



## EARLY ONSET NEONATAL SEPSIS WITH PREMATURE RUPTURE OF MEMBRANES IN PRETERM BABIES

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### ABSTRACT

**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.<sup>1,2</sup> 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. PPRM is defined as a rupture of the amniotic membranes before 37 weeks of gestation and before onset of labor.<sup>3,4</sup>

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

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.<sup>7</sup> Early onset neonatal sepsis implies that the infection presented before 72 hours of life.<sup>7</sup> Respiratory distress is the most common presenting feature. Neonates with sepsis may have non-specific signs and symptoms including temperature instability, hypotension, poor perfusion.<sup>8,9</sup> 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.<sup>10</sup>

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 GSL General Hospital Rajahmundry from July 2017 to June 2018. Neonates of singleton pregnancies complicated by PPRM 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, GSL general hospital, Rajahmundry. 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  $>0.6$  mg/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  $<35.5$  or  $>37.5$  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 PPRM 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 as 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: 18-36 years). Mean gestational age was 34 weeks (Range: 30-36 weeks). Sepsis was suspected in 26 (43%) babies on clinical grounds. Initial C-reactive protein (done within 6 hours of birth) was

raised in 3 (5%) babies while at 48 hours 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 PPRM 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 PPRM. 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 PPRM than those caused by idiopathic preterm labor (27% versus 15.1%,  $p<0.002$ ). PPRM affects 32 to 40% preterm deliveries, with 60 to 80% of these patients entering spontaneous labor within 48 hours, and the subsequent neonatal sequelae 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. It is classified into Early onset sepsis (EOS) within 1st 72 hours and late onset sepsis (LOS) afterwards. 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. Even late preterm infants have a fourfold higher risk of sepsis than term infants. 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 in 33.7%. 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. The sensitivity and specificity of CRP in the present study is 55.17% and 81% respectively. Chauhan et al study<sup>13</sup> showed sensitivity and specificity of 92.30% and 85.71%. Where as Boma et al study<sup>14</sup> 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 *E. coli*, *Acinetobacter*, *Staphylococcus aureus*, coagulase negative staphylococci. The findings of our study are similar to those of the National neonatal perinatal database<sup>15</sup> where *Klebsiella* was the commonest isolate followed by *Staph aureus*. In another study conducted by Kerur basavaraju et al study<sup>16</sup> the commonest isolate was *E. coli*.

Considering the influence of PPRM 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 PPRM with the latency of more than 48 hours and occurring between 30-33 weeks 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.

#### CONFLICT OF INTEREST:

This study has no conflict of interest to declare by any author.  
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#### REFERENCES:

- Bang AT, Bang RA, Bactule SB, Reddy HM, Deshmukh MD. Effect of home based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. *Lancet* 1999; 354: 1955-61.
- Stoll BJ. The global impact of neonatal infection. *Clin perinatol* 1997; 24: 1-21.
- Al riyamani N, Al-Ruheili, Al-shezawi F, Al-khabori M. Extreme preterm premature rupture of membranes; Risk factors and fetal maternal outcomes. *Oman med J* 2013; 28(2):108-11.
- Caughey AB, Robinson JN, Norwitz ER. Contemporary diagnosis and management of preterm premature rupture of membranes. *Rev obstet gynecol* 2008, 1(1):11-22.
- Nilli F, Ansari AAS. Neonatal complications of premature rupture of membranes. *Acta medica Iranica* 2003; 41(3): 175-9.
- Cotton DB, Hill LM, Strassner HT. Use of amniocentesis in preterm gestation with ruptured membranes. *Obstet Gynecol* 1984; 63: 38-48.
- Singh M, Narang A, Bhakoo ON. Predictive perinatal score in the diagnosis of neonatal sepsis. *J trop pediatr* 1994 dec; 40(6): 365-8.
- Kayange N, Kamugisha E, Mshana E. Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza, Tanzania. *BMC pediatr*. 2010; 10:39.
- Karen m puopolo, Clohert and stark's manual of neonatal care 2017; 49: 684-85.
- Kornacki J, Kornack A, Skrzypczak J et al. The influence of preterm premature rupture of membranes on maternal and neonatal outcome. *Arch med sci* 2009; 5(2): 222-28.
- Jaiswal A, Murkhi S, Gaddam P, Reddy A. Early neonatal morbidities in late preterm infants. *Indian pediatr* 2011; 48(8): 607-11.
- Benitz WE. Adjunct laboratory tests in the diagnosis of early onset neonatal sepsis. *Clin perinatol*. 2010; 37(2): 421-38.
- C-reactive protein in early diagnosis of neonatal septicaemia. *Setal B Chauhan, Viren Vagharia, Bimal B Chauhan. Natl J med. Res.* 2012; 2(3): 276-278.
- Prospective evaluation of the usefulness of C-reactive protein in the diagnosis of neonatal sepsis in a sub Saharan African region Boma A west, Oliemen peterside, Rosemary O Ugwu and Augusta U Eneh. *Anti microb resist infect control*. 2012; 1; 22...doi: 2047-2094.
- National neonatal perinatal database NNPD 2002-2003.
- Maternal genital bacteria and surface colonization in early neonatal sepsis Basavaraju M, B. Vishnu bhat, BN Harish, S. Habeebullah and C. Uday kumar Department of paediatrics, Jawaharlal Institute of post graduate medical education and research, Pondicherry, India. *Indian J pediatr* 2006; 73(1): 29-32