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Early Onset Neonatal Sepsis with Premature Rupture of Membranes in Preterm Neonates

Dr. Buthu Divya[1], Dr. S. Narasimha Rao[2*], Dr. Kundan Gorikapudi[3], Dr. Manisha[4]

[1]Post Graduate Department of Paediatrics, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India
[2]Professor of Paediatrics Department of Paediatrics, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India
[3]Medical Student, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India
[4]Post Graduate Department of Paediatrics, Kamineni Academy of Medical Sciences and Research centre, Hyderabad, Telangana, India

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***Corresponding author:** Dr. S. Narasimha Rao
Professor of Paediatrics Department of Paediatrics, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India

Abstract **Original Research Article**

Objectives: To determine the frequency of early onset neonatal sepsis with premature rupture of membranes in preterm babies in a tertiary care hospital. ***Materials and Methods***: Neonates of singleton pregnancies complicated by premature rupture of membranes with delivery occurring between 30 and 36 weeks gestation were included in the study. The frequency of neonatal sepsis was assessed based on clinical and laboratory parameters. Incidence of sepsis in relation to gestational age and duration of rupture of membranes was studied. ***Results:*** Out of 60 babies, 38(63%) were female and 22(37%) were male. Mean maternal age was 24 years (range 18-35years). Mean gestational age was 34 weeks (30-36weeks). Sepsis was suspected in 26(43%) babies on clinical examination. C-reactive protein raise was observed in 13 (22%) neonates. There was statistically significant difference between clinical versus laboratory diagnosis (p=0.000). Frequency of neonatal sepsis was significantly higher in mothers with longer duration of rupture of membranes (p=0.041). ***Conclusion***: Frequency of neonatal sepsis was observed to be 22% of babies. Frequency also increased with longer duration of rupture of membranes. Incidence of sepsis is more in early preterm. premature rupture of membranes is an important risk factor for early onset neonatal sepsis.

Keywords: Premature rupture of membranes, Early onset neonatal sepsis, Sepsis screen, Blood culture.

INTRODUCTION

Sepsis is the commonest cause of neonatal mortality, it is responsible for about 30-50% of total neonatal deaths in the developing countries [1, 2]. The major cause of neonatal morbidity and mortality is preterm birth. It is divided into three categories; preterm premature rupture of membranes (PPROM), preterm labor and early delivery resulting from medical intervention. PPROM is defined as a rupture of the amniotic membranes before 37 weeks of gestation and before onset of labor [3, 4].

PPROM complicates only 3-4.5% pregnancies but is associated with 40% of preterm deliveries and can result in significant morbidity and mortality [5]. The three causes of neonatal death associated with PPROM are prematurity, sepsis and pulmonary hypoplasia. Infants born with sepsis have a mortality rate four times higher than those without sepsis [6].

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. The incidence of neonatal sepsis according to the data from national neonatal perinatal database (NNPD) is 30 per 1000 live births [7]. Early onset neonatal sepsis implies that the infection presented before 72 hours of life [7]. Respiratory distress is the most common presenting feature. Neonates with sepsis may have non- specific signs and symptoms including temperature instability, hypotension, poor perfusion [8, 9]. The risk of developing neonatal sepsis increases progressively with the time elapsed between rupture of membranes and eventual delivery. A five fold rise in sepsis is seen when comparing incidences at 24 hours

versus 72 hours of premature rupture of membranes. Neonatal screening can be carried out using clinical guidelines as well as selected laboratory investigations. Serum c-reactive protein levels have been shown to be highly sensitive and specific for neonatal sepsis [10].

This study aims to observe the frequency of neonatal sepsis in mothers with various duration of premature rupture of membranes, using serum c-reactive protein levels and clinical parameters as indicator of infection. It will also provide an early screening protocol for neonatal sepsis and allow timely treatment of neonates at risk of developing infections, while at same time reducing admissions and antibiotic use in neonates not likely to develop sepsis neonatorum.

MATERIALS & METHODS

This cross-sectional study was conducted at Kamineni Academy of Medical Sciences and Research centre, Hyderabad, Telangana from September 2021 to September 2022. Neonates of singleton pregnancies complicated by PPROM with delivery between 30 and 36 weeks of gestation were included in the study. Women with incomplete information, a preterm delivery resulting from medical intervention as well as women who delivered elsewhere were excluded from the study. 60 babies were included through non-probability convenience sampling. In all patients rupture of membrane was diagnosed by sterile speculum examination. All pregnant women were hospitalized in the department of Gynecology and Obstetrics, Kamineni Academy of Medical Sciences and Research centre, Hyderabad, Telangana. All patients were between 30 and 36 weeks of pregnancy as estimated by LMP, and confirmed by ultrasonography.

C-reactive protein was estimated in all cases at birth and repeated after 48 hours. For the purpose of this study, C-reactive protein levels of >0.6mg/dl were taken as positive and any one or more of the following signs and symptoms were constituted clinical evidence of sepsis: unexplained respiratory distress, temperature instability (temperature 37.5 degree centigrade), lethargy, poor perfusion and hypotension. Blood culture were done in all patients with suspected sepsis while urine cultures, CSF analysis, x-ray chest were done in relevant cases. All neonates were admitted in Neonatal Intensive Care Unit. A single course of Betamethasone was administered to all mothers prior to the delivery. All patients received antibiotics as per the protocol. Relationship of neonatal sepsis with duration of rupture of membranes was also studied. Duration of rupture of membranes was categorized into two categories as interval between PPROM and delivery between 18-24 hours and 24-72 hours. Data had been analyzed through SPSS version 16. Descriptive statistics were used to describe the results. Chi-square test was applied to study the relationship of neonatal sepsis with duration of rupture of membranes. Comparison of the frequency of sepsis as judged by clinical and laboratory parameters basis was also made through chi-square test. A p-value<0.05 was considered significant.

RESULTS

Total 60 babies were included in the study. Of these, 38 (63.3%) were female and 22 (36.6%) were male. Mean maternal age was 24 years (Range: 18-36years). Mean gestational age was 34 weeks (Range: 30- 36weeks). Sepsis was suspected in 26 (43%) babies on clinical grounds. Initial C-reactive protein (done within 6hours of birth) wasraised in 3 (5%) babies while at 48hours C-reactive protein level was raised in 13(22%) neonates. There was statistically significant difference between clinical versus laboratory diagnosis (p=0.000).

Clinical evidence of sepsis showed respiratory distress in 15 neonates (25%), unexplained low APGAR without fetal distress in 6 (10%) and poor perfusion and hypotension found in 5 (8.3%). Blood culture were positive in 13 neonates. Klebsiella (46.1%) was the commonest organism followed by E.coli (23%), Acinetobacter (15%), Staphylococcus aureus (7.6%) and coagulase negative staphylococci (7.6%).

Frequency of neonatal sepsis was significantly higher in mothers with longer duration of rupture of membranes, (p=0.041).

DISCUSSION

Preterm premature rupture of membranes (PPROM) affects 5 to 10% of pregnant women and is responsible for around 30% preterm deliveries. The diagnosis of PPROM is made by obtaining a history of leaking amniotic fluid, clinical assessment. Additionally, ultrasound evaluation of amniotic fluid volume may be helpful in diagnosis of PPROM [10]. The independent relationship with perinatal complications has been illustrated by Arias and Tomich, who have prospectively shown higher rates of severe neonatal morbidity in pregnancies complicated by PPROM than those caused by idiopathic preterm labor (27% versus 15.1%, p<0.002). PPROM affects 32 to 40% preterm deliveries, with 60 to 80% of these patients entering spontaneous labor within 48 hours, and the subsequent neonatal sequeale of preterm delivery ensuing.

Sepsis is the commonest cause of neonatal mortality. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes [2]. It is classified into Early onset sepsis (EOS) within 1 st 72 hours and late onset sepsis (LOS) after wards [7]. Prematurity predisposes to sepsis: premature infants with a birth weight<1000g are particularly at risk with an inverse correlation between gestational age, birth weight and sepsis [2]. Even late preterm infants have a fourfold higher risk of sepsis

than term infants [11]. Thus bacterial infections remain the most common cause for mortality and morbidity in early human life. In our study sepsis was suspected on clinical grounds in 26(43.3%) neonates. Nili and Ansari found suspected cases of sepsis in33.7% [5]. Signs of infection may be difficult to assess, particularly when the infection has been partially treated.

C-reactive protein (CRP) is the most extensively studied acute phase reactant so far and despite the ongoing rise (and fall) of new infection markers it still remains the preferred index for diagnosis of neonatal sepsis in many neonatal intensive care units. The sensitivity of CRP is known to be lowest during the early stages of infection.CRP is currently considered as the most reliable method with highest sensitivity and specificity for early diagnosis of both EOS and LOS [12]. The sensitivity and specificity of CRP in the present study is 55.17% and 81% respectively. Chauhan Setal *et al*., study [13] showed sensitivity and specificity of 92.30% and 85.71%. Where as Boma a west *et al*., study [14] sensitivity and specificity are lower with 74% and 74.1% respectively. CRP passes the placenta only in very low quantities, therefore any elevation in the neonate always represents endogenous synthesis. In diagnosis of early onset sepsis previous studies reported on widely differing sensitivities and specificities of CRP ranging from 29 to 100% and from 6 to 100% respectively. These extreme variations are a result of different reference values, test methodologies, inclusion criteria, sampling time.

We observed that gram negative organisms were the commonest organisms causing neonatal sepsis. Most common organism isolated was klebsiella followed by Ecoli, Acinetobacter, staphylococcus aureus, coagulase negative staphylococci. The findings of our study are similar to those of the National neonatal perinatal database [15] where klebsiella was the commonest isolate followed by staph aureus. In another study conducted by Kerurbasavaraju *et al*., study [16] the commonest isolate was Ecoli.

Considering the influence of PPROM on neonatal mortality and morbidity, we found significant relation between length of interval between rupture of membranes and delivery on the incidence of neonatal infection, though only in neonates born after PPROM with the latency of more than 48 hours and ocurring between 30- 33weeks of gestation. Frequency also increased with longer duration of rupture of membranes.

CONCLUSION

Frequency of neonatal sepsis was observed to be 22% of babies. Frequency also increased with longer duration of rupture of membranes. Incidence of sepsis is more in early preterm. premature rupture of membranes is an important risk factor for early onset neonatal sepsis. CRP is an effective and readily available tool for diagnosis of neonatal sepsis especially in resource constrained setups. Gram negative organisms are the commonest organisms implicated in early onset neonatal sepsis.

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