

Research Article

Preterm premature rupture of membranes: correlates and pregnancy outcome in a tertiary care setting

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ABSTRACT

Background: Prelabour membrane rupture before 37 weeks of gestation is referred to as preterm premature rupture of membranes (PPROM). Incidence of PPRM is about 2% of all pregnancies. This prospective study aims to determine fetal and early neonatal outcome of pregnancies with PPRM.

Methods: The study was conducted in 190 antenatal women with PPRM between 24 weeks to 36 weeks of gestation over a period of 18 months. Their babies were followed up till discharge from Pediatric new born unit.

Results: Prevalence of PPRM was 0.8%, accounting for 19% of preterm deliveries. 61% of women with PPRM showed evidence of lower genito-urinary tract infection, 28% had anemia, 48% gave history of coitus during pregnancy. Mean gestational age of membrane rupture was 32 weeks, the mean latency between membrane rupture and delivery was 4.4 days. Chorioamnionitis developed in 13% of women with PPRM, cord prolapse in 4% and abruption in 3%. The gestational age wise survival was 40% in babies weighing less than 1.5kg, 88% in babies weighing 1.5 to 2.5kg and 93% in those more than 2.5kg. The predominant causes of neonatal mortality were hyaline membrane disease (HMD) in babies born before 28 weeks, HMD and sepsis between 29 to 33 weeks and sepsis in babies born after 34 weeks.

Conclusions: Screening and treatment of risk factors may contribute to prevention of PPRM. Neonatal survival depends on gestational age and availability of advanced NICU facilities. Patients and family members should be counseled regarding the outcome of pregnancies with PPRM. A team effort by the obstetrician and neonatologist in a tertiary care setting can ensure a healthy and fruitful life for mother and baby.

Keywords: Fetal outcome, Early neonatal outcome, PPRM, Risk factors

INTRODUCTION

Prelabour membrane rupture before 37 weeks of gestation is referred to as preterm premature rupture of membranes (PPROM). Incidence of PPRM is about 2% of all pregnancies.¹ The consequences of PPRM for the neonate fall into three major overlapping categories. The first is the significant neonatal morbidity and mortality associated with prematurity. Secondly the complications during labor and delivery increase the risk for neonatal resuscitation and thirdly infection.² The relative

contributions of prematurity and perinatal infections to perinatal mortality are responsible for most of the controversy surrounding the optimal management of PPRM. Complications such as respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC) contribute to most of the cases of neonatal mortality.

Since the goal of management in PPRM is prolongation of pregnancy, the most commonly accepted management scheme less than 36 weeks is expectant, with patient

admitted in the hospital and observation for signs of infection, fetal distress or labor, in an effort to gain time for fetal growth and maturation.³ This expectant approach is complicated by controversies surrounding the efficacy of tocolytic agents to stop uterine contractions, prophylactic antibiotics, corticosteroids to accelerate fetal lung maturation, and amniocentesis for diagnosis of occult infection and fetal lung maturity. In any event, where adequate facilities for intensive perinatal and neonatal care is lacking, it is prudent to refer the patient to a center where such facilities are available.⁴

Premature rupture of the fetal membranes is an obstetric enigma and several aspects of management of PPRM remain controversial. Clinical judgment, physician experience, and careful individualization of management will often come into play.

METHODS

This is a prospective study conducted in a tertiary care centre in South Kerala, India over a period of 18 months.

Inclusion criteria

All women with singleton pregnancies complicated by PPRM between gestational ages 24 to 36 weeks, who were admitted in the labor room during the period of study were included. The perinatal group involved the fetus in-utero of the women with PPRM, still births, neonatal deaths and babies surviving to discharge from pediatric newborn unit.

Exclusion criteria

All cases of multiple pregnancy, diabetes, severe pre-eclampsia, fetal congenital anomaly and Intra uterine fetal demise were excluded.

Patient details such as age, parity, socioeconomic status, obstetric history, complications and mode of delivery were noted. Clinical examination, sterile speculum examination and routine investigations were done in all cases. Ultrasound to determine amniotic fluid index and biophysical profile was done where possible.

Special investigations like TC, DC, CRP was done to rule out chorioamnionitis. Antibiotics (ampicillin or cephalosporin for 5 days) were given to all patients and steroids (Betamethasone 12 mg 2 doses 24 hour apart) were given to all patients between 28 to 32 weeks unless delivery occurred prior to this period. Tocolytics were avoided in PPRM.

All stable patients with PPRM prior to 34 weeks were managed conservatively after confirming fetal viability and ruling out congenital anomalies. The mother and fetus were monitored closely in the ward for evidence of chorioamnionitis, abruption, cord prolapse or other complications. Induction of labor was done after 34

weeks, or earlier if patient developed complications. Labor was monitored and mode of delivery was noted. After delivery, detailed neonatal examination was done to determine the APGAR score, gestational age, birth weight, birth asphyxia, respiratory distress, IUGR and evidence of sepsis. Neonatal ICU admission was sought if necessary. All still births and neonatal deaths were recorded

Statistical tool

Data was analyzed using computer software Statistical package for Social Science (SPSS) version 10. To elucidate the associations and comparisons between different parameters, chi square test was used as nonparametric test. For all statistical evaluations a two-tailed probability of value <0.05 was considered significant.

RESULTS

The prevalence of PPRM is 4% in this study. This accounts for 19% of all preterm deliveries in SAT hospital. The mean age was 24 years (SD \pm 3.8). 71% of the population were from rural area while 29% are from urban area. 65% of patients were from low socioeconomic status, 32% were from middle class and 3% from high socioeconomic status. Primipara accounted for 59% of study population while multipara constituted 41%.

47% patients were booked, 51% were referred, 2% constituted unbooked patients. 6% of cases in the study group had a history of PPRM in their previous pregnancies, 5% had preterm labour and 2% had undergone cervical cerclage in previous pregnancies. 72% had regular antenatal visits while 28% had irregular ANC in this study. In the present pregnancy, 43% had abnormal discharge pervaginum, 28% had anemia, 18% had UTI, 3% underwent cervical cerclage, and 48% gave history of sexual intercourse during pregnancy.

The mean gestational age of membrane rupture as 33 weeks. 8% occurred between 24-28 weeks, 40% between 29-33wks and 52% between 34-36 weeks. The mean latency between membrane rupture and delivery was 4.4 days. The duration of latency decreased with advancing gestational age. Presentation of fetus was vertex in 52%, breech in 15% and transverse lie in 2%. Chorioamnionitis developed in 13%, cord prolapsed in 4%, abruption in 3% following PPRM.

65% of patients had vaginal delivery, 30% underwent caesarian section, 3% had forceps delivery. Postpartum haemorrhage developed in 11%, postpartum fever in 22%, wound infection in 14% and pelvic abscess in 0.5%. The mean duration of hospital stay was 9.8 days. The mean birth weight was 1.9 kg (SD \pm 0.57). 95% of babies were live born, 4% still born and 1% were IUD. 24% of neonates developed respiratory distress, 25% had sepsis,

10% had birth asphyxia, 19% had neonatal jaundice, 3% had NEC, 0.5% had IVH and 2% had congenital pneumonia. The gestational age-wise survival was 7% below 29wks, 73% between 29-33wks and 93% above 34 wks. The birth weight wise survival was 40% below 1.5kg, 88% between 1.5-2.5kg and 93% above 2.5kg. The predominant cause of neonatal mortality was HMD (89%) below 28 week, HMD (50%) and sepsis (36%) between 29-33 weeks and sepsis (83%) above 34 weeks.

DISCUSSION

The mean age in this study was 24.4 years (SD±3.8) 52.1% of patients were in the age group 20 to 24 years. The mean age of obstetric admissions was 24.9 years. Thus, age may not be a significant factor in PPRM. 58.9% of patients were primiparous which is comparable to the percentage of primipara in total hospital admissions (56.3%). Therefore parity may not be the important determinant of PPRM. In the current study, 51.1% patients were booked outside (referred from peripheral hospitals). The higher percentage of referrals reflects the fact that the hospital is a tertiary center.⁴

In this study, 71.1% of patients belong to the rural population. This may be due to the fact that 65% of people live in rural areas in India, and there may be an increased referral of patients with PPRM from rural areas ($p<0.001$). In this study, 5.8% of patients had a history of PPRM and 4.8% had a history of preterm labor in their previous pregnancies. Therefore PPRM may recur in subsequent pregnancies.⁵

In the present study, 1.6% of patients with PPRM had undergone cervical cerclage in their previous pregnancy. A combination of short cervical length and previous preterm birth caused by PPRM was highly associated with preterm delivery caused by PPRM in the current gestation ($p<0.001$). In the study 13.8% of patients with PPRM had a history of first trimester abortion. Previous abortions or fetal loss had increased risk for subsequent preterm birth with or without rupture of membranes (Ekwore, 1993).

In the present study 28.4% of patients with PPRM had irregular antenatal visits during the current pregnancy ($p<0.001$). Fewer antenatal visits are associated with unfavorable maternal and neonatal outcome in PPRM according to Phupong V et al.² In the study 56.6% of patients were found to have abnormal discharge per vaginum indicating the presence of cervicovaginal infection. Cervicovaginal infections were significantly associated with PPRM, preterm delivery and PROM.⁶

48.0% of patients, in the present study, gave history of sexual intercourse during pregnancy. Sexual activity has long been suspected to be potential causes of preterm delivery and several biologic mechanisms could explain the adverse effect of sexual activity on preterm delivery. Maternal orgasm might release oxytocin and initiate

uterine contraction. Prostaglandins in seminal fluid also have oxytocic properties. Coitus during pregnancy can increase exposure to infectious agents that could result in preterm delivery⁷. In this study 17.9% of patients with PPRM had urinary tract infection in the current pregnancy.

However in a study, microbial colonization of urine was not associated with PPRM, but reduced prevalence of lactobacilli, coryne-bacteria and coagulase negative staphylococci in the cervix were associated with PPRM beyond 26 weeks.⁸

In the current study PPRM occurred following cervical cerclage in 2.6% patients, The cervical sutures were retained till the onset of labour or till 34 weeks. Retention of cerclage sutures in patients with PPRM (managed with both corticosteroids and antibiotics) was not associated with increased maternal morbidity or neonatal mortality.⁹

Table 1: Mode of delivery.

Mode of delivery	Frequency	Percentage
Vaginal Delivery	123	64.80%
Instrumental outlet (forceps)	6	3.20%
Caesarian Section	56	29.50%
VBAC	2	1.10%
Asst. breech delivery	3	1.60%

Chi square: 8.019; >0.05

In the present study, 28.4% of patients with PPRM suffered from anemia (hemoglobin values ranged from 6.2g% to 10.9g%). In India, prevalence of anemia complicating pregnancy is estimated to be as high as 60% to 80%. A lower prevalence of anemia in this study may reflect a better nutritional status and health awareness in Kerala compared to other states in India.

Table 2: Indications for caesarian section.

Indication	Frequency	Percentage
Breech, PPRM	19	34.0%
Transverse lie, PPRM	3	5.3%
Previous cesarean section, PPRM	9	16.1%
Previous CS, Placenta previa type 3	1	1.8%
Placenta previa type 3&4	4	7.1%
Abruption	2	3.6%
Failed induction	4	7.6%
Failed induction, maternal fever	6	10.7%
Fetal distress	7	14.3%
Elderly primi, treated for infertility	1	1.8%

Anemia increases maternal and perinatal mortality and morbidity rates consequent to preterm delivery and low stores ($p < 0.001$). The mean gestational age at rupture of membranes in this study was 31.1 weeks. 51.6% of PPROM occurred between 34-36 week, 40.5% between 29-33 weeks and 7.9% between 24-28 weeks. The latency period between the onset of membrane rupture to delivery was less than 24hrs in 62% of patients. The mean latency was 7.95 days between 24-28 weeks, 3.80 days between 29-33 weeks and 3.25 days between 34-36 weeks. The mean gestational age at delivery in this study was 32.2 weeks and the mean latency period between membrane rupture and delivery was 5.95 days.

Table 3: Perinatal loss.

Perinatal loss	Frequency	Percentage
Still birth	6	2.6%
Intrauterine demise	3	1.60%
Neonatal death	34	18.6%

Chi square 6.88 > 0.05

Maternal morbidity as a consequence of PPROM in the antenatal period included chorioamnionitis in 8.4% of patients and abruption in 3.2% of patients in the study. In studies by certain investigators, the incidence of

chorioamnionitis increased with increasing length of latent period, while others found no such increase. Women who underwent digital vaginal examination following PPROM had a significantly shorter latent period, more maternal infection and more positive amniotic fluid cultures. Thus routine vaginal examinations should be avoided until labour develops in patients with PPROM.

In this study 3.8% of patients developed blood staining of liquor of which one-third (30%) were detected to have placenta previa on ultrasound, while two-third (60%) were diagnosed with abruption placenta, there was one still birth due to abruption while the remaining delivered live babies.

Gonen R et al found that among patients with prolonged PPROM, those who experienced vaginal bleeding before the onset of labour had ten times higher risk for abruption placenta than who did not bleed.⁹ The association between abruption and PPROM was also studied. They found that in pregnancies complicated by PPROM that are managed expectantly, there is a significant risk for abruption placenta which may predispose to intrapartum fetal distress.¹⁰

Table 4: Gestational age wise fetal outcome.

Gestational age (weeks)	Survival	SB	IUD	NND	Total
24-28	1 (6.67%)	3 (20%)	3 (13.3%)	9 (60%)	15
29-33	56 (72.73%)	2 (2.6%)	1 (1.3%)	18 (23.37%)	77
34-36	91 (92.86%)	-	-	7 (7.14%)	98
Total	148 (77.9%)	5 (2.63%)	3 (1.58%)	34 (17.9%)	190

Chi square: 69.820 < 0.001

Cord prolapse occurred in 3.7% patients with PPROM in this study, out of which 28% were still born while 72% of the babies survived. Babies delivered after cord prolapse in PPROM had normal neuro-developmental outcome at 2 years of follow up provided the decision delivery interval was kept short.³ In the present study 0.5% patients had meconium stained amniotic fluid. A prospective study found that histologic chorioamnionitis and reduced nutrition in the fetus co-existed with meconium stained liquor in 80% of preterm infants. These neonates were more prone for fetal distress in labour and respiratory distress in the neonatal period¹¹.

In this study, 77.9% of patients had ultrasound estimated AFI less than 5 while 22.1% had AFI between 5 had 10. PPROM with AFI less than 5 was more likely to be delivered by caesarian section due to non-reassuring fetal status. This group also had significant increase in the frequency of chorioamnionitis. However, the latency and perinatal morbidity or mortality was not significantly

influenced by AFI.¹² Two does of steroids were given to 74% of patients with PPROM while 26% received only one does as labour supervened before the course could be completed in the later group.

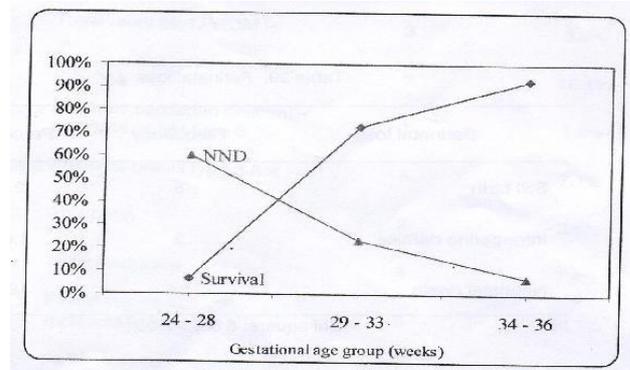


Figure 1: Gestational age wise fetal outcome.

The National Institute of Health (NIH) consensus conferences concluded that the risk of maternal and infant infection may be increased with corticosteroid use after PPROM but the magnitude of this risk was small. The benefits of steroids with PPROM before 28 weeks were not firmly established. Another study found that multiple course of antenatal corticosteroid therapy was associated with increased risk of clinical chorioamnionitis and seemed not to reduce the incidence of respiratory distress and other neonatal morbidities in patients with PPROM.¹³ The issue of steroids in PPROM is being studied by large multicentric trials like ACTORDS and NICHD-MFMU.

The prevalence of non vertex presentation was 17.9% in this study, out of which breech accounted for 84%. A study was conducted by Demol S, et al to assess the prevalence of malpresentation among preterm births between 24-36 weeks and to evaluate the clinical significance of malpresentation as a predictor of neonatal complications in preterm delivery in their study. The prevalence of malpresentation was 13.8% in their study. Higher perinatal mortality rates were observed in the non-vertex group as compared to the vertex births. There was also a clinically significant association between the presence of breech presentation and neonatal mortality (OR2.2) The larger question of whether prolonging the latency in women with PPROM significantly improves the neonatal outcome was addressed by Ramsey and Colleagues of the National Institute of Health and Development in 2003. They noted that a longer latency was associated with greater neonatal morbidity, including perinatal death and respiratory distress syndrome. Much more study is needed to explore this interesting finding given the increased morbidity of delivery at earlier gestation. This information however does imply that conservative management of PPROM at later gestational ages may not be optimal.³

Table 6: Birth weight wise fetal outcome.

Birth weight (kg)	Survival	SB	IUD	NND	Total
< 1.0	2 (10.5 %)	4 (21.05%)	2 (10.5%)	11 (57.9%)	19
1-1.5	14 (66.6%)	-	-	7 (33.3%)	21
1.6-2	42 (77.7%)	1 (8.5%)	1 (8.5%)	10 (18.5%)	54
2-2.5	77 (93.9%)	-	-	5 (6.1%)	82
2.6-3	12 (92.31%)	-	-	1 (7.6%)	13
>3	1 (100%)	-	-	-	1

Chi square: 78.773, < 0.001

The mode of delivery in early preterm infants is another important area of controversy. A few studies have suggested that a policy of elective caesarian in case of breech presentation of fetuses weighing less than 1-1.5 kg would be beneficial, however, majority of studies show that there is no evidence to suggest improved outcome. This will probably constitute an important area of research in the future. 11% of caesarian sections in this study were due to fetal distress (Table 2). A study by

Table 5: Neonatal complications.

Neonatal complications	Frequency	Percentage
Birth asphyxia	19	10.40%
Congenital pneumonia	3	1.6%
Respiratory distress	47	24.7%
Intraventricular hemorrhage	1	0.5%
Necrotising enterocolitis	6	3.3%
Neonatal jaundice	34	18.6%
Neonatal death	48	26.2%
Sepsis	34	18.6%

The optimal mode of induction in PPROM is being investigated by several randomized control trials. The prelabour rupture of membranes study assessed induction with oxytocin versus vaginal prostaglandin E2, and found that neonatal infection and operative delivery rates were similar in both groups. However, oxytocin induction resulted in a lower risk of maternal infection than vaginal prostaglandins¹⁴. The overall caesarian rate in this study was 29.5%.

Non vertex presentations (Breech and transverse lie) accounted for 37.5% of caesarian sections (Table 1). Reducing the incidence of cerebral damage in preterm infants has become the major objective of perinatal medicine. Prematurity and intrauterine infections are a few of the main risk factors associated with cerebral palsy. Those measures that have had demonstrable benefit in improving preterm infants were, a policy of prenatal transfer to tertiary level units, antenatal corticosteroid therapy and administration of antibiotics to women with preterm premature rupture of membranes.²

Sedighah showed that oligohydramnios associated with PPROM was associated with higher likelihood of caesarian section is due to non-reassuring fetal rate patterns. This was consistent with findings of other studies as well.⁷

Failed induction was responsible for 16% of caesarian sections in this study. The incidence of failed induction and operative morbidity is higher at earlier gestational

ages according to Julien SK et al. The overall neonatal survival was 77.9% in this study with perinatal mortality of 22.1%. The survival rate between gestational ages 24-28 weeks was 6.7%, survival between 29-33 weeks was 72.7% and between 34-36 weeks, neonatal survival was 92.9% (Figure 1). Neonatal deaths accounted for 17.9% of perinatal loss (Table 3, Table 4). The survival rate in this study was similar to the survival rate among other babies in the IBN showing that prematurity rather than PPROM is the main contributor to neonatal mortality. The causes of neonatal mortality in this study were hyaline membrane disease in 56%, sepsis in 31%, birth asphyxia in 6%, intraventricular haemorrhage and kernicterus in 3% respectively.

From data derived from NNPD (National Neonatal Perinatal Database) 2002-2003, HMD was the cause of death in 51.6% of preterm neonates, sepsis in 25.8%, birth asphyxia in 16% and IVH in 6.5% of neonates. The relative proportion of death due to sepsis was higher in my study and this underlines the need for enforcing strict aseptic precautions among health personal caring for laboring women and neonates.¹⁷

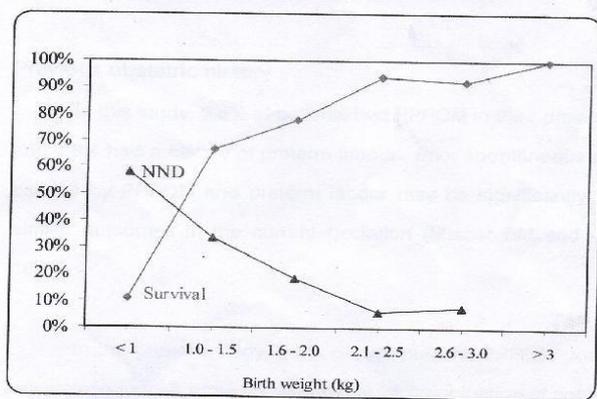


Figure 2: Birth weight wise fetal outcome.

The relative proportion of deaths between 24-28 weeks was HMD in 89% cases, between 29-33 weeks 50% of deaths were due to HMD and 30% due to sepsis, while between 34-36 weeks 83% were caused by sepsis and 16% by HMD. This suggests that lung immaturity and HMD is the primary cause of neonatal mortality less than 28 week, while prolongation of pregnancy beyond 34 weeks may increase the risk of neonatal deaths due to sepsis (Table 5).

Cause of morbidity in neonate included sepsis in 33%, respiratory distress in 21%, birth asphyxia in 13%, and neonatal jaundice in 20%. NEC and congenital pneumonia accounted for the remainder ($p < 0.001$). In this study, 6% of preterm babies were given assisted ventilation while 4.7% were given surfactant for treatment of HMD. Among the very low birth weight babies who were given surfactant, 24% survived. In a study of survival and morbidity in extremely low birth weight babies, they found that 60% of infants weighing

more than 750 g could be salvaged without surfactant (18). This is reassuring given the fact that surfactant may not be available for all preterm infants with respiratory distress in a developing nation like India. Infants weighing less than 750 g remains a high risk group with barely one-fourth surviving to discharge without surfactant and almost two-third requiring ventilation (Table 6, Figure 2).

This would have significant implications for units planning to take care of preterm babies. Adequate ventilation facilities and infection control measures would be necessary to achieve reasonable outcomes in the high risk neonates.¹¹ Sepsis is an important preventable cause of morbidity and mortality in these neonates. In this study the average duration of neonatal ICU stay for infants was 3.3 days. The overall duration of neonatal ICU stay decreased with increasing gestational age. The duration of NICU stay between 24-28 weeks was on an average 4.2 days, between 29-33 weeks, 3.4 days and between 34-36 weeks, 2.4 days.⁹ This may reflect the lesser incidence of neonatal morbidity at higher gestational ages. The average duration of maternal hospital stay was 9.4 days. This is more compared to the average hospital stay in this hospital (3 days following vaginal delivery, 6 days following caesarian section). The total maternal and neonatal hospital stay comprised significantly more days in PPROM especially below 34 weeks (Phupong and Taneepanichskul, 1997).²

This imposes significant economic burden on the patient and her family members. Despite the pivotal importance of accurate data regarding major and minor neonatal morbidities in pregnancies complicated by PPROM, few studies have attempted to fully characterize these morbidities to identify an optimal gestational age for delivery of pregnancies complicated by PPROM. In the current study, an attempt is made to provide a comprehensive assessment of maternal and neonatal morbidities and mortality, in women with PPROM who were managed under a standardized management protocol. There is a marked decrease in the incidence of respiratory distress beyond 34 weeks. In addition, the length of neonatal ICU stay was shorter after 34 weeks.

CONCLUSION

Expectant management of PPROM may be the preferred treatment between 28-34 weeks given the higher neonatal morbidity in this group, provided other maternal or fetal contraindication does not exist. However, parental preference is likely to assume greater importance in the management of PPROM in less than 24 weeks considering the problems of pulmonary hypoplasia and lung immaturity in this group. The management of PPROM beyond 34 weeks is not well elucidated by randomized trials.

Expectant management may result in prolonged antenatal hospitalization with antibiotic treatment, regular

monitoring and intensive care of the neonate in the event of sepsis. On the other hand, planned early delivery may necessitate intensive care for the neonate for problems associated with prematurity. Additional number of days admitted to the hospital will increase the economic burden, particularly neonatal intensive care

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