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Research Article

PROSPECTIVE ANALYSIS OF PRETERM LABOUR: ITS ETIOLOGY AND OUTCOME

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ABSTRACT
Preterm birth has emerged as the most common cause of perinatal morbidity and mortality.The incidence of preterm labour has been increasing over the last few decades. This study was undertaken to analyse the risk factors and aetiology of preterm labour, mode of delivery and neonatal outcome so that the analysis could be used to identify the high risk patients and help improve neonatal survival. A prospective study was conducted between December 2010 and March 2012 on 100 pregnant women presenting to the labour room of Dayanand Medical College and Hospital, Ludhiana between 24 – 37 weeks of gestation with spontaneous preterm labour. In patients <34 weeks gestation, tocolysis was started, if not contraindicated, to delay delivery by ≥48 hours. Injection betamethasone 12 mg I/M, 2 doses, 24 hours apart were given. The patients were followed up till delivery. Gestational age at the time of delivery, mode of delivery and neonatal outcome in terms of birth weight, morbidity and mortality were recorded. Genitourinary infection was the most common risk factor identified and E coli was the most common causative organism found in urine and vaginal cultures. Other important risk factors identified included previous history of preterm labour and abortions, Preterm Premature Rupture of Membranes (PPROM), multiple pregnancy and Ante Partum Haemorrhage (APH). Tocolytics helped prolong the pregnancy by ≥48 hours in 65% patients with Bishop Score ≤5 at admission. Vaginal delivery was the more common mode of delivery at lesser gestation (80% at <28 weeks).The most common neonatal complications seen were jaundice, Respiratory Distress Syndrome (RDS) and sepsis. The incidence of RDS was high in babies <28 weeks gestation and weighing <1000 grams at birth. In patient who received both doses of betamethasone, incidence of RDS was significantly reduced. The perinatal mortality rate in our study was 12.84% and it was highest in babies born <28 weeks of gestation and with birth weight <1000 grams. Hence it was concluded that preterm labour has identifiable risk factors. Extreme prematurity has a high morbidity and mortality rate. Identifying risk factors to prevent onset of preterm labour, tocolysis to delay delivery by ≥48 hours in order to give two doses of antenatal steroids and an advanced neonatal care unit can help decrease neonatal morbidity and mortality.

Keywords: *Preterm Labour, Aetiology, Neonatal Outcome, Prematurity, Low Birth Weight*

INTRODUCTION
Preterm birth remains a major cause of perinatal mortality and long term sequelae in surviving infants. In industrialized countries, 5-11% of infants are preterm (<37 weeks gestation), and the rate has been increasing since the early 1980s. 10.6% neonates born in USA in 1990 were preterm, in the year 2000 the incidence increased to 11.6% and in 2004 to 12.5% (Gabbe *et al.,* 2007). According to a survey published in The Lancet (2012), India tops the list of the 10 countries with the greatest number of preterm births. The importance of preterm labour lies in the fact that 75% of all perinatal deaths occur in preterm infants (Arias, 2009). Though a wide spectrum of causes and demographic factors has been implicated, aetiology remains obscure in a large number of cases. Possible etiological factors include increase in maternal age, increased incidence of underlying maternal health problems such as diabetes and hypertension, greater use of infertility treatments leading to increased rates of multiple pregnancies and changes in obstetric practices such as more caesarean births before term. The rising rate of preterm birth represents the failure of modern obstetrics to understand the complexity of the phenomena and to develop effective preterm birth prevention interventions. The obstetrician has to decide whether to try and conserve the pregnancy a

little longer so as to improve the chances of healthful survival of the baby or to resign to the inevitability of premature delivery. The neonatologist has the onerous task of looking after the preterm neonate and seeing it through the turbulent period when the baby tries to attain maturity. In the past several decades major progress has been made in improving the survival of extremely premature neonates, mostly attributable to the timely access to effective interventions that ameliorate prematurity associated mortality and morbidity such as antenatal administration of corticosteroids and exogenous surfactant therapy. This study analyses the risk factors and the aetiology of preterm labour and the outcome of such pregnancies in a tertiary care centre in our country, so that this analysis can be used in early identification of high risk patients and help improve the neonatal survival.

MATERIALS AND METHODS

A prospective study was conducted on 100 pregnant women with preterm labour admitted in the Labour Room of Dayanand Medical College and Hospital, Ludhiana from December 2010 to March 2012. Pregnant women with gestational age between 24-37 weeks getting uterine contractions ≥ 4 in 20 min or ≥ 8 in 1 hour with effacement > 80% and cervical dilatation≥1 cm were included in the study.

At the time of admission a detailed history was taken and thorough general physical, systemic and obstetric examination was done paying special attention to the presence of conventional risk factors for preterm labour. Gentle per speculum examination and if required a per vaginum examination and Bishop scoring was done. Complete haemogram, urine routine examination, urine culture and sensitivity, vaginal culture and sensitivity and CRP levels were sent. Ultrasonography was conducted as and when required to document fetal gestational parameters, rule out multiple pregnancy, congenital malformations and fetal growth restriction, Amniotic Fluid Index, placental localization and grading and also to assess the cervical length and status of the cervical os. The patient and her attendants were counseled regarding the need for surfactant, cost of nursery care and prognosis. Women< 34weeks of pregnancy at the time of admission were given 2 doses of betamethasone 12 mg I/M 24 hours apart. For tocolysis, parenteral infusion of isoxsuprine hydrochloride was started at 60µg/min and stepped up by 60µg/min every 20 min till contractions stopped, avoiding tachycardia (pulse rate >120/min) and hypotension (<100/60mmHg). The infusion was continued for 24 hours before shifting to oral isoxsuprine 40 mg sustained release preparation twice a day. Tocolytics were not given to women in active phase of labour (> 3 cm dilatation), > 34 weeks of gestation, any evidence of chorioamnionitis, ante partum haemorrhage, hypertensive disorder of pregnancy, fetal distress, severe IUGR or with dead or congenitally malformed fetus. Women with medical conditions contraindicating tocolysis like diabetes, cardiac disease and hyperthyroidism were also not started on tocolytics. Antibiotic was given according to culture and sensitivity report. These patients were followed up till delivery. 95 patients delivered in DMC & Hospital. Gestational age at the time of delivery, mode of delivery and neonatal outcome in terms of birth weight, morbidity and mortality were recorded.

Statistical analysis of the results was done using unpaired T test.

RESULTS

Incidence of preterm deliveries in our institute during the study period was 20.4% and that of spontaneous preterm labour was 13.8%. At the time of admission 57.8% subjects had gestational age of 32 -36 weeks, 29% were with gestational age 28-31 weeks and 13% subjects were less than 28 weeks. We found a higher incidence of preterm labour in young women < 30 years of age and in females with body mass index less than 25 kg/m^2.

As seen in Table1, past obstetric history had an impact on the outcome of the present pregnancy. 21% patients presenting with preterm labour had a past history of abortions and 12 % had a history of preterm delivery in a previous pregnancy also. Genitourinary tract infection was found to be the most common risk factor related with preterm labour in this study. 39% patients had either vaginal infection (26%) or urinary tract infection (20%), or both, as evidenced by positive cultures. Total leucocyte count and C-reactive protein which are markers of infection were raised in 26% and 33% females respectively.

Table 1: Distribution of subjects according to risk factors

RISK FACTORS	%age
Past obstetric history	
Abortions	21
Previous preterm delivery	12
Cervical incompetence	3
Present Obstetric history	
Threatened abortion	6
Genitourinary infections	39
Vaginal infection	26
UTI	20
Chorioamnionitis	6
PPROM	29
Ante partum haemorrhage	11
Abruption	9
Placenta praevia	2
PIH	9
Multiple Pregnancy	13
Twins	12
Spontaneous	2
ART	10
Triplets	1
Spontaneous	0
ART	1
Polyhydramnios	4
Malpresentation	7
Co morbid gynaecological conditions	
Infertility	6
Fibroid uterus	2
Uterine malformations	2
Co morbid medical conditions	
Diabetes Mellitus	4
Acute febrile illness	10

Table 2: Organisms Causing Genitourinary Infections

Organism	Urine (20)		Vagina (26)	
	No.	%	No.	%
E – coli	8	40	9	34.61
Enterococcus	4	20	6	23.07
Klebsiella	2	10	3	11.53
Staph aureus	3	15	4	15.38
Proteus mirabilis	1	5	1	3.85
Pseudomonas	1	5	1	3.85
Non-hemolytic Streptococcus	1	5	-	-
Candida	-	-	2	7.69
MRSA	-	-	-	-

E. coli was the most common organism isolated both in urine culture (40%) and vaginal culture (34.61%). Other common organisms identified were enterococcus, Staphylococcus aureus and Klebsiella (Table 2).

Premature rupture of membranes preceded onset of preterm labour in 29% cases. A strong correlation was found between multiple pregnancy, use of artificial reproductive techniques and prematurity. Of the 12 twin pregnancies, 83.3% were conceived by artificial reproductive techniques. Majority of them (58.3%) delivered before 32 weeks of gestation. Another important risk factor identified in this study was antepartum haemorrhage (11%) of which abruption placentae was the cause in 81.81% cases (Table 1).

The mean Bishop score at admission in our study was 7.59 with a standard deviation of 2.52. 76.9% of patients with Bishop Score ≤ 5received tocolysis. Pregnancy was prolonged by ≥ 48 hours in 65% patients in this group. In patients with Bishops score 6-10 tocolytics were given in 46.67% patients of whom pregnancy could be prolonged by ≥48 hours in only 23%.This difference was found to statistically significant.

Out of 100 patients enrolled in the study 95 subjects delivered in DMCH and 5 were lost to follow up. 109 babies were born in our institute. 32.63% were delivered by caesarean section the common indications for which were malpresentation (22.58%), foetal distress (19.35%) and antepartum haemorrhage (16.13%). Vaginal delivery was the more common mode of delivery at lesser gestation (80% at < 28 weeks). Caesarean section rate increased with increase in gestation being 20% at < 28 weeks and 50% at ≥ 37 weeks.

Majority of the babies (57.8%) were born at 32-36 weeks and 10.09% babies were < 28 weeks gestation at birth. 12.84% babies were extremely low birth weight (ELBW) i.e. weighing <1000 grams, 21.10% were very low birth weight (VLBW) weighing between 1000 grams to 1500 grams and 49.54% were low birth weight (LBW) babies (<2500 grams). 81.82% babies born before 28 completed weeks of gestation were ELBW (<1000 Grams). All babies born after 37 completed weeks weighed >2500 g (Table3).

Table 3: Relationship between Gestational Age and Birth Weight

Gestational Age (weeks)	No. (%)	<1000g	1000 – 1499g	1500 – 1999g	2000 – 2499g	>2500g
		No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
<28	11 (10.09)	9 (81.82)	2 (18.18)	0 (0)	0 (0)	0 (0)
28 – 31	29 (26.61)	5 (17.24)	17 (58.62)	6 (20.69)	1 (3.45)	0 (0)
32 – 36	63 (57.80)	0 (0)	4 (6.35)	25 (39.68)	22 (34.82)	12 (19.05)
>37	6 (5.50)	0 (0)	0 (0)	0 (0)	0 (0)	6 (100)
Total	109 (100)	14 (12.84)	23 (21.10)	31 (28.44)	23 (21.10)	18 (16.51)

P value 0.00187 (Significant)

As shown in table 4, preterm babies suffered from various complications like jaundice, respiratory distress syndrome, sepsis, coagulopathy, hypocalcaemia, hypoglycemia, necrotizing enterocolitis and congenital malformations. The frequently seen complications included Jaundice (28.44%), RDS (15.6%) and sepsis in 12.84% cases.

Table 4: Neonatal Morbidity Associated With Prematurity

Neonatal Morbidity	No.	%age
Respiratory distress syndrome	17	15.60
Transient tachypnea of newborn	1	0.92
Congenital pneumonia	1	0.092
Jaundice	31	28.44
Coagulopathy	10	9.17
Hypocalcemia	3	2.75
Hypoglycemia	3	2.75
Sepsis	14	12.84
Necrotizing enterocolitis	2	1.83
Congenital malformation	5	4.59

Table 5: Relationship of gestation with RDS

Gestational Age (weeks)	Total births (109)		RDS	
	No.	%age	No.	%age
<28	11	10.09	6	54.55
28 to 31	29	26.61	10	34.48
32 to 36	63	57.80	1	1.59
>=37	6	5.50	0	0.00

P-value 0.01147 (Significant)

Table 6: Relationship of Birth Weight with RDS

Weight (grams)	Total Births (109)		RDS	
	No.	%age	No.	%age
<1000	14	12.84	7	50.00
1000-1499	23	21.10	9	39.13
1500-1999	31	28.44	1	3.23
2000-2499	23	21.10	0	0.00
>=2500	18	16.51	0	0.00
Total	109		17	15.60

P-value 0.00254 (significant)

There was a statistically significant decrease in the incidence of RDS as the gestational age and birth weight increased (Tables 5 and 6). At <28 weeks gestation incidence of RDS was 54.55% and it decreased to 1.59% at 32-36 weeks. 50% of the extremely low birth weight babies developed RDS. 40.36% babies received both doses of betamethasone and 30.27% babies could receive only single dose of antenatal steroid as they delivered before the second dose could be given. Standard dose of antenatal steroid had better protection for RDS than single dose as RDS was seen in only 13.63% when 2 doses were given and in 21.21 % when one dose was given.
Perinatal mortality rate was 12.84% in our study.

Table 7: Relationship of Birth Weight with mortality

Weight (g)	No.	Mortality	
		No.	%age
<1000	14	8	57.14
1001-1499	23	3	13.04
1500-1999	31	2	6.45
2000-2499	23	0	0.00
>2500	18	1	5.56
Total	109	14	

P-value 0.00167

Mortality was more in the extremely low birth weight babies (57.14%) and mortality decreased as the birth weight increased (Table 7).

Table 8: Relationship of gestation with mortality

Gestational Age (weeks)	Total Births	Deaths	
		No.	%
<28	11	5	45.45
28 to 32	29	6	20.69
32 to 37	63	3	4.76
>= 37	6	0	0.00
	109	14	12.84

P-value 0.00347

Mortality was maximum (45.45%) in extremely premature babies and mortality decreased as gestational age increased (Table 8).
Mortality was more in patients who delivered vaginally (16%) than by caesarean section (5.8%).

DISCUSSION

In our institute 20.4% patients delivered before 37 completed weeks of gestation during the study period. This is significantly more than the incidence of preterm birth given by researchers like Sumana and Misra (2006) who reported an incidence of 5-12% and Singh M (2010) who reported an incidence of 10-12%. The high incidence of preterm births in our institute is probably because, being a tertiary care center dealing with high risk pregnancies, this includes those patients who were delivered before term in view of other obstetric indications. The incidence of spontaneous preterm deliveries was 13.8% which is also higher than that reported by other workers. This may be because patients in preterm labor are referred here from other centers to avail nursery care.

Aetiology of preterm labour was found to be multifactorial. We found a correlation between past obstetric history and the reproductive outcome in the present pregnancy. 21% patients presenting with preterm labor had a past history of abortions.Our results were consistent with the findings of Trivedi *et al.,* (1995), Chhabra *et al.,* (2001) and Singh *et al.,* (2007) where 22.6% 18%, and 14.4% subjects respectively had history of previous abortions. 12% patients in our study had history of preterm delivery in the previous pregnancies also. Singh Uma *et al.,* (2007) also found that 14.4% patients had history of previous preterm delivery. Pandey *et al.,* (2010) also concluded that prior preterm birth is a risk factor for preterm labour and it was identified in 14.14% (41/290) subjects in their study group. Therefore a detailed past obstetric history should be taken in all antenatal patients and those with a prior history of spontaneous abortions or preterm births should be counselled regarding the risk of preterm labour in the present pregnancy and managed accordingly.

The commonest risk factor for preterm labour in our study was genitourinary tract infection. 26% subjects in our study had vaginal infection. Singh *et al.,* (2007) found positive vaginal culture in 12.25% patients and Deka *et al.,* (1997) found that cervical infection was present in as many as 55% patients with preterm labor. Similarly Chhabra *et al.,* (2001) found that genital tract colonization was a common risk factor for preterm labour seen in 28% patients. We found that E. coli was the most common organism isolated both in urine culture (40%) and vaginal culture (34.61%). Other common organisms were Staphylococcus aureus, Klebsiella and enterococcus. Singh *et al.,* (2007) also found that E. coli and Staph aureus were the commonest organisms (32% each) isolated. In the study conducted by Deka *et al.,* (1997) most commonly isolated organisms were Staphylococcus aureus, micro aerophilic gram positive non sporing bacilli and Peptostreptococcus.

20% patients in the study group had urinary tract infections. Similar finding were reported by Pandey *et al.,* (2010), Chhabra *et al.,* (2001) and Singh *et al.,* (2007) who found an incidence of 20.34%, 14% and 8.4% respectively confirming that UTI is an important risk factor for preterm labour.This means that it is important to diagnose UTI early and treat it aggressively to prevent preterm labour.

Another important cause of preterm labour in our study was preterm premature rupture of membranes which was associated with 29% preterm births. This is in accordance with Singh *et al., 's* study (2007) where preterm premature rupture of membranes was associated with 25.9% preterm births and was the commonest cause of preterm labour.

Multiple pregnancy was found to be associated with preterm labour in 13% of our patients. Arias (2009) also reported that multiple pregnancy was responsible for 12-25% of all preterm deliveries. Artificial Reproductive Techniques (ART) accounted for an increase in multifetal pregnancies and resulted in 58.3% babies being born before completing 32 weeks of gestation in this study. This has been corroborated by other workers like Martin and Park (1999) and Sonkusare *et al.,* (2009) who found the use of assisted reproductive technology to be an important contributor to the increase in the rate of low birth weight in the United States. ART was found to be associated with low birth weight because it is associated with a higher rate of multiple birth which, in turn, is associated with low birth weight (Venkat

et al., 2003). Ante partum haemorrhage contributed to 11% preterm births in our study of which 81.81% had abruptio placenta. Tocolysis was not offered to these patients and they were allowed to deliver. This is in accordance with the findings of Singh *et al.,* (2007) who also found that antepartum haemorrhage either led to spontaneous onset of preterm labour or induction of labour in view of abruptio placentae in 10.8% patients.

Isoxsuprine hydrochloride was the tocolytic used to arrest preterm labor in our study. An inverse relation was found between bishop score at admission and prolongation of pregnancy. Review of recent literature did not yield any study using isoxsuprine as a tocolytic agent. However many other workers have found a similar inverse relation using nifedipine or ritodrine to arrest preterm labour. Thus health care providers need to be sensitized that the outcome of preterm labor improves with early referral to higher centers as lower the Bishop score at admission more are the chances of being able to prolong pregnancy by at least 48 hours with the help of tocolytics thus giving time for antenatal steroids to act.

In our study 66.37% patients delivered vaginally and 32.63% had caesarean section. This is almost similar to the findings of Sonkusare *et al.,* (2009) and Venkat *et al.,* (2003) where 56.5% and 61% subjects respectively delivered vaginally. In the present study 80% patients with gestational age <28 weeks delivered vaginally. In a study conducted by Jotwani *et al.*, (2001).

92 % patients presenting in preterm labour delivered vaginally.

The most common neonatal complications in our study group were jaundice (28.44%), RDS (15.6%) and sepsis (12.84%). Sonkusare *et al.,* (2009) reported the incidence of jaundice as 50.80%, RDS as 20.16% and sepsis as 23.39%.These were also the common complications in studies carried out by Singh (2007) and Venkat *et al.,* (2003). The incidence of RDS was maximum (54.55%) in extremely premature babies and reduced significantly with increasing birth weight, gestation and in patients who received 2 antenatal doses of Injection betamethasone.

In our study perinatal mortality rate was 12.84%.A slightly higher mortality rate of 18.18% was reported by Venkat *et al.,* (2003) and Sonkusare *et al.,* (2009) found the mortality rate to be 14.5%.However Jotwani *et al.,* (2001) reported a much higher mortality rate of 35.04%.This shows that over the last few years there is significant reduction in the mortality rate. Mortality was highest (45.45%) in the extremely premature babies i.e. < 28 weeks gestation. As the gestational age increased mortality rate decreased and survival rate increased. A similar trend was reported by Venkat *et al.,* (2003),Trivedi and Nagpal (1995) and Singh *et al.*, (2007).

Conclusion

Hence it can be concluded that various risk factors that lead to preterm labor are identifiable. Preterm infants suffer from many complications and have high mortality. Early identification of risk factors and early interventions in the form of treating the underlying risk factor, employing tocolysis, antenatal steroid prophylaxis and shifting mother to a tertiary care center with advanced neonatology unit can improve the neonatal survival and decrease morbidity and mortality due to prematurity.

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