A Prospective Assessment of the Causes and Complications Associated with Preterm Birth in A Tertiary Care Hospital, Erode

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ABSTRACT
Objective(S): To assess the probable causes of pre-term labor (PTL) also to identify the complications associated with PTL. Method(S): This prospective study was conducted over a period of 6 months (April to September 2018), in which 100 antenatal women were admitted in the hospital with antepartum hemorrhage, premature rupture of membrane, and weak cervix. The complications associated with preemies, gestational age at delivery, causes and neonatal outcome were analyzed and recorded. Results: The results revealed a comparatively low incidence of pre-term birth. Pre-term birth was mostly observed between the age group of 20-22 years. Among the cases, the most common causes of pre-term delivery was premature rupture of membrane 24(48%), 12(24%) cases were due to ante-partum hemorrhage. The study showed that nifedipine was able to induce tocolysis for at least 1 day in 08% of patients. Furthermore, nifedipine was able to induce tocolysis for at least 2 days in 06% of patients. Conclusion(S): The significant causes of preterm birth found in this study were (i) premature rupture of membrane and (ii) ante-partum hemorrhage respectively. Respiratory distress syndrome was the major complication associated with preemies. Prolongation of delivery for 48 hours by administering tocolytics for deriving the benefit of nifedipine coverage was found to reduce the morbidity due to RDS, but the same did not reduce the overall neonatal mortality below 34 weeks.

Keywords: Ante-partum hemorrhage, respiratory distress syndrome, tocolytic.

INTRODUCTION
The World Health Organization (WHO) defined pre-term labor (PTL) as a fetus delivered earlier than 37 weeks or less than 259 days from the first day of last menstrual period (LMP)1. It complicates approximately 5-10% of pregnancies and accounts for about 75% of perinatal deaths2. Based on gestational age pre-term birth can be classified into three categories of births from 20 to 27 weeks of gestation, from 28 to 31 weeks, and from 32 to 36 weeks3. These categories reflect very marked differences in the probability of survival, in the need for, and cost of, intensive care, and in long term health and disability outcomes. Premature infants classified by birth weight:

- Low birth weight: birth weight < 2500g
- Very low birth weight: birth weight < 1500g
- Extremely low birth weight: birth weight < 1000g

Premature infants can be classified by (i) gestational age, (ii) late preterm - defined as who is born between the gestational ages of 34 weeks and 0/7 days through 36 weeks and 6/7 days4,5. Very preterm is defined as any fetus born before 32 weeks of gestational age. Extremely preterm is defined as who any infant born before the 28 week of gestational age. The causes of pre-term birth are multifactorial and include a complex interaction between fetal, placental, uterine and maternal factors. Fetal factors are: fetal distress, multiple pregnancy, erythroblastosis, and anasarca-nonimmune. Placental factors are placental dysfunction, placenta previa, and placental abruption. Uterine factors are bicornuate uterus, cervical incompetence. Maternal factors are preeclampsia, chronic diseases, infections, drugs6. Women who have more than one drink per day, on average, or intake of about one drink/day or more has consistently been shown to be associated with reduced birth weight and intrauterine growth restriction7 and heavy maternal alcohol consumption is consistently found to be associated with malformations8 mental retardation, as well as behavioral and psychosocial problems in childhood and adolescence9. Animal models have shown that alcohol increases the production of prostaglandins (PGs), including prostaglandins of the E series10. PGs increase the cAMP activity thereby decreasing cell division,3 and an association between high levels of cAMP and low birth weight has been described. In humans, increased secretion of PGs and thromboxanes (TXs) has been found in alcoholics and their offspring11. Cocaine users experience an approximately two fold increased risk of pre-term birth compared with that for nonusers, also increasing the risk through inhalation of combustion products alone12. Premature rupture of membranes (PROM) refers to a patient who is beyond of 37 weeks' gestation and has presented with rupture of membranes (ROM) prior to the onset of labor13. At term, programmed cell death and activation of catabolic enzymes, such as collagenase and mechanical forces, result in ruptured membranes14.
Preeclampsia, the most common manifestation of hypertensive disorders, is attributed to inadequate placentalation and reduced utero-placental blood flow, causing ischemia reperfusion and release of various mediators involved in the pathophysiology of the disease, including cytokines and products of oxidative stress\textsuperscript{16}. It was demonstrated that for women with more than one induced abortion, a cervical length <25mm obtained by transvaginal ultrasound between 14 and 24 weeks is predictive of spontaneous pre-term birth\textsuperscript{17}. There has been concern that mechanical dilation may result in injury to the cervix,\textsuperscript{18} which may increase the risk of cervical insufficiency and pre-term birth. In case of an incompetent cervix, the cervix might begin to open too soon causing the gestating woman to give birth too early.

The risk of complication increases if the baby is born early\textsuperscript{19}. The most common complications of preterm birth include respiratory distress syndrome (RDS), broncho-pulmonary dysplasia (BPD), apnea of prematurity, patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL).

The efforts or prevention have been primarily aimed to improve survival and health of preterm infants. There is significant evidence that long term (>1 year) use of folic acid supplement preconceptionally may reduce premature birth and birth defects\textsuperscript{20}. Reducing smoking is expected to benefit pregnant women and their offspring\textsuperscript{21}. Healthy eating can be instituted at any stage of the pregnancy including nutritional adjustments, use of vitamin supplements, and\textsuperscript{22}, calcium supplementation in women who have low dietary calcium reduces a number of negative outcomes including preterm birth, pre-eclampsia, and maternal death, WHO suggests 1.5-2.0g of calcium supplements daily, for pregnant women who have low levels calcium in their diet\textsuperscript{22}. Self-care methods to reduce the risk of preterm birth include proper nutrition, avoiding stress and infections, seeking appropriate medical care, control of preterm birth risk factors (e.g. working long hours while standing on feet, carbon monoxide exposure, domestic abuse, and other factors), self-monitoring vaginal pH followed by yogurt treatment or clindamycin treatment if the pH was too high, all seem to be effective at reducing the risk of preterm

Clinical factors associated with pre-term PROM include: low socioeconomic status, low body mass index, tobacco use, pre-term labor history, urinary tract infection, vaginal bleeding at any time in pregnancy, cerclage, and amniocentesis. PPROM is associated with 30-40% of preterm deliveries and is the leading identifiable cause of preterm delivery\textsuperscript{15}. Antepartum hemorrhage (APH) is defined as bleeding from or in to the genital tract, occurring from 24+0 weeks of pregnancy and prior to the birth of the baby. The most important causes of APH are placenta previa and placental abruption, although these are not the most common.
Table 3: Neonatal outcome.

<table>
<thead>
<tr>
<th>Infant Data</th>
<th>No. of births (n=50)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight(g)</td>
<td>&lt;1500</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>1501-2000</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>2001-2500</td>
<td>5</td>
</tr>
<tr>
<td>NICU</td>
<td>&lt;5</td>
<td>6</td>
</tr>
<tr>
<td>admission(days)</td>
<td>&gt;5-10</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>&gt;10</td>
<td>30</td>
</tr>
<tr>
<td>Mortality</td>
<td>Early neonatal death</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>First 10 days after delivery</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>First 15 days after delivery</td>
<td>0</td>
</tr>
</tbody>
</table>

birth. Reduction in activity by the mother-pelvic rest, limited work, and bed rest may be recommended although there is no evidence if it is useful with some concerns or harmful. An increasing medical care by more number of frequent visits and better education/awareness has not been shown to reduce preterm birth rates.

MATERIALS AND METHODS

Study design and site

The prospective observational study was conducted in a tertiary care hospital, Erode, Tamil Nadu.

Study period

The study was conducted between April 2017 to September 2017.

Study criteria

Inclusion criteria

Pre-term labor patients admitted in Neonatal Intensive Care Unit (NICU)

Women aged between 17-30 years.

Gestational age <28 weeks and 36 weeks

Pregnant woman who undergone tocolytic therapy.

Exclusion criteria

Individuals who undergone normal delivery.

Gestational term of >40 weeks.

Pregnancies resulted by in vitro fertilization and artificial insemination.

Source of data

The required information for the study were obtained from the case sheets of each subjects. Observable interventions were also collected from physicians and nursing staffs in 24 hr Neonatal Intensive Care Unit (NICU).

Sample size

This study involved 50 subjects of whom 32 were male and 18 were female.

Design of questionnaire

A questionnaire containing demographic data’s’ of mother, type of delivery they had undergone, causes of preterm delivery (uterine factor, maternal factors) neonatal outcome and preemies information. Standardized Appearance Pulse Grinace Activity Respiration (APGAR) scoring was also included in the questionnaire.

Collection of data

Initially, the purpose of the study was explained to the concern hospital staffs. We had interacted with mother of each participant. The potential causes, possible risk factors and precaution for caring preemies were fully explained. Based on our questionnaire, the required information’s were collected. Case summary of each participant were noted and documented. The reliable causes were discussed with physician and noted, all the data were categorized based on the informations collected.

The study design, protocol, and informed consent were approved by the Institutional Ethics Committee. The procedures, possible discomforts or risks, and potential benefits were fully explained to the review board. Written informed consent was obtained from the parents of all premies in this study before the investigation.

RESULTS

Out of the 50 cases, 32 (64%) preemies were males and 18 (36%) preemies were females. While assessing the cases, it was found that the most common mode of delivery was Emergency Lower Segment Caesarean Section (LSCS). Pre-term birth was mostly observed between the age group of 20-22 years. The incidence of pre-term birth was mostly seen in young adults. While early childbearing has often been regarded as a social issue, there is mounting evidence that young maternal age may be linked to adverse infant outcomes including low birth weight (LBW), preterm birth, and intrauterine growth restriction, as well as neonatal mortality. In this analysis, most common complications were associated with respiratory system. Out of 50 cases, 30 experienced respiratory distress syndrome and 20 cases had complication of sepsis. Among the preemies respiratory distress syndrome was mostly seen in males. Among the cases, the most common cause of pre-term delivery was premature rupture of membrane. 24(48%) cases were reported with premature rupture of membrane. Bleeding during pregnancy may also lead to pre-term labor. Out of 50 cases, 12 (24%) cases were due to antepartum hemorrhage. Among the 50 preterm births, 17(34%) cases were reported with very low birth weight (VLBW). At the same time, more number 28(56%) infants having birth weight between 1501-2000grams. The study showed that out of 50 cases, 30 infants (60%) were admitted in neonatal intensive care unit more than 10 days, 14 infants (28%) admitted for 5 to 10 days and 30 infants (60%) admitted for >10 days. As seen from table 3, neonatal mortality is significantly low. Only 3 cases were reported with early neonatal death.

The APGAR score described the condition of a new born infant immediately after birth and when properly applied is a tool for standardized assessment. From the APGAR scoring, it was found that most of the infants had APGAR score between 5-7. Out of 50 infants, 20 (40%) were...
completely pink, while 39 (22%) of them had heart rate >100.

While analyzing the association of gestational age with complication (Figure 2), it was found that sepsis was noted in one preemie whose gestational age was <28 weeks, two with sepsis whose gestational age was between 28-31 weeks, 30 with RDS and 17 with sepsis whose gestational age was between 32-36 weeks. Tocolytics were associated with significant decrease in the likelihood of delivery within 24 hr, 48 hr. In the present study, nifedipine was observed to induce tocolysis for at least 1 day in 08% of patients. Furthermore, nifedipine was also able to induce tocolysis for at least 2 days in 06% of patients.

CONCLUSION

Pre-term onset of labor is a heterogeneous condition with multifactorial etiology. Due to the various complications and consequences associated with pre-term labor, it has become a great burden, both socially and economically. The significant causes of preterm birth found in this study were premature rupture of membranes and ante partum hemorrhage respectively. Premies were mostly affected by respiratory distress syndrome. Maternal betamethasone in pre-term labor helps in enhancing the fetal pulmonary maturity and reduces the incidence of RDS. Deliveries in the hospital have facilities for neonatal care, which improve the perinatal outcome in preterm labor. Generally, with respect to the above and due to the role and importance of mother-infant health in community health, it is necessary that the health care system improve health education with regard to appropriate number of pregnancies, diagnosis, and cure disease during pregnancy and recognize mothers with maternal pressure or lack of support and help them.

REFERENCES


Table 4: Appearance Pulse Grimace Activity Respiration (APGAR) score at 5 minutes.

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Cases (n=50)</th>
<th>Male (n=32)</th>
<th>Female (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue or pale</td>
<td>11 (22%)</td>
<td>07</td>
<td>04</td>
</tr>
<tr>
<td>Acrocynotic</td>
<td>19 (38%)</td>
<td>13</td>
<td>06</td>
</tr>
<tr>
<td>Completely pink</td>
<td>20 (40%)</td>
<td>12</td>
<td>08</td>
</tr>
<tr>
<td>Heart rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>00 (00%)</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>&lt;100</td>
<td>11 (22%)</td>
<td>09</td>
<td>02</td>
</tr>
<tr>
<td>&gt;100</td>
<td>39 (78%)</td>
<td>23</td>
<td>16</td>
</tr>
<tr>
<td>Reflux irritability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No response</td>
<td>00 (00%)</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Grimace</td>
<td>12 (24%)</td>
<td>08</td>
<td>04</td>
</tr>
<tr>
<td>Cry</td>
<td>38 (76%)</td>
<td>24</td>
<td>14</td>
</tr>
<tr>
<td>Muscle tone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limp</td>
<td>07 (14%)</td>
<td>05</td>
<td>02</td>
</tr>
<tr>
<td>Some flexion</td>
<td>27 (54%)</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Active motion</td>
<td>16 (32%)</td>
<td>12</td>
<td>04</td>
</tr>
<tr>
<td>Respiration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>00 (00%)</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Weak cry</td>
<td>38 (76%)</td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td>Good crying</td>
<td>12 (24%)</td>
<td>09</td>
<td>03</td>
</tr>
</tbody>
</table>


