PRETERM BIRTH AND PERINATAL OUTCOME: AN OBSERVATIONAL COHORT STUDY

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A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Preterm birth is a common cause for neonatal morbidity and mortality worldwide.

Aim of the study: To compare perinatal outcomes in preterm and term neonates.

Material and methods: The present cohort study was conducted in the Obstetrics and Gynecology Department of MMIMSR, Ambala, a rural tertiary care center of Northern India over a one-year period (January-December 2018). 2,997 antenatal women were recruited at gestation (≥28 weeks) with singleton live pregnancies. All participants were divided into two groups: Group I: Antenatal women delivering at gestation (≥37 weeks) and Group II: Antenatal women delivering at gestation (≥28 to <37-weeks. Onset of labor, mode of delivery, perinatal outcome including birth weight, Apgar scores, Neonatal Intensive Care Unit (NICU) admission, need for intubation, complications, and mortality were compared between groups.

Results: Of 2,997 deliveries, 2,528 (84.4%) were full-term, 469 (15.6%) preterm [48(10.2%) very preterm and 421(89.8%) late preterm] deliveries. The most common mode of delivery in both full-term and preterm participants was spontaneous vaginal delivery (62.8% vs 60.4%) followed by cesarean section (36.6% vs 39.2%). Preterm neonates (especially very preterm) had significantly lower birthweights (p<0.001, OR: 0.898; 95% CI: 0.108-7.48), 1-minute (p=0.018; OR: 7.812; 95% CI: 1.06-57.69) and 5-minutes Apgar scores (p=.000; OR: 3.410; 95% CI: 1.79-6.48) as compared to moderate- to- late preterm neonates. NICU admission rate, need for intubation, neonatal complications, stillbirth and early neonatal deaths were significantly higher in preterm neonates (p=.000). The most common complication in preterm neonates was Respiratory Distress Syndrome 172(55.1%) followed by sepsis 41(54.7%).

Conclusions: Preterm delivery, especially very preterm, was significantly associated with adverse perinatal outcome as compared to full-term delivery.

KEYWORDS: pregnancy, infant, newborn, intensive care units

BACKGROUND

The World Health Organization (WHO) has defined preterm birth as birth before 37 completed weeks of gestation from the first day of a woman's last menstrual period (LMP). Preterm birth is subdivided into three groups based on the gestational age: extremely preterm (<28 weeks); very preterm (28 to<32 weeks); moderate or late preterm (32 to <37 completed weeks of gestation) [1,2]. An estimated 15 million neonates are born preterm (more than 1 in 10 newborns) worldwide, annually [1], with India alone accounting for the maximum contribution to the world's total prematurity burden. According to the WHO 2013 fact sheet, India accounts for 3,519,100 preterm births which is 23.6% of the total preterm births in the world [3,4]. Preterm birth is one of the leading causes of neonatal mortality, accounting for approximately 1 million deaths of children every year due to its complications [5]. Furthermore, preterm birth is responsible for 70% of neonatal deaths and around 75% of neonatal morbidity, including long-term neurocognitive, ophthalmologic disorders, and pulmonary dysfunction [6].

The exact reason for preterm birth is still unclear; however, it can be due to multiple factors of which preterm premature rupture of membranes (PPROM) is one important cause. Other causes include cervical incompetence, uteroplacental insufficiency, multifetal gestation and polyhydramnios [3,7,8].

Aim of the study

The present study was conducted with the aim to compare the overall perinatal outcome in women with preterm (≥28 weeks to <37 weeks) and full-term (≥37weeks) deliveries in a rural tertiary care center of Northern India.

Material and Methods

Study design, setting and duration

The present Observational cohort study was conducted in the Department of Obstetrics and Gynecology of a rural tertiary care center of Northern India over one year from January 2018 to December 2018.

Study Population

2,997 live singleton pregnancies at gestation ≥28 weeks were divided into two groups: Group I Full-term: 2,528 and Group II Preterm: 469, admitted in the labor ward of Department of Obstetrics and Gynecology.

Inclusion criteria

All admitted antenatal women with a single live fetus at gestation ≥28 weeks with or without spontaneous onset of labor were enrolled as participants.

Exclusion criteria

Antenatal women at gestation <28weeks, multifetal gestation, with intra-uterine dead or anomalous fetus, women with a history of substance or tobacco abuse and those who were not able to give formal consent were excluded from the study.

Study size

Consecutive sampling was done and all the subjects fulfilling the inclusion criteria were enrolled over the period of one year.

Ethical Considerations

The study was conducted after ethical approvals were obtained from the MMIMSR Institutional Ethical Committee (IEC No.: 1120).

Methodology

The present study was conducted according to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement. After obtaining ethical approval from the Institutional Ethical Committee and informed written consent from each of the participants in their own language, the socio-demographic parameters including age, gravidity, parity, gestation, were recorded by trained staff members. A thorough medical history of all of the participants and their general and systemic examinations including per-abdominal and vaginal examination were recorded. Based on gestation at the time of delivery, all of the participants were divided into two groups: Group I: antenatal women delivering at term (≥37 weeks) and Group II:

women delivering at gestation (≥28-<37 weeks). Group II was further subdivided into very preterm (28–<32 weeks) and moderate-to-late preterm (≥32–<37weeks). The onset of labor, mode of delivery, perinatal outcome including birth weight, Apgar scores at 1-and 5-minutes, NICU admission, need for intubation, neonatal complications, stillbirth and early neonatal deaths were recorded and compared between the groups. The birth weight was measured using a tabletop-beam weighing scale by trained nursing staff. Neonatal Apgar scores, NICU admission and overall outcome was assessed and recorded by a trained pediatrician on duty at the time of delivery.

Statistical Analysis

Statistical analysis was performed using SPSS software version 22.0. For comparison of two continuous variables such as neonatal birthweight and Apgar scores, unpaired t-test/Mann-Whitney U-test was performed. For comparison between more than two groups such as age and gestation, an ANOVA/Kruskal-Wallis test was performed. The qualitative variables such as NICU admission, neonatal complications, and perinatal mortality were correlated using a Chi-Square test A p value of ≤ 0.05 was considered statistically significant.

Results

Of a total 2,997 live births at gestation (≥28 weeks), 2,528 (84.4%) were full-term and 469 (15.6%) were preterm births. The mean age (±SD) for full-term participants was 25.08±3.193 years and for preterm was 25.55±3.653 years with the majority of participants (88.7%) belonging to the 21-30 years of age group. The average gestation in Group I was 38.82±1.121 weeks and for Group II was 34.77±2.001 weeks. The majority of the participants in both groups were multigravida and multiparous. The most common maternal high-risk factors associated with preterm birth were hypertensive disorders of pregnancy, anemia, malpresentations, antepartum hemorrhage and Rhesus factor (Rh) incompatibility. The most common mode of delivery in both of the groups was spontaneous vaginal delivery (62.8% vs 60.4%). The comparison of socio-demographic features between the two groups is described in Tab. 1.

Preterm birth was found to be significantly associated with adverse perinatal outcome including low birth weight (p<0.001; OR:10.369; 95% CI: 8.29-12.96), poor 1-minute (p<0.001; OR: 1.925; 95% CI:1.45-2.56) and 5-minutes Apgar scores (p<0.001; OR: 9.940; 95% CI: 6.91-14.31), increased rate of NICU admission (p<0.001; OR: 8.914; 95% CI: 7.07-11.21), need for intubation (p<0.001; OR:10.880; 95% CI: 7.01-16.87), neonatal complications (p<0.001; OR:5.034; 95% CI: 4.07-6.22), stillbirth (p<0.001; OR:9.561; 95% CI: 2.78-32.79) and neonatal deaths (p<0.001; OR:9.158; 95% CI: 3.312-25.32) as described in Tab. 2. Furthermore, the neonatal outcome was significantly worse in very preterm as compared to moderate-to-late preterm neonates as described in Tab. 3.

Table 1. Socio-demographic features.

Parameters		Term N (%)	Preterm N (%)	Chi-square test	p-value	Odds Ratio	95% Confidence Interval
Age (Years)	≤20	141(5.6%)	25(5.3%)	13.637	0.001	-	-
	21-30	2259(89.4%)	400(85.3%)				
	>30	128(5.1%)	44(9.4%)				
Gravidity	Primigravida	1018(40.3%)	171(36.5%)	2.397	0.122	1.175	0.95-1.44
	Multigravida	1510(59.7%)	298(63.5%)				
Parity	Nulliparous	1180(46.6%)	197(42.0%)	3.478	0.062	1.209	0.99-1.47
	Multiparous	1348(53.4%)	272(58.0%)				
Mode of Delivery	Vaginal	1588(62.8%)	283(60.4%)	4.920	0.085	-	-
	Cesarean Section	925(36.6%)	184(39.2%)				
	Instrumental	15(0.6%)	02(0.4%)				
Perinatal outcome	Live	2518(99.6%)	452(96.4%)	18.630	0.001	9.470	2.63-31.68
	Stillbirth	04(0.2%)	07(1.5%)	19.260	0.001	9.561	2.78-32.79
	Neonatal death	06(0.2%)	10(2.1%)	26.749	0.001	9.158	3.312-25.32

Table 2. Comparison of neonatal outcome between term and preterm neonates.

Neonatal Parameters		Term N (%)	Preterm N (%)	Chi-square test	p-value	Odds Ratio	95% Confidence Interval
Birth weight (Kg)	<2.5	487(19.3%)	334(71.2%)	536.815	0.001	10.369	8.29-12.96
	≥2.5	2041(80.7%)	135(28.8%)				
1-minute Apgar score	<7	1963(77.7%)	408(87.0%)	20.899	0.001	1.925	1.45-2.56
	>7	565(22.3%)	61(13.0%)				
5-minutes Apgar score	<7	52(2.1%)	81(17.3%)	215.918	0.001	9.940	6.91-14.31
	>7	2476(97.9%)	388(82.7%)				
NICU admission	Yes	211(8.3%)	210(44.8%)	434.828	0.001	8.914	7.07-11.21
	No	2317(91.7%)	259(55.2%)				
Need for Intubation	Yes	33(1.3%)	59(12.6%)	169.906	0.001	10.880	7.01-16.87
	No	2495(98.7%)	410(87.4%)				
Neonatal Complications	Yes	372(14.7%)	218(46.5%)	252.495	0.001	5.034	4.07-6.22
	No	2156(85.3%)	251(53.5%)				
Stillbirth	Yes	04(0.2%)	07(1.5%)	19.260	0.001	9.561	2.78-32.79
	No	2524(99.8%)	462(98.5%)				
Neonatal Death	Yes	06(0.2%)	10(2.1%)	26.749	0.001	9.158	3.312-25.32
	No	2522(99.8%)	459(97.9%)				

Table 3. Comparison of neonatal outcome between moderate to late preterm and very preterm neonates.

Neonatal Parameters		Moderate to Late Preterm N (%)	Very Preterm N (%)	Chi-square test	p-value	Odds Ratio	95% Confidence Interval
Birth weight (Kg)	<2.5	286(67.9%)	48(100%)	21.613	0.001	0.898	0.108-7.48
	≥2.5	135(32.1%)	00(0%)				
1-minute Apgar score	<7	361(85.7%)	47(97.9%)	5.639	0.018	7.812	1.06-57.69
	>7	60(14.3%)	01(2.1%)				
5-minutes Apgar score	<7	63(15.0%)	18(37.5%)	15.315	0.001	3.410	1.79-6.48
	>7	358(85.0%)	30(62.5%)				
NICU admission	Yes	166(39.4%)	44(91.7%)	47.548	0.001	16.890	5.96-47.91
	No	255(60.6%)	04(8.3%)				
Need for Intubation	Yes	37(8.8%)	22(45.8%)	53.76	0.001	8.782	4.54-16.99
	No	384(91.2%)	26(54.2%)				
Neonatal Complications	Yes	178(42.3%)	40(83.3%)	29.192	0.001	6.826	3.12-14.94
	No	243(57.7%)	08(16.7%)				
Stillbirth	Yes	06(1.4%)	01(2.1%)	0.127	0.722	1.472	0.173-12.48
	No	415(98.6%)	47(97.9%)				
Neonatal Death	Yes	02(0.5%)	08(16.7%)	54.133	0.001	41.910	8.60-204.05
	No	419(99.5%)	40(83.3%)				

The most common neonatal complication observed in preterm neonates was Respiratory Distress Syndrome 172(55.1%) followed by sepsis 41(54.7%), whereas in full-term neonates, it was jaundice 186(88.2%) followed by hypoglycemia 12(75.0%) as shown in Fig. 1.

DISCUSSION

In the present study of total 2,997 neonates delivered, 2,528(84.4%) were term and 469(15.6%) preterm with 421(89.8%) moderate to late preterm and 48(10.2%) very preterm. The mean (±SD) gestational age in term group was 38.82±1.121 weeks and in preterm group 34.77±2.001 weeks. Similar results were reported by a study conducted in Trinidad and Tobago on 129 preterm neonates with 59.7% moderate to late preterm, 33.3% very preterm and 7.5% extremely preterm neonates and concluded that preterm delivery was associated with increased risk of neonatal morbidity and mortality with 12.4% neonatal deaths before discharge, and 11.6% survived with major disabilities [9]. Another similar study conducted in Greater Paris on 2,172 live births found that 13.6% (95% CI 12.2–15.1) of newborns were preterm. The median gestation for full-term neonates was 39 weeks and for preterm neonates was 35 weeks [10].

In this study, the majority of the women having preterm delivery were multiparous and belonged to the 21-30 years of age group (mean±SD: 25.55±3.65 years) with spontaneous vaginal delivery (60.4%) as the most common mode of delivery. Another similar study conducted on 21,075 women delivering at gestation (≥ 20 weeks) reported that the incidence of preterm delivery was 5.8%, of which 85% belonged to the 32 to36 weeks of gestation group and was least common in women of the 20 to 35 years of age group. The authors observed that preterm birth was more com-

mon with male fetuses and in primigravida. They also concluded that preterm neonates were significantly at higher risk of perinatal morbidity and mortality as compared to full- term neonates [11]. Similar to our study, many authors have reported that preterm births were more common in multiparous women [11–14]. Many other studies have reported that preterm birth was more common in young (<20 years) and advanced (≥40 years) age mothers [14,15].

In this study, it was observed that preterm neonates have a significantly adverse outcome with low birth weight (p<0.001; OR:10.369; 95% CI: 8.29-12.96), poor 1 minute (p<0.001; OR:1.925; 95% CI: 1.45-2.56) and 5-minutes (p<0.001; OR:9.940; 95% CI: 6.91-14.31) Apgar scores, increased NICU admission (p<0.001; OR: 8.914; 95% CI: 7.07-11.21), need for ventilator (p<0.001; OR:10.880; 95% CI: 7.01-16.87), neonatal complications (p<0.001; OR:5.034; 95% CI: 4.07-6.22), stillbirth (p<0.001; OR:9.561; 95% CI: 2.78-32.79) and early neonatal deaths (p<0.001; OR:9.158; 95% CI: 3.312-25.32) as compared to term neonates. Furthermore, very preterm neonates were more significantly associated with adverse perinatal outcome as compared to moderate to late preterm neonates (p<0.05). Similar results were reported by a study which concluded that neonates in preterm group were significantly associated with adverse perinatal outcomes, such as low birth weight, poor 1 and 5-minutes Apgar score, compared with term neonates (*P* < 0.05) [16]. Another study reported that the Apgar scores were significantly affected by advancing gestational age (*P*< 0.001), neonatal birthweight (*P*< 0.001), head circumference (*P*< 0.001) and placental weight (*P*< 0.001) [17]. A recent study observed that preterm newborns had a 3.8-fold higher risk of infant mortality than full-term neonates (RR 3.8, 95%CI 2.7–5.2) and 4-fold higher risk of neonatal (RR 4.3, 95% CI 2.9–6.6) and 3-fold higher risk for post-neo-
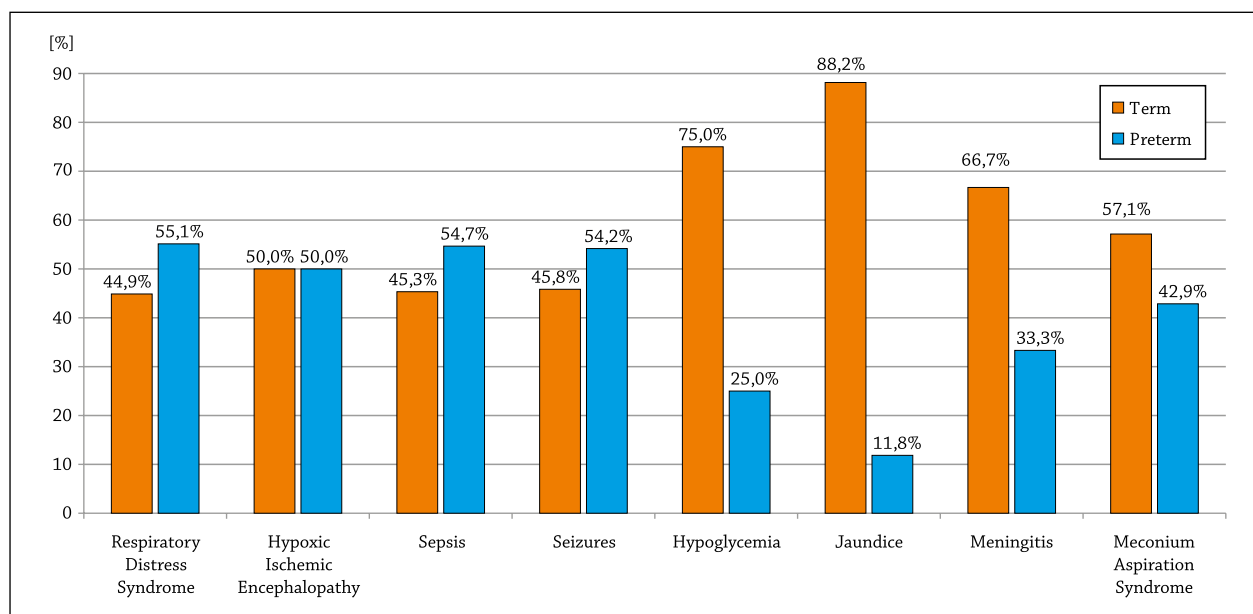

Figure 1. Comparison of neonatal complications in full-term and preterm neonates.

natal deaths (RR 3.0, 95% CI 1.7–5.2) [10]. In this study, 3.6% preterm neonates had perinatal mortality (7 stillbirths and 10 early neonatal deaths) as compared to 0.4% (4 stillbirths and 6 early neonatal deaths) in term neonates (p<0.001), accounting for 63.0% of total perinatal deaths. Similar to this study, another recent study conducted in Bangladesh reported that the preterm neonates were associated with 46% of all neonatal deaths, with 40% in the late preterm group, 20% in moderately preterm and 40% in very preterm neonates. They also concluded that the preterm neonates carry a 3.5 times higher mortality risk as compared to term neonates (RR=3.5, 95% CI=2.9 to 4.3) [18]. Similar results of adverse perinatal outcomes and an increased risk of mortality in preterm neonates as compared to full-term neonates was reported by many other studies [7,19–21].

A recent global survey has shown that India ranks first amongst the top ten countries with the greatest number of preterm births, around 35,019,100 preterm births every year [4]. The table 4 shows the comparison of preterm births in this study with different parts of India, different countries of Asia and global comparison.

Table 4. Comparison of preterm births in india and all over the world.

Comparison amongst states in India	
States	**Estimated Preterm births (N or %)**
Present Study	15.6%
Maharashtra	6.1% [22]
Gujrat	8.9% [23]
South India	23.3% [24]
North India	5.8% [25]
Comparison amongst different countries in Asia [4]	
India	3 519 100
China	1 172 300
Pakistan	748 100
Bangladesh	424 100
Global Comparison [26]	
Asia	7 847 643
Sub-Saharan Africa	4 182 440
Latin America and the Caribbean	1 062 800
Europe	690 931
North America	491 297

The common reasons for preterm births identified in developing countries, especially in India, are maternal anemia, hypertension in pregnancy, diabetes, tobacco use, obesity and domestic violence [27]. By providing appropriate antenatal care to mothers, the risk of preterm births can be significantly reduced.

Limitations of the study

The present study was conducted over a short period and small sample size. In future studies, a larger population size (including preterm deliveries) at centers other than ours in India will be considered. Furthermore, various maternal risk factors will be correlated with preterm births and their complications.

Clinical Implications

Preterm births carry the major burden for perinatal morbidities and mortalities all over the world. Preterm neonates are at an increased risk of birth asphyxia, poor Apgar scores, increased rate of NICU admission, need for ventilators, hypothermia and hypoglycemia [16,17]. They are also prone to developing long-term complications in their childhood and adulthood such as delayed development of milestones, retarded growth, learning disabilities, attention-seeking problems and speech disorders. The risk of preterm births can be prevented to some extent by identifying women at increased risk of preterm births such as those having history of any previous preterm births, ultrasound for cervical length, vaginal infections, particularly Group B Streptococcal infections, and women with multifetal gestation. Women identified as having an increased risk of preterm births can be managed by progesterone supplementation, cerclage operations, and antibiotic therapy [28].

According to the WHO, more than three quarters of premature neonates can be saved easily by using cost-effective methods such as providing essential maternal and neonatal care during childbirth and in the postnatal period to mothers and neonates. Antenatal steroid injections can be given to women at increased risk of preterm births(to hasten fetal lung maturity), kangaroo mother care, thermal care and frequent breast feeding to all preterm neonates, delayed cord clamping (to prevent anemia in these neonates and antibiotic treatment to newborns with infections or sepsis. The described methods have led to a major reduction in the incidence of neonatal morbidities and mortalities associated with preterm births [29].

CONCLUSIONS

Preterm birth was associated with adverse overall perinatal outcome with increased risk of neonatal morbidity and mortality as compared to full-term neonates. Very preterm neonates were more adversely affected than moderate-to-late preterm and therefore, carried a higher risk of developing chronic complications in later life including neurocognitive disorders due to poor development of the brain. The majority of the preterm births described in the present study are due to preventable causes and can be avoided by identifying these problems and treating them at an early gestation period, which could reduce the overall burden of preterm births in India.

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