

# Incidence, risk factors and consequences of preterm birth – findings from a multicentric observational study in Nepal

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## Research

**Keywords:** preterm, risk factors, stillbirth, neonatal mortality, Nepal

**Posted Date:** January 28th, 2020

**DOI:** <https://doi.org/10.21203/rs.2.22050/v1>

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**Version of Record:** A version of this preprint was published on July 17th, 2020. See the published version at <https://doi.org/10.1186/s13690-020-00446-7>.

# Abstract

**Background:** Preterm birth is a worldwide epidemic and a leading cause of neonatal mortality. In this study, we aimed to evaluate the incidence, risk factors and consequences of preterm birth in Nepal.

**Methods:** This was an observational study conducted in 12 public hospitals of Nepal. All the babies born during the study period were included in the study. Babies born <37 weeks of gestation were classified as preterm births. For the association and outcomes for preterm birth, univariate followed by multiple regression analysis was conducted.

**Results:** The incidence of preterm was found to be 93 per 1000 live births. Mothers with age less than 20 years (aOR 1.21; 1.09-1.34) and 35 years and above (aOR 1.30; 1.05-1.63) had a high risk for preterm birth. Similarly, education of the mother was a significant predictor for preterm birth: illiterate mothers (aOR 1.90; 1.66-2.19), literate mothers (aOR 1.48; 1.33-1.65) and mothers having basic level of education (aOR 1.25; 1.14-1.38). Socio-demographic factors such as smoking (aOR 2.02; .84-2.22) and use of polluted fuel (aOR 1.38; 1.28-1.50); obstetric factors such as nulliparity (aOR 1.44; 1.28-1.61), multiple delivery (aOR 1.92; 1.33-2.76), severe anemia during pregnancy (aOR 2.43; 1.55-3.82), antenatal visit during second trimester (aOR 1.10; 1.02-1.19) and third trimester (aOR 1.44; 1.30-1.60) were found to be significant risk factors of preterm birth. Preterm has a risk for pre-discharge mortality (10.60; 9.28-12.10).

**Conclusion:** In this study, we found high incidence of preterm birth. Various socio-demographic, obstetric and neonatal risk factors were associated with preterm birth. Risk factor modifications and timely interventions will help in the reduction of preterm births and associated mortalities.

## Background

Preterm birth (< 37 weeks of gestation) is one of the leading causes of neonatal morbidity and mortality and a significant public health burden [1, 2]. Every year, there are 15 million (11.1%) preterm births worldwide, and 13.3% of these births occur in South Asia alone [1]. In order to reduce neonatal mortality due to preterm births and its complications and also achieve this target set by Sustainable Development Goal 3, it is critical to address the burden of preterm births [3].

Several factors have been identified as risk for preterm birth. Socio-demographic factors such as ethnicity, older age of mothers and smoking have been reported as risk factors for preterm birth [4, 5]. Poor education levels of mothers have been documented as risk factors for preterm birth by many studies [6–8]. Primiparity has been linked as an obstetric risk factor for preterm birth [9]. Studies have also been conducted showing provider-initiated interventions like induction of labor and caesarean section are attributable to preterm births [10–12].

Babies born preterm have a higher risk of dying as reported from a multi-country study of low- and middle-income countries (LMICs) [13]. The greater risk of dying has been mostly associated with neonatal infections [14]. In comparison to term infants, they are more prone to short and long-term

neurocognitive and motor impairments together with increased risk of malnutrition, chronic diseases and early deaths [15, 16].

Despite the increase in burden of preterm births worldwide, the data available from developing countries like Nepal is very scarce [12]. Also, very few studies have been conducted assessing the risk factors with preterm births in Nepal. For developing suitable interventions for preventing morbidities and mortalities associated with preterm, it is essential to understand the underlying risk factors linked with preterm births. Hence, we aimed to evaluate the incidence, risk factors and consequences related to preterm births.

## **Method**

### **Aim**

The study aimed to evaluate the incidence, risk factors and consequences of preterm birth in Nepal.

### **Study design and setting**

This observational study among a large number of births was conducted in 12 hospitals of Nepal [17]. These hospitals are government-funded providing referral level obstetric and neonatal care services. This study was conducted for a period of 14 months from 1 July 2017 to 29 August 2018.

### **Study participants**

### **Inclusion criteria**

All babies who were delivered in the selected hospitals were included for this study.

### **Exclusion criteria**

The babies whose mothers who did not provide consent were excluded.

### **Data collection and management**

A data surveillance system was established in all the hospitals to collect data on babies and their mothers. For obstetric information, data were extracted from Maternity Register using a data retrieval form (Additional file 1). For sociodemographic variables, data were collected through semi-structured interviews with mothers before discharge (Additional file 2). The forms that were completed were then assessed by the data coordinator at the hospital for completeness and those completed were indexed. The data entry and management team then sorted and indexed the forms and reassessed for completeness. The data were entered and cleaned in Census and Survey Processing System (CSPPro). The cleaned data were exported into Statistical Package for the Social Sciences (SPSS) for further data analysis.

### **Variables**

## **Outcome variable:**

Preterm births – Babies born before 37 weeks of gestation

Pre-discharge mortality – The death of newborn before discharge

## **Demographic variables**

Maternal age, ethnicity, education and smoking history were included

## **Antenatal variables**

Antenatal care (ANC) visit, time for ANC visit, parity and severe anemia during pregnancy were included

## **Intrapartum variables**

Induction of labor, mode of delivery, multiple deliveries, major malformation and sex of the baby were included

## **Statistical analysis**

The incidence of preterm births was calculated based on maternal age, ethnicity, mode of delivery and induction of labor. For socio-demographic and obstetric characteristics, binary logistics regression was done to analyze the level of association with preterm births. P-value of  $< 0.05$  was considered to be significant. Missing values were excluded from the analysis. Multiple regression analysis was done for variables that were significant in univariate analysis.

## **Results**

A total of 63,099 women were admitted and 60,742 deliveries were conducted during the study period. Among the delivered, 54,778 were term babies while 5,964 babies were born preterm (Fig. 1). The incidence of preterm births was found to be 98 per 1,000 total births while it was 93 per 1,000 live births (Fig. 2).

In univariate analysis, socio-demographic characteristic such as age of mother, education level, smoking history and type of fuel all showed significant association ( $p < 0.001$ ) with preterm births. Similarly, obstetric characteristics such as multiple delivery, primiparity, ANC visit, time of first ANC visit, major malformation and severe anemia during pregnancy were found to be significantly associated with preterm births. Female babies were significantly associated with preterm births (Table 1).

Table 1  
Socio-demographic, obstetric and neonatal characteristics

Variables	Preterm (n = 5964)	Non-Preterm (n = 54778)	Total (n = 60742)	p- value	OR (95% CI)
Age of mother	23.53 ± 4.7	23.96 ± 4.33			
20-<35 years	4640(77.8%)	46077(84.1%)	50717(83.5%)	< 0.001	Ref
< 20 years	1116(18.7%)	7322(13.4%)	8438(13.9%)	< 0.001	1.51(1.41–1.62)
> 35 years	208(3.5%)	1379(2.5%)	1587(2.6%)	< 0.001	1.50(1.29–1.74)
Level of education (n = 50424)					
Secondary and above	2587(60.3%)	31743(68.8%)	34330(68.1%)	< 0.001	Ref
Illiterate	352(8.2%)	2186 (4.7%)	2538(5.0%)	< 0.001	1.98(1.75–2.23)
Literate	572(13.3%)	4763 (10.3%)	5335(10.6%)	< 0.001	1.47(1.34–1.62)
Basic education	776(18.1%)	7445 (16.1%)	8221(16.3%)	< 0.001	1.28(1.18–1.39)
Smoking (n = 50422)					
No	3664(85.5%)	41071(89.0%)	44735(88.7%)		Ref
Yes	622 (14.5%)	5065 (11.0%)	5687 (11.3%)	< 0.001	1.38(1.26–1.51)
Type of fuel (n = 50209)					
Clean	2886(67.6%)	34628(75.4%)	37514(74.7%)		Ref
Polluted	1384(32.4%)	11311(24.6%)	12695(25.3%)	< 0.001	1.47(1.37–1.57)
Sex of the baby					
Boy	2962(49.7%)	29788(54.4%)	32570(53.9%)		Ref
Girl	3002(50.3%)	24990(45.6%)	27992(46.1%)	< 0.001	1.21(1.15–1.27)
Multiple delivery					
No	5786(97.0%)	54576(99.6%)	60362(99.4%)		Ref

Variables	Preterm (n = 5964)	Non-Preterm (n = 54778)	Total (n = 60742)	p- value	OR (95% CI)
Yes	178 (3.0%)	202 (0.4%)	380 (0.6%)	< 0.001	8.31(6.78–10.19)
Parity					
Multipara	1084(18.2%)	9325 (17.0%)	10409(17.1%)	< 0.001	Ref
Nullipara	3168(53.1%)	26647(48.6%)	29815(49.1%)	0.55	1.02(0.95–1.10)
Primipara	1712(28.7%)	18806(34.3%)	20518(33.8%)	< 0.001	0.78(0.72–0.85)
ANC visit (n = 50424)					
Yes	4229(98.6%)	45669(99.0%)	49898(99.0%)		Ref
No	58 (1.4%)	468 (1.0%)	526 (1.0%)	0.04	1.34(1.02–1.76)
Time of first ANC visit (n = 49898)					
First trimester	1537(36.3%)	19316(42.3%)	20853(41.8%)	< 0.001	Ref
Second trimester	1818(43.0%)	19105(41.8%)	20923(41.9%)	< 0.001	1.20(1.11–1.28)
Third trimester	874(20.7%)	7248(15.9%)	8122(16.3%)	< 0.001	1.52(1.39–1.65)
Major malformation					
No	5,953(99.8%)	54,742(99.9%)	60,695(99.9%)		Ref
Yes	11 (0.2%)	36 (0.1%)	47 (0.1%)	0.003	2.81(1.43–5.52)
Severe anaemia during pregnancy					
No	5,915(99.2%)	54,642(99.8%)	60,557(99.7%)		Ref
Yes	49(0.8%)	136(0.2%)	185(0.3%)	< 0.001	3.33(2.40–4.62)
Outcome (n = 60062)					
Pre-discharge mortality	460(50.1%)	459(49.9%)	919(1.5%)	< 0.001	10.60(9.28–12.10)

Half the total pre-discharge mortalities (50.1%) were due to preterm births and its complications. Similarly, preterm births had 11-times more risk of pre-discharge mortality (OR 10.60; 9.28–12.10)

(Table 1).

The significant variables in univariate were taken for multivariate analysis. In comparison to mothers aged 20-<35 years, the risk of preterm birth was 1.2 times (aOR 1.21; 1.09–1.34) with mothers aged 20 years and younger and 1.3 times (aOR 1.30; 1.05–1.63) with mothers aged 35 years and above. In comparison to mothers with secondary and higher education level, the risk of preterm births with illiterate mothers was 1.9 times (aOR 1.90; 1.66–2.19), literate mothers were 1.48 times (aOR 1.48; 1.33–1.65) and mothers having basic level of education was 1.25 times (aOR 1.25; 1.14–1.38). Similarly, the risk of preterm births among nulliparous mothers was 1.44 times (aOR 1.44; 1.28–1.61) compared to multiparous mothers. Time for ANC visits was significantly associated with preterm births with those mothers going for ANC visits in the second trimester having a risk of 1.1 times (aOR 1.10; 1.02–1.19) and third trimester having a risk of 1.44 times (aOR 1.44; 1.30–1.60). The risk of preterm birth was found to be 2.02 times (aOR 2.02; .84-2.22) for mothers who had a history of smoking. Further, polluted fuel (aOR 1.38; 1.28–1.50), multiple deliveries (aOR 1.92; 1.33–2.76) and severe anemia during pregnancy (aOR 2.43; 1.55–3.82) were also significantly associated with preterm births (Table 2).

Table 2

Multivariate analysis of factors associated with preterm birth (n = 49898)

Variables	$\beta$ – coefficient	p-value	aOR (95% CI)
Age of mother			
20-<35 years	Ref		
< 20 years	0.190	< 0.001	1.21 (1.09–1.34)
> 35 years	0.265	0.018	1.30 (1.05–1.63)
Education level of mother			
Secondary and higher	Ref		
Illiterate	0.644	< 0.001	1.90 (1.66–2.19)
Literate	0.391	< 0.001	1.48 (1.33–1.65)
Basic education	0.225	< 0.001	1.25 (1.14–1.38)
Parity of mother			
Multipara	Ref		
Nullipara	0.361	< 0.001	1.44 (1.28–1.61)
Primipara	0.029	0.628	1.03 (0.92–1.16)
Time of first ANC visit			
First trimester	Ref	< 0.001	
Second trimester	0.091	0.025	1.10 (1.02–1.19)
Third trimester	0.365	< 0.001	1.44 (1.30–1.60)
Smoking			
No	Ref		
Yes	0.702	< 0.001	2.02 (1.84–2.22)
Type fuel			
Clean	Ref		
Polluted	0.325	< 0.001	1.38 (1.28–1.50)
Severe anaemia			
No	Ref		
Yes	0.889	< 0.001	2.43 (1.55–3.82)

Variables	$\beta$ – coefficient	p-value	aOR (95% CI)
Multiple delivery			
No	Ref		
Yes	0.650	< 0.001	1.92 (1.33–2.76)
Sex of the baby			
Boy	Ref		
Girl	0.002	0.956	1.00 (0.93–1.08)
Major malformation			
No	Ref		
Yes	0.708	0.223	2.03 (0.65–6.33)

## Discussion

The study describes the incidence, risk factors and consequences associated with preterm births based on data available from 12 public hospitals across Nepal. The incidence of preterm births was found to be 9.8% among total births while it was 9.3% among live births. In a systematic review conducted with data available from 107 countries, the global preterm birth rate was reported at 10.6% [18] and a systematic analysis based on data available from 184 countries reported an estimated preterm births of 11.1% [1]. Similarly, studies conducted in the United States (9.62%) [19] and Australia (8.6%) [4] have also reported similar estimates. A previous study conducted in a tertiary hospital in Nepal reported at incidence of 8.1% for preterm births [20]. These findings suggest that Nepal's preterm birth rate is in line with developed countries, suggesting an improvement over the national and global estimates.

The study looked at some of the potential risk factors for preterm births. The risk of preterm births was higher among both mothers younger than 20 years and above 35 years. Several other studies have also reported linking both younger and older maternal age with preterm births [4, 21–25]. The risk of preterm births was also higher among mothers with education lower than secondary level had a higher risk of having preterm births. Other studies have also shown similar associations related to lower education levels [7, 9, 26]. This suggests that better educational status of mothers has a direct effect on the birth outcomes. Further, mothers with a history of smoking had higher risk for preterm births. Other studies have also shown similar associations for preterm births [4, 27–29]. Also, the risks were higher for mothers who did not use clean fuel. A recent study conducted in China showed no any significant association with the type of fuel used [30]. However, another study conducted in East India looking at the impact of the fuels in pregnancy outcomes showed a significant association for preterm births [31]. The variations could be due to the difference in sample sizes.

Our study showed that the risk was higher among nulliparous mothers. The findings have also been supported by previous studies [32, 33]. Babies born to mothers who seek ANC visits during second and third trimesters also had a higher risk of being preterm. Seeking ANC visits later in pregnancies can increase the risks of preterm births, studies have shown [21, 23, 34].

The risk of preterm births was also higher among women who had severe anemia during pregnancy. The finding is corroborated by other studies which showed severe anemia increased the risk of preterm births significantly [35–37]. However, a study conducted in Tanzania showed no association with preterm birth, though the study only compared anemia without specifying the type and there were only 2 preterm birth cases [38]. Further, mothers who had multiple deliveries had higher risk of having preterm births. A Korean study also showed similar associations [39]. However, a systematic review and meta-analyses assessing interventions aimed at preventing preterm births among twin pregnancies found that no interventions reduced the risk significantly [40].

The risk was also higher among women whose babies had major malformations although the association was not significant. However, previous studies have shown significant associations [41, 42]. One of the reasons could be the low numbers reported from our study. Sex of the child had no any risks for preterm births. This was in line with another study who also showed no significant association between sex of the child and preterm births [43]. However, several studies have linked male babies with preterm births [44–46].

We also analyzed the consequences of preterm birth. The pre-discharge mortality was 11-times higher for preterm babies. Other studies have also reported similar findings [20, 47, 48].

There are some limitations in the study. The study did not analyze some of the risk factors (e.g. previous medical history, previous preterm births, cervical length, etc.) that have been discussed in the research articles as these data were either not collected in our study or they were underreported. Also, not all mothers took part in the interviews and for those who took part, the information might not be reliable due to recall bias. Further, we only analyzed pre-discharge mortality so we do not know about the consequences thereafter. Having said that, this is a large representative sample from 12 different hospitals. Hence, the results are a likely representation of the incidence of preterm births in Nepal.

## **Conclusion**

Preterm birth has multi-factorial risk factors. Despite the lower than anticipated incidence, it is still high and while some of the risk factors are modifiable and others can be prevented with timely interventions, strategies aiming at better access to education, healthcare services and skilled care at birth are required to further reduce the incidence.

## **Abbreviations**

LMICs:low- and middle-income countries; ANC:antenatal care; CSPro:Census and Survey Processing System; SPSS:Statistical Package for the Social Sciences.

## **Declarations**

### **Ethics approval and consent to participate**

Written informed consent were taken from the mothers before the interview and confidentiality on the information was maintained. The study was approved by Ethical Review Board of Nepal Health Research Council (reference number 26-2017).

### **Consent for publication**

Consent was taken from the individuals prior to the data collection. The information was coded prior to analysis for anonymity. All records have been kept confidentially, following strict ethical guidelines.

### **Availability of data and materials**

The datasets analyzed for this study will be made available by the corresponding author upon request. Data collection forms (data extraction and exit interview) are provided along with the manuscript as additional files 1 and 2.

### **Competing interests**

The authors declare that they have no any competing interests.

### **Funding**

No any funding was received for this paper. The study was funded by Einhorn Foundation, Swedish Foundation for International Cooperation in Research and Higher Education (STINT), Swedish Research Council (VR), Laerdal Foundation for Acute Medicine, Norway and UNICEF Nepal country office.

### **Authors' contributions**

AG, AK, PP and AKS conceived and planned the study. AG and AKS performed the analysis. AG prepared the first draft of the manuscript. MM, JW, NR, YNB, AP, AKS and AK reviewed the manuscript. All authors read and approved the final manuscript.

### **Acknowledgements**

The authors would like to acknowledge the data collectors and Omkar Basnet at Golden Community.

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## Figures

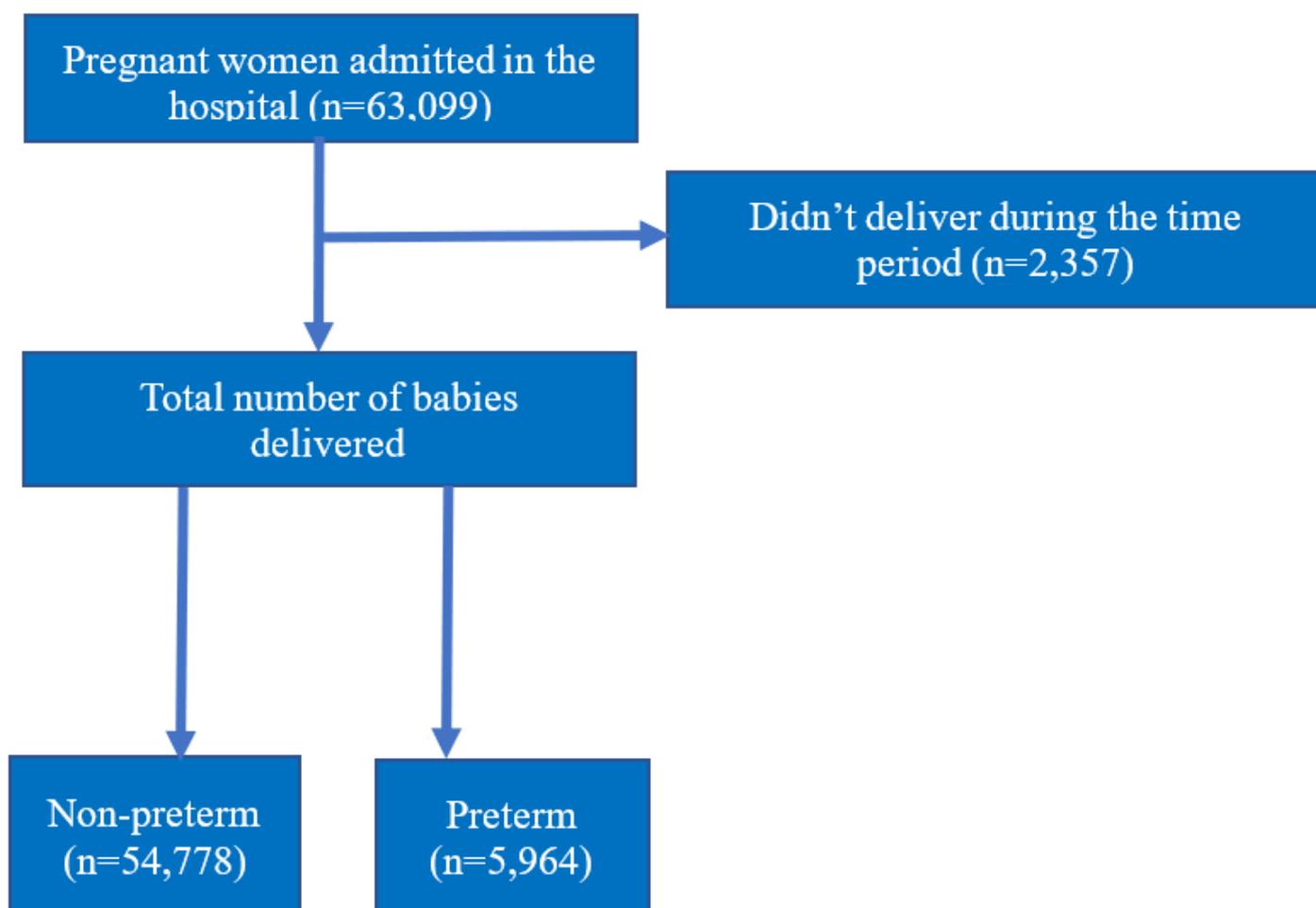
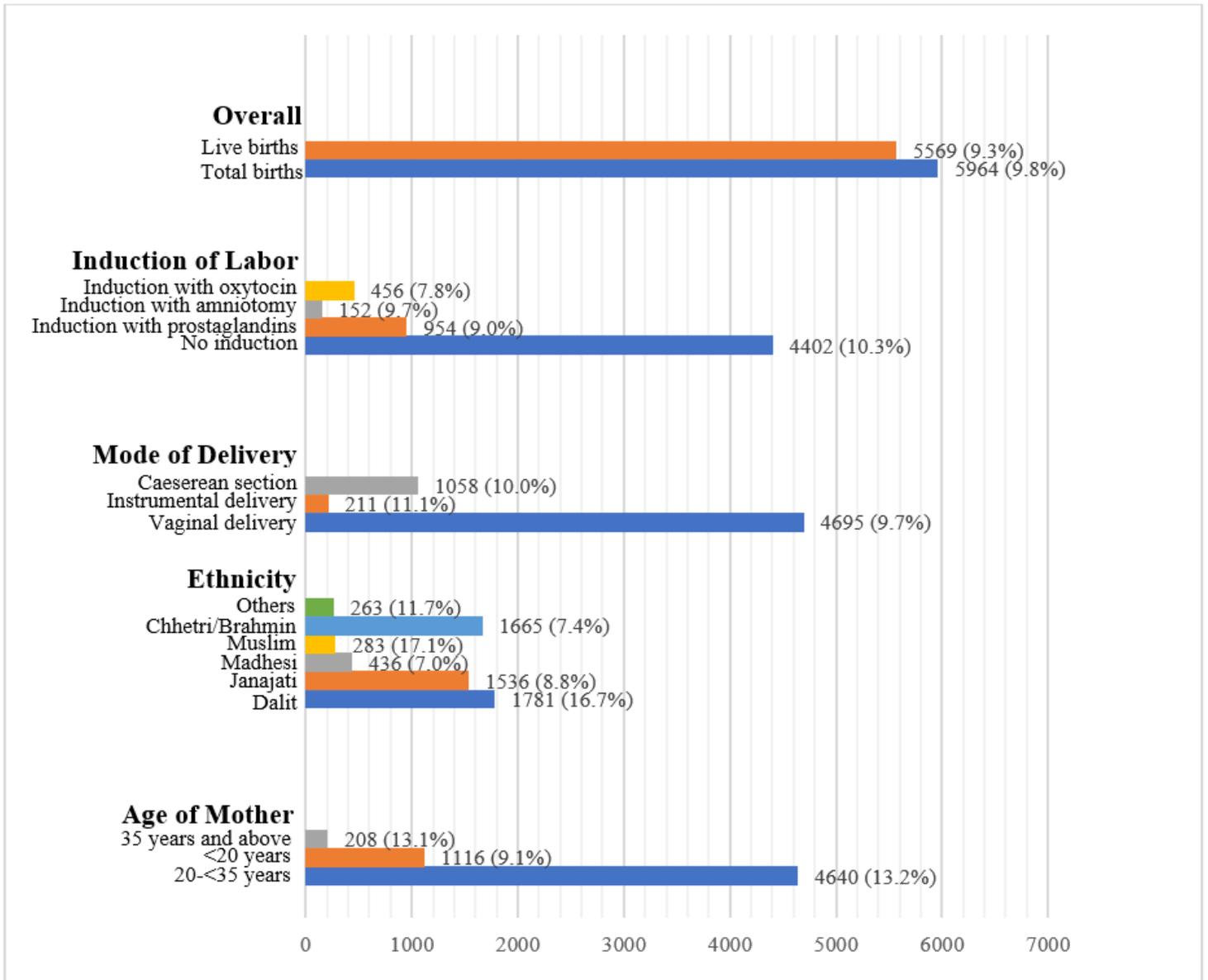


Figure 1

STROBE flow diagram



**Figure 2**

Incidence of preterm (n=60742)

## Supplementary Files

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