



A prospective analysis of etiology and outcome of preterm labor

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OBJECTIVE(S) : To identify etiological factors and to assess the neonatal mortality and morbidity associated with preterm labor and delivery.

METHOD(S) : In this prospective cohort study conducted over a 8 months period (January to August 2005) 416 antenatal women admitted with threatened preterm labor and in preterm labor, with or without rupture of membranes, were recruited. They were followed up from admission till delivery and discharge. Gestational age at onset of preterm labor, associated risk factors, response to tocolytics if given, gestational age at delivery, and neonatal outcome were recorded and analyzed.

RESULTS : Incidence of preterm labor was 22% and that of preterm deliveries 20.9% Preterm rupture of membranes and infection were the commonest causes of preterm labor. Irrespective of the use of a course of betamethasone, neonatal mortality was significantly high ($P < 0.0001$) in babies delivering before 34 weeks (30.4%) as compared to that in babies delivering after 34 weeks (3.4%). Septicemia, respiratory distress syndrome (RDS) and birth asphyxia were the important causes of neonatal morbidity. RDS was significantly reduced in those who completed steroid cover ($P = 0.029$).

CONCLUSION(S) : There is a high incidence of preterm labor and preterm births in our set up, compared to developed countries. Infection is one important modifiable risk factor which can be curtailed. Prolongation of delivery for 48 hours by giving tocolysis for getting the benefit of betamethasone coverage reduces morbidity due to RDS but does not reduce overall neonatal mortality below 34 weeks.

Key words : preterm labor, preterm delivery, uterine tocolytics, preterm neonate, rupture of membranes

Introduction

Preterm labor and delivery are very challenging obstetric complications encountered by obstetricians, as are preterm neonates for the pediatricians. Preterm labor is defined as the onset of labor prior to 37 completed weeks of gestation i.e. 359 days from first day of last menstrual period. Preterm delivery affects one in 10 births (11%) in USA¹ and even greater births in developing countries and causes 40-75% neonatal deaths. Due to continued innovation in neonatal intensive care facilities and obstetric interventions, fetal survival is now possible even at 20 weeks gestation in

developed countries. However, in even the best setups in developing countries, salvage is rare below 28 weeks of gestation. Incidence of preterm labor is 23.3% and of preterm delivery 10-69% in India. It is rising world over because of increased frequency of multiple births due to assisted reproductive techniques (ART), more working mothers, increasing psychological stress and medically induced prematurity. Hence it is a time felt need to ascertain the causes and outcome of preterm labor and delivery and also the neonatal care resources available in most Indian nurseries.

Methods

Four hundred and sixteen antenatal women admitted with preterm labor at less than 37 weeks gestational age were recruited. They were evaluated by history taking, clinical examination, and ultrasonography. ACOG criteria (1997) were used to document preterm labor and threatened preterm labor viz., four uterine contractions in 20 minutes with or without cervical dilatation greater than 1 cm or effacement 80% or greater. Leaking i.e., rupture of membranes was diagnosed

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by speculum examination and confirmed by ferning. Detailed history taking, and general, systemic and obstetrical examinations were done paying special attention to presence or absence of conventional risk factors for preterm labor.

All women with preterm labor were investigated for presence of infection by complete hemogram, and urine and vaginal swab culture. Antibiotics were provided to those with ruptured membranes or significant pathogen count on urine or vaginal culture. Women with gestational age greater than 36 weeks, those in active phase of labor (>4cm dilatation), those with signs and symptoms of chorioamnionitis, and those with antepartum hemorrhage, those with fetal distress due to any reason and those with any medical contraindication to tocolytics were not given tocolysis. This group comprised of 216 patients. Tocolytics were given to the other 200 women in either of two forms viz., nifedipine orally or isoxsuprine orally / parentally as per treating obstetrician's choice. The aim of using tocolytics was to delay delivery for at least 48 hours in women with ruptured membranes and through 36 completed weeks of gestation in those whose membranes were intact. Tocolysis was stopped and pregnancy terminated in those with chorioamnionitis, progression to active phase of labor and development of fetal distress.

All those with less than 34 weeks gestation (n=172) were given 12 mg betamethasone intramuscularly at the time of admission and again after 24 hours. Women with rupture of membranes (n=108) were kept on strict bed rest with foot end elevated and given 2g ampicillin intravenously at the time of admission followed by 1g 6 hourly. The type of antibiotic was changed after urine or vaginal culture sensitivity reports. Only 31 of the women with ruptured membranes were given tocolysis. Women were followed till delivery. Risk factors related to preterm labor and neonatal outcome were recorded and analyzed.

Results

Amongst the 1884 antenatal admissions during the study period, 416 were admitted with preterm labor giving an incidence of 22%. At the same time, out of the total 1614 live births, 338 delivered prior to 37 completed weeks giving a 20.9% incidence of preterm births.

The distribution of cases of preterm labor according to gestational age is shown in Table 1. Maximum number of women (48.5%) were in the gestational age group of 34-36 weeks. Out of 416 cases of preterm labor, 200 (48.1%) were given tocolysis. Out of these 200 cases, 25 (12.5%) reached term, 53 (26.5%) were discharged satisfactorily and 122 (61.0%) delivered prematurely. Remaining 216 (52%) were allowed delivery on admission due to reasons shown in Table 2.

Table 1. Gestational age.

Gestational age (weeks)	Admission for preterm labor		Tocolysis Number	Preterm deliveries Number
	Number	Percent		
< 28	15	3.6	9	12
28.34	157	37.7	96	111
34-36	202	48.6	95	173
>36	42	10.1	-	42
Total	416		200	338

Table 2. Reasons for allowing delivery on admission (n=216).

Reason	Number	Percent
Active phase of labor	148	68.5
Antepartum hemorrhage	29	13.4
Acute fetal distress	22	10.2
Severe preeclampsia	8	3.7
Chorioamnionitis	9	4.2

Table 3 shows the various risk factors for preterm labor and delivery. Premature rupture of membranes was found to be the most common cause of preterm labor (25.96%). Amongst the 108 cases with rupture of membranes, 77 were allowed spontaneous labor while 31 were given tocolysis. Seventeen of the 31 (54.8%) crossed 48 hours interval. Twelve of these successful women were electively induced after 48 hours due to chorioamnionitis or oligohydramnios. Remaining five delivered spontaneously within 1 week of tocolysis.

Infection was the next common risk factor seen in 86 (20.7%) women. Urinary tract infections (UTI) were found in 35 (8.4%) of these women in whom *E. coli* accounted for 75% while *klebsiella*, *staphylococcus* and *citrobacter* were present in few. Vaginal swab culture was positive in 51 (12.25%) women, *E. coli* and *Staphylococcus aureus* contributing 32% each, *candida* 18.2%, and *klebsiella* and *trichomonas* 9% each.

As seen from Table 4, neonatal mortality was quite high (30.4%) in babies less than 34 weeks gestation compared to 3.4% in those with more than 34 weeks gestation. The difference was highly significant ($P < 0.0001$). Neonatal mortality was not affected in babies below 34 weeks by gaining 48 hours through tocolysis for the beneficial effect of betamethasone ($P = 0.961$). Neonatal morbidity was significantly reduced ($P = 0.043$) in cases where some time was gained for betamethasone coverage. The incidence of respiratory distress syndrome (RDS) was significantly less ($P = 0.029$) in this group.

Table 3. High risk factors for preterm labor (n=416).

Risk factors	No. of cases	Percentage
Preterm rupture of membranes	108	25.9
Infections		
Urinary	35	
Vaginal	51	
Antepartum hemorrhage	45	10.8
Multiple gestation	17 (Twins 14, triplets 3)	4.1
Polyhydramnios / (AFI > 20)	14	3.4
Malpresentation	60	14.4
Maternal disease	92	22.1
Fetal anomaly	4 (Anencephaly)	1
Uterine anomaly	3 (Bicornuate uterus)	0.7
Extremes of age		
>35 years	24	13.5
< 18 years	32	
History of abortions		
1 st trimester	45	
2 nd trimester	15	14.4
History of preterm deliveries		
One	44	14.4
Two	16	
Short stature (height < 140 cm)	12	2.9
Kuppuswami socioeconomic class IV and V	92	22.1
Maternal weight < 50 kg	72	17.3
Idiopathic	98	23.6

Table 4. Neonatal outcome in 338 preterm deliveries (358 babies) ^a.

Outcome	< 34 weeks (n=119)		> 34 weeks (n=239)
	Steroid uncovered (71)	Steroid covered (48)	
Intrauterine demise	2	-	-
Live birth	69	48	239
Admissions to neonatal intensive care unit	30	20	16
Neonatal death	22	14	8
Neonatal mortality	30.98% ^b	29.16% ^b	3.4%
Respiratory distress syndrome (RDS)	19 ^c	5 ^c	1
Septicemia	10	10	20
Neonatal encephalitis	8	3	2
Neonatal morbidity	52.1% ^d	37.5% ^d	1%

^a Twins 14, Triplets 3 ^b = P < 0.0001 ^c P = 0.029 ^d P = 0.043

Table 5. Incidence of preterm birth and trends.

Country	Preterm labor	Preterm birth	Trend
USA (Martin et al ²)	-	12.3%	Increasing
United Kingdom (Bibby and Stewart ¹⁵)	10%	7%	Increasing
Australla (Robert et al ¹⁶)	14.1%	5.5%	Stationary
Sweden (Morten et al ¹⁷)	-	5-6%	Decreasing
China (Leuing et al ¹⁸)	-	7.4%	Increasing
Zimbabwe (Shingairai et al ¹⁹)	-	16.4%	Increasing
India (Present study)	22.0%	20.9%	-

Discussion

Preterm labor and delivery are not rare. McPheeters et al ¹ state that incidence of first time hospitalization for preterm labor is 9% with only 38% delivering in their first episode. According to annual vital statistics in USA percentage of infants delivering before 37 weeks is continuously rising from 11% in 1998 to 12.3% in 2003 ². Incidence of preterm labor is showing an increasing trend due to assisted reproduction leading to an increase in multiple births, early and late procreation, and better obstetrical intervention. Table 5 compares the incidence of preterm labor, preterm births and their trends in different countries. Amongst the developing countries, India has a very high incidence of preterm labor (23.3%) corroborating our 22% incidence. Our incidence of preterm birth was 20.9%. Thirty-two women (15.9%) had previous episodes of preterm labor treated successfully in index pregnancy.

Etiology of preterm labor is multifactorial. Van der Pool ³ found that approximately 30% of preterm births are associated with rupture of membranes. In our study also, preterm rupture of membranes was associated with 25.9% preterm births.

According to Gonclaves et al ⁴ intrauterine infections are a major cause of preterm labor, with or without intact membranes and accounts for approximately 25% of cases. Lamont ⁵, concludes that infection is responsible in 40% of cases and earlier the abnormal genital tract colonization is detected the greater is the risk of adverse outcome. Wright et al ⁶ identified urinary tract infection (UTI) as a significant risk factor, contributing to 7% of preterm births. In our study, genitourinary infection is the second commonest cause (20.7%). UTI was present in 8.4% while vaginal culture was positive in 12.25%.

Carey and Klebanoff ⁷ state that increases in *E coli* (commonest) and *Klebsiella pneumoniae* in vagina are independent risk factors for preterm birth. It has been shown that *E. coli* is the organism that can permeate living intact chorioamniotic membranes. According to Cram et al ⁸ asymptomatic bacteriurea, gonococcal cervicitis and bacterial

vaginosis are strongly associated with preterm labor and the role of chlamydia, candida, trichomonas and urea plasma is less clear. In our study, *E coli* and *Staphylococcus aureus* were the most commonly found organisms (32% each) in vaginal culture followed by candida, klebsiella and trichomonas. During prenatal care, standard practices should be applied for screening for gonorrhoea, chlamydia infection and bacterial vaginosis in patients at high risk of preterm labor. Patients in preterm labor with or without membranes should be provided group B streptococcus prophylaxis till delivery.

EPIPAGE study results show that women with history of induced abortion were at higher risk of preterm delivery ⁹. Carr-Hill and Hall ¹⁰ have shown that in women with history of one preterm delivery there is 15% chance of next preterm delivery and after two preterm deliveries there is 32% chance. In our study 60 out of 416 (14.4%) had history of preterm deliveries, 44 (10%) had one preterm delivery, and 16 (4.8%) had two or more. Sixty (14.4%) women had history of prior abortions, out of which 15 (3.6%) had second trimester abortions.

Age, parity, socioeconomic status, anthropometry, education and small intervals between births are the other affecting variables (Table 3). It has been reported that risk of preterm labor is highest (15.8%) in adolescents and teenage pregnancies (<18 years age). It decreases to a minimum of 6% in reproductive age (20-45 years) and again rises, reaching a new peak of 9.9% around 45 years. Diallo et al ¹¹ found that early and late age of procreation (7.95% and 3.9%), first and last parities (7.75% and 5.31%), and poor and rich women groups (7.34% and 3.84%), are the important risk factors. They state that 83% of maternal causes could be controlled by efficient prenatal care. Begum et al ¹² state that weight less than 45 kg (OR 4.9), height less than 150 cm (OR 3.4), BMI less than 19 kg/m² (OR 2.9), education less than 5 years (OR 2.7), monthly income less than 2000 rupees (OR 5.05) and birth interval less than 12 months (OR 6.39) were significant risk factors for preterm labor. In the present study 32 (7.7%) women were less than 18 years old, 24 (5.8%) more than 35 years old, 72 (17.3%) weighed

less than 50 kg, and 92 (22.2%) belonged to lower socioeconomic group (Kuppuswami class IV & V). There were 95 (47%) primigravidas and 107 (53%) multigravidas in the study.

In our study two babies died in utero, both before 32 weeks gestational age. One was associated with preeclampsia and consequently had severe placental abruption, while the other had severe oligohydramnios with chorioamnionitis following rupture of membranes for 1 week.

According to Sehgal et al¹³, neonatal hyperbilirubinemia (78%) and RDS (65%) were the most common causes of morbidity in extremely low birth weight babies. Sing et al¹⁴ reported that there was 21% overall mortality amongst preterm babies delivered at hospital and managed in the nursery. According to them intraventricular hemorrhage was the most common cause of death (42%) followed by septicemia 31%.

In contrast, our institution has an overall mortality of 12.7% among preterm births which indicates a comparatively better neonatal care and outcome. There were 36 neonatal deaths (30.4%) in babies of less than 34 weeks gestational age while only eight (3.4%) in those of more than 34 weeks gestational age ($P < 0.0001$). This indicates a clear cut benefit of prolonging pregnancy beyond 34 weeks in cases of preterm labor.

In less than 34 weeks gestational age, mortality was almost same in both betnesol (steroid) covered and uncovered groups (30.98 vs 29.16%). But neonatal morbidity was significantly high in betnesol uncovered group (52.1% vs 37.5%; $P=0.043$). Similarly, incidence of RDS was significantly high in babies without steroid coverage than in those with (26.8% vs 10% ; $P=0.029$). One baby of more than 34 weeks gestation developed RDS as the mother was having impaired glucose tolerance. Septicemia and hypoxic ischemic encephalopathy were the two most common causes of neonatal morbidity and mortality after RDS, accounting for 16.8% and 9.2% respectively in less than 34 weeks gestational age group. Hyperbilirubinemia developed in approximately 50% of preterm babies irrespective of gestational age. Delay in delivery and steroid coverage decrease neonatal morbidity due to RDS but overall mortality is not reduced if baby is delivered before 34 weeks.

Conclusion

Preterm labor and preterm births require early and prolonged hospitalization posing great financial and psychological burden on family. Most etiological factors are modifiable, and preconception counseling should emphasize family planning, good nutrition, safe sex, good hygiene, treatment of sexually

transmitted diseases, and avoidance of tobacco, alcohol, abusive drugs and harmful work conditions. All efforts should be made to prolong the pregnancy beyond 34 weeks for better neonatal outcome. Tocolytics help by giving time for steroid coverage so that morbidity due to RDS can be decreased.

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