bhutan, Thimphu.

ABSTRACT

Background: Preterm birth is the child birth before 37 completed weeks .Prematurity is one of the leading causes of neonatal morbidity and mortality due to the complications associated with it. The objective of the study was to determine the maternal risk factors associated with all preterm birth in singleton pregnancy at National hospital.

Methods: Hospital based unmatched case control study was conducted between March 2021 to December 2021 at National hospital, Thimphu, Bhutan. Case to control ratio was 1:2.Data were collected using interviewer – administered structured questionnaires. The collected data were entered into Epi-data and exported into SPSS for analysis. Independent variables with p-valves<0.05 in the univariate analysis were entered to multi variable logistic model to estimate the strength of association .P-valve <0.05 was considered significant.

Results: Total of 107 cases and 201 controls participated with a response rate of 95.95%.Multiple logistic regression showed that mothers with ANC follow ≤ four[aOR 9.58(7.36-28.86)], previous history of preterm delivery [aOR 2.99(1.5-15.77)], previous caesarean section [aOR 5.72(2.19-14.92)], prelabour rupture of membrane [aOR 8.67(3.78-19.73)], fetal growth restriction [aOR 7.28(2.11-25.11)] , and pre-eclampsia [aOR 10.99(6.75-85.29) were the risk factors positively associated with preterm birth .

Conclusions: This study highlights that preeclampsia, number of antenatal care visits ≤ four, prelabour rupture of membrane, fetal growth restriction, previous caesarean section and previous preterm delivery were the risk factors for preterm birth. This show the need of early screening and prevention of preeclampsia, strengthening of antenatal care follow-up, and treatment of infection to prevent prelabour rupture of membrane, reducing primary caesarean section and more attention and care with previous preterm birth .

Keywords: Case control study; preeclampsia; preterm birth; risk factors.

INTRODUCTION

Preterm birth is the childbirth before 37 completed weeks.[1] Approximately 9, 00,000 children die due to complications related to preterm birth and majority were born in South Asia and Sub-Sahara Africa. [2, 3] In Bhutan, 21.6% to 29.27% of the neonatal mortality was due to complications of prematurity and among survivors had lifetime complications. [4-6]

Some of the preterm birth occurs due to interplay of multiple factors or risk factors leading to the spontaneous or medical indicated birth.[6-8] Common maternal risk factors are age,[9-11] Occupations,[12,13,] and lifestyle factors such as stress, physical work, smoking and alcohol consumption,[14-16] obstetrics complications such as miscarriages,[9] previous preterm labour, [17,18] caesarean section,[19-21] antepartum hemorrhage,[11] pre-labour rupture of membrane(PPROM) ,[13,17] and preeclampsia. [22, 23]

In Bhutan, majority of neonatal mortality were due to the complications of prematurity. [4, 5,24] Therefore, this study was carried out to identify modifiable maternal risk factors, to provide important insights into the factors leading to preterm birth among the Bhutanese

Correspondence: Sonam Gyamtsho, Department of Obstetrics and Gynecology. Jigme Dorji Wangchuck National Referral Hospital. Thimphu. Email: sgyamtsho@jdwnrh.gov.bt, Phone: +97517637011

pregnant women.

METHODS

This Hospital based unmatched case control study was carried out at Jigme Dorji Wangchuck National Referral Hospital (JDWNRH), Thimphu, Bhutan from 1st March 2021 till 31st December 2021. The study was approved by Research Ethic Board of Bhutan Vide letter no REBH/Approval/2021/019 dated 24th February 2021.

The JDWNRH is the apex tertiary care hospital in the country which conducts annually more than 4300 deliveries including majority of the preterm birth and complicated high risk pregnant women . Approximately more than 35 % of the annual deliveries of the country were conducted in this Hospital. [25]

All singleton pregnant women who were admitted for delivery during the study period were recruited into this study. From this study population, all mother who had preterm delivery (Gestational age between 26 weeks to 36 week + 6 days) were recruited as case and mother who had term delivery (≥37 weeks but ≤42 weeks) were included as controls. Women who were sick and unable to answer the questions or multiple pregnancies or with intrauterine fetal death (IUFD) were excluded from the study.

Information on gestational age were calculated based on last menstrual period (LMP) and early ultrasound and followed the American colleges of Obstetrician and Gynecologist guideline for calculation of gestational age. [26]

The sample size was calculated using Open Epi. [27] The sample size calculation was done using 95% confidence interval(CI) with margin error of 5%, 80% power keeping a ratio of cases to controls of 1:2. Considering the proportion of previous miscarriage in control (32.50%) and proportion of miscarriage in cases (49.44%) as risk factors for preterm birth in a study done by Min Jiang et al in Taiwan. [28] The total sample size was 320 with 107 cases and 214 controls. For the selection of cases, systemic sampling technique was done by selecting every 2nd preterm delivery followed by selection of two consecutive term deliveries following preterm birth as controls.

Data were collected using face to face interview with the mother within 24 hours of delivery using interviewer-administered structured questionnaires.

The questionnaires consisted of socio-demographic characteristics, obstetrics, medical and behavioral questions relevant to this present pregnancy. The data were collected by trained nurses and resident doctors working in the maternity ward and birthing center after obtaining a written informed consent. The same person interviewed both the case and the controls. Mothers were interviewed in private room to ensure their privacy and to encourage participation.

The data was cleaned; double entered using EPI DATA Version 3.1 statistical software, and then exported to SPSS Version 22.0 for analysis. Results were presented as tables and figures. Hosmer –lemeshow test was done to check for goodness of fit.

Association between risk factors and preterm birth were assessed using a Chi-square (x2) test. Variables which showed statistically significance during univariate analysis at P-value <0.05 were entered to multivariable logistic regression. Adjusted Odd ratio (aOR) with 95% CI were estimated to assess the strength of association and statistical significant was considered if P-valve < 0.05.

RESULTS

In this study, 107 cases and 201 controls were included after excluding 13 controls due to incomplete data, thereby indicating a response rate of 95.95%. Majority of the mother were aged between 21 to 30 years (59.81% cases and 69.65% control). Among the cases 11.21% of the women were below the age of 20 years in compared to 2.99% control groups which was statistically significant (p=0.025) (Table 1).

In terms of level of education (p=0.281), employment (p=0.052) and income (p=0.630), there were no statistical difference between the case and control groups as shown in Table 1.

Similarly, for first antenatal care (ANC) visit and past history of miscarriage there were no significant difference between the two groups. However, a lower proportion of mothers from study group had at least four or more visits compared to control group (p<0.001) as shown in Table 2.

A significantly (p<0.001)) higher proportion of mothers in study group had history of previous preterm birth, prelabour ruptures of membrane (PROM), previous caesarean section and fetal growth restriction compared to the controls group as shown in table 2.

Table 1. Socio-demographic characteristics of case and control with preterm birth among pregnant women admitted at National Hospital, Thimphu, Bhutan (March 2021 to December 2021).			
Variables	Cases(n=107)	Control(201)	P-valve
Age			
15-20	12 (11.21)	6 (2.99)	0.025
21-30	64 (59.81)	140 (69.65)	
31-40	29 (27.10)	50 (24.88)	
41-50	2 (1.87)	5 (2.49)	
Level of education			
No schooling	16 (14.95)	25 (12.44)	0.281
Non Formal education	3 (2.80)	6 (2.99)	
Primary	9 (8.41)	11 (5.47)	
Lower secondary	12 (11.21)	28 (13.93)	
Higher secondary	39 (36.45)	95 (47.26)	
Degree/ master/PhD	28 (26.17)	34 (16.92)	
Others	0 (0.00)	2 (1.00)	
Occupation			
Housewife	56 (52.34)	132 (65.67)	0.052
Civil servant	18 (16.82)	19 (9.45)	
Corporate employee	8 (7.48)	16 (7.96)	
Manual labourer	2 (1.87)	0 (0.00)	
Private business	20 (18.69)	33 (16.42)	
Student	3 (2.80)	1 (0.50)	
Family income(Nu)			
<20000	43 (40.19)	81 (40.30)	0.630
20000-40000	44 (41.42)	93 (46.27)	
40001-50000	9 (8.41)	13 (6.47)	
>50000	11 (10.28)	14 (6.97)	

Nu: Ngultrum Bhutanese currency.

Table 2.Univariate analysis of the maternal and obstetrics risk factors associated with case and control for preterm birth among pregnant women admitted at National Hospital , Thimphu ,Bhutan(March 2021 to December 2021).				
Variables		Cases (n=107)	Controls(n=201)	p-valve
First ANC* booking	≤ 12 weeks	46(43)	102(50.75)	0.216
	>12 weeks	61(57)	99(49.25)	
Total Number of ANC visits	≤4 visits	57(53.27)	14(6.97)	<0.001
	>4 visits	50(46.73)	187(93.03)	
Previous miscarriage	Yes	16(14.95)	23(11.44)	0.378
	No	91(85.05)	178(88.56)	
Previous preterm birth	Yes	9(8.41)	3(1.49)	0.003
	No	98(91.59)	198(98.51)	

Table 2.Univariate analysis of the maternal and obstetrics risk factors associated with case and control for preterm birth among pregnant women admitted at National Hospital , Thimphu ,Bhutan(March 2021 to December 2021).				
Variables		Cases (n=107)	Controls(n=201)	p-valve
Previous caesarean section	Yes	22(20.56)	8(3.98)	<0.001
	No	85(79.44)	193(95.02)	
PROM/PPROMß	Yes	28(26.17)	10(4.98)	<0.001
	No	79(73.83)	191(95.02)	
Fetal growth restriction	Yes	23(21.50)	4(1.99)	<0.001
	No	84(78.50)	197(98.01)	
Preeclampsia	Yes	28(26.17)	3(1.49)	<0.001
	No	79(73.83)	198(98.51)	
Chronic hypertension	Yes	8(7.48)	3(1.49)	0.007
	No	99(92.52)	198(98.51)	
Pre gestational Diabetes mellitus	Yes	6(5.61)	3(1.49)	0.041
	No	101(94.39)	198(98.51)	
Vaginal bleeding during pregnancy	Yes	18(16.82)	17(8.46)	0.028
	No	89(83.18)	184(91.54)	
Smoking	Ye s	5(4.57)	6(2.99)	0.447
	No	102(95.33)	195(97.01)	

*Antenatal care

ß Preterm prelabour rupture of membrane

Table 3. Multivariate logistic regression analysis showing the association of independent variables with preterm birth among pregnant women admitted at National Hospital, Thimphu, Bhutan (March 2021 to December 2021).				
Variables		Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-valve
Total ANC visits	≤ 4 weeks	10.27	9.58(7.36-28.86)	<0.001
	>4 weeks	Ref		
Previous preterm delivery	Yes	6.06	2.99(1.5-15.77)	<0.001
	No	Ref		
Previous caesarean section	Yes	6.22	5.72(2.19-14.92)	<0.001
	No	Ref		
PROM	Yes	6.77	8.67(3.78-19.73)	<0.001
	No	Ref		

Table 3. Multivariate logistic regression analysis showing the association of independent variables with preterm birth among pregnant women admitted at National Hospital, Thimphu, Bhutan (March 2021 to December 2021).

Variables		Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p-valve
Fetal growth restriction	Yes	13.49	7.28(2.11-25.11)	0.002
	No	Ref		
Preeclampsia	Yes	12.39	10.99(6.75-85.29)	<0.001
	No	Ref		
Chronic hypertension	Yes	5.33	3.40(0.70-16.57)	0.129
	No	Ref		
Pregestational Diabetes mellitus	Yes	3.92	1.91(0.37-9.80)	0.438
	No	Ref		
Vaginal Bleeding during pregnancy	Yes	2.19	2.18(0.93-5.10)	0.073
	No	Ref		

ANC: Antenatal care.

OR: odd ratio.

CI: Confidence Interval.

PROM: Prelabour rupture of membrane

Similarly, a higher proportion of mothers in study group developed preeclampsia compared to controls (26.17% and 1.49% respectively) (p<0.001) and 7.48% of cases had chronic hypertension compares to only 1.49% of control (p =0.007) as shown in table 2.

Nearly 6 % of the study group had pregestational diabetes mellitus and vaginal bleeding during pregnancy was twice higher among the study group compared to control (p=0.028).

There is no difference in the proportion of mother among the cases and controls with regards to behavioral habits like intake of alcohol, and smoking (Table 2).

Factors like first ANC booking, previous miscarriage, smoking, and alcohol intake were statistically not significant.

The following variables, total numbers of ANC visits, previous preterm birth, previous caesarean section, PROM, fetal growth restrictions, preeclampsia, chronic hypertension, pregestational diabetes mellitus, and vaginal bleeding during pregnancy had P<0.05 during the univariate analysis were subjected to multivariate logistic regression analysis to assess the strength of association.

The adjusted ORs (aOR) for preterm birth by each variable are shown in Table 3.

These findings demonstrate that those women who had ≤4 antenatal checkup compared to >4 visits had increased the risk of preterm delivery by 10 times (aOR= 9.58(CI: 7.36-28.86) (Table 3).

Previous histories of preterm delivery among multiparous women were associated with three times increased risk of preterm delivery (aOR=2.99, CI: 1.5-15.77).

Having delivered previously by caesarean section increased the risk of preterm delivery by 5.72 times (aOR=5.72, CI: 2.19-14.92) and in PROM and fetal growth restriction increased the preterm birth by 8.67 times

(AOR=8.67, CI: 3.78-19.73), and 7.28 times (aOR=7.28, CI: 2.11-25.11) respectively (Table 3)

Women with Preeclampsia in the present pregnancy had the highest odd of delivering preterm which was increased by 11 folds (AOR=10.99, CI: 6.75-85.29) (Table 3).

The Hosmer- Lemeshow test of goodness of fit gave a p valve of 0.83 for the preterm birth model, suggesting a good fit.

DISCUSSION

The study indicates that mothers who had preeclampsia were 11 times more likelihood of having preterm birth than those mothers without preeclampsia. This finding is higher than some of the studies done in South Ethiopia,[29] Kenya,[14] Tanzania,[18] and China.[22] This increased risk in this study compared to others studies could be due to delayed in prevention, early identification and intervention during the antenatal care visits, thereby causing maternal or fetal complications leading to increased rate of medical indicated preterm birth.[4,6] The other reason could be due to complication of preeclampsia causing vascular damage to the placenta, which induces oxytocin receptors resulting in spontaneous preterm birth. It is thus more meaningful to focus on preeclampsia and provide prenatal and medical interventions to prevent the development of preeclampsia.

Our findings revealed that women who had ANC visits of less than four times were about 10 times more likely to have preterm birth compared to women who had attended ANC more than four times. This is consistent with study done by Bernadette et al in Tanzania,[18] Rwanda, [30] and Ethiopa.[31] Another study reported 10 folds increased risk of preterm birth among mothers, who had no ANC visits.[16] This could be due to the fact that women with less ANC visits, there is delay in early detection of maternal as well as obstetrics complications. Therefore increasing numbers of ANC visits lead to early detection and interventions to prevent preterm birth.

In this study, prelabour rupture of membrane (PROM) was 8.67 times more likely to be associated with preterm birth compared to those who had no PROM. This finding of significant increase in preterm birth is in consistent to many of the studies done. [14, 17, 18] Majority of the cases of PROM were associated with spontaneous preterm delivery, due to subclinical chorioamnionitis and other unidentified infections like bacterial vaginosis or Chlamydia infection which may trigger release of inflammatory mediators like interleukin 1 or tumor necrosis factor α leading to release of prostaglandins from uterine deciduas that induce preterm labour.[11,13,14] Most of these were related to infections, therefore proper infection control, and early initiation of antibiotics is recommended during prenatal and antenatal care.

This study found that mother with fetal growth restriction (FGR) were 7 times likely to have a preterm birth, this was higher than a study done in Northern Ethiopia (aOR 2.78: CI 1.39-5.55).[15] These increased could be due to early identification of FGR and interventions by obstetricians before the growth restricted fetus were severely affected leading to medically indicated preterm birth.

In this study, women who underwent caesarean section in the previous birth were 6 times more likely have preterm birth, compared to those who had natural vaginal delivery .This finding is similar to studies done in Tigray, Ethiopa, [31] Tanzania, [18] and Kenya.[14] A systemic review and meta-analysis carried out by Yingghul Zhang et al found that women who had previous caesarean section had a significantly higher risk of preterm birth even after adjusting the confounding factors.[19] Carolina Eriksson et al, also found that when the first caesarean section done with low fetal station or with full dilatation of cervix, were associated with significant risk of spontaneous preterm birth. [20, 21] The increased risk of subsequent preterm birth following previous caesarean section could be due to uterine structure or intrauterine micro environmental changes following previous caesarean section exposing the risk to preterm birth or due to disruption of cervical integrity following lower uterine incision and there by affecting the function of the cervix.[19] In order to reduce the risk of preterm birth following caesarean section, there is a need to revisit the indications and reduce primary caesarean sections.

In this study, previous preterm birth was associated with 3 times increased risk of recurrent preterm birth in the current pregnancy. This finding is similar to the study done in Japan, [17] Brazil,[12] and Ethiopia.[29] The mechanism of how recurrent preterm birth happens is not well understood.[12] History of preterm birth in Bhutanese mothers is important risk factors for recurrent preterm birth, and more attention and care during the ANC visits may lead to decrease in the rate of preterm birth.

This study found that the history of miscarriage was not significantly associated with the risk of preterm birth in this study, but increased risk of preterm birth with

history of miscarriages was reported by many studies. [10, 11, 15] It is imperative to be mindful of the fact that there could be underreporting by our pregnant mother about miscarriages due to socio-cultural reasons.

This study revealed that there was no statistically significant association between alcohol consumption and smoking during pregnancy with increased risk of preterm birth. This is in contradiction to others studies done of Teresa Cobo et al and BayewKelkay, [10, 15] where there were significant increases in preterm rate among pregnant women who smoked and drank alcohol during the pregnancy. This discrepancy in this study could be due to underreporting of alcohol consumption and smoking by pregnant women in Bhutan due to the fear of stigmatization and sociocultural ground.

The study also found no statistically significant association of income, previous miscarriage, pregestational diabetes mellitus and vaginal bleeding in pregnancy with preterm birth.

The strength of this study is that it provides important information regarding the common significant risk factors that were associated with preterm deliveries in Bhutan, which will be useful in identification of pregnant women at risk and guide clinicians to monitor and treat these groups of women.

One of major limitation, it was a single institution based study, and this study may not represent the general population. There was a possibility of recall bias on some of the data especially given the nature of collection of data by face to face interviews and on some of the data like history of abortions, smoking or intake of alcohol.

CONCLUSIONS

This study highlights that preeclampsia, number of antenatal care visits ≤ four, prelabour rupture of membrane, fetal growth restriction, previous caesarean section and previous preterm delivery were the risk factors for preterm birth. This show the need for strengthening early screening and prevention of preeclampsia, create increase awareness and strengthening of antenatal care follow-up, treatment of infection to prevent PROM, Strengthen decision making for primary caesarean section to decrease the number of previous caesarean section cases Women with a previous preterm birth were also in a high risk for recurrent preterm birth and health care providers should pay more attention and care during the ante natal care.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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