Neonatal positivity of CRP test in early onset neoanatal sepsis in relation to duration of PROM vs PROM delivery Interval (PDI)

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Abstract

Aim: To know, which one, PROM duration or PDI is in high risk for CRP positive early onset neonatal sepsis to start antibiotic in treatment to prevent perinatal morbidity and mortality.

Methodology: Total 150 newborn cases admitted to NICU, diagnosed as EONS associated with their maternal history PROM were taken. The information in all the neonate, enrolled into the study as sex, gestational age, weight, with maternal duration of PROM and PROM delivery interval were recorded. In all the cases CRP was done by latex agglutination test and blood culture was sent to confirm sepsis.

Results: There were 40% cases of CRP positivity in EONS with 6 hour of PROM in comparison to 63% positivity associated with PDI of 12 hour duration. CRP was positive in all cases that presented beyond 24 hour of rupture of membrane. The risk of developing EONS was higher (100%) in cases that delivered beyond 24 hours of PDI compared to the cases that delivered within 24 hours. There was a statistical significant relationship of CRP with PROM and PDI (P value-<0.05).

Conclusion: Preventive measures should focus on recognition of factor according to the risk, such as PROM even if 6 hour is high for neonate, PDI should be considered first, with prompt laboratory screening for sepsis. Early institution of empirical antibiotic in treatment to prevent need for neonatal intensive care without increase in perinatal morbidity and mortality.

Key Word: Early onset Sepsis (EOS), ( ), C- Reactive Protein (CRP), Premature rupture of membrane(PROM) PROM delivery interval(PDI).

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Introduction

Neonatal sepsis is defined as a clinical syndrome of bacteraemia with systemic signs and symptoms of infection in the first 4 weeks of life. It can be classified into two subtypes depending upon whether the onset of symptom is before 72 hours of life (early onset) or later (late onset). The major risk factor for early onset neonatal sepsis are maternal colonisation with GBS, rupture of membrane>18 hr, prolonged labour >24hrs and maternal sign and symptom of intra amniotic infection. Early onset infections are caused by organism prevalent in the maternal genital tract or in the delivery area. PROM is rupture of membranes before the onset of labour after 37 completed weeks of gestation. Intra amniotic infection is an acute inflammation of the membrane and chorion of the placenta, typically due to ascending polymicrobial bacterial infection in the setting of membrane rupture. In 50% of affected women labour starts spontaneously within 12 hours, 70% within 24hours, 85% within 48 hours.

A wide variety of acute phase reactant has been evaluated in neonate with suspected bacterial sepsis. However, only C- reactive protein (CRP) and procalcitonin concentration have been investigated in sufficiently largely studies[1]. C-reactive protein is a substance produced by the liver that increases in the presence of inflammation in the body. CRP named for its capacity to precipitate the somatic C-polysaccharide of streptococcus pneumonia, was the first acute phase protein to be described and is an exquisitely sensitive marker of early infection and tissue damage. This response appears much earlier than the pyrogen response leading to constitutional symptoms and signs. Whereas, a single blood culture in a sufficient value is required for all neonates with suspected sepsis to confirm sepsis.

In our study, we want to present the, percentage of chance of infection, support by positivity of CRP test in neonate with EONS in relation to duration of PROM, to the interval between PROM and delivery. So that, we will be more cautious and supportive and use of antibiotics in treatment to prevent need for neonatal intensive care without increase in perinatal morbidity and mortalty.

Material & Methods

This prospective study was conducted in our tertiary level neonatal unit of KIMs medical college over two year period. All the babies born at the obstetric unit of this hospital and admitted to nicu were

enrolled in this study. Those mother attended t antenatal clinic towards term pregnancy with history of leaking or confirmed PROM were booked in Obstetrics and Gynecology department of KIMs. Total 150 babies diagnosed as EONS (The confirmed (Blood culture + but CRP –ve) and suspected cases(CRP positive ± clinical feature suggestive of EONS) and absent cases (CRP negative but clinical feature suggestive of EONS)) delivered from booked cases during the study period were taken.

The information in all the neonate, enrolled into the study as sex, gestational age, weight, length, Head circumference were recorded at birth by standard technique. The details of delivery viz, induced or spontaneous, vaginal or operative, colour of liquor and the APGAR score at birth, need for resuscitation, presentation and vitals at the time of admission were recorded. Sepsis screen was sent for all babies diagnosed as EONS in specific importance to CRP (±). Blood culture was sent from peripheral site to confirm sepsis.

Relevant antenatal history of maternal age, parity, infection including TORCH, drug intake, pregnancy induced hypertension(PIH), gestational diabetes, Abruptio placenta chorioamnionitis, PROM, fetal distress were recorded from all booked cases. Clinical PROM was confirmed by speculum examination and the duration was recorded. All cases managed actively and the interval between PROM and delivery were recorded in obstetric unit of this hospital.

Inclusion Criteria

1. All pregnant women attended antenatal clinic in third trimester with cofirmed premature rupture of membrane
2. All babies diagnosed as EONS ((The confirmed (Blood culture + but CRP –ve) and suspected cases(CRP positive ± clinical feature suggestive of EONS) and absent cases (CRP negative but clinical feature suggestive of EONS))
3. Singleton pregnancy

Exclusion Criteria

1. Pregnant women with other complication except PROM attended antenatal clinic
2. Neonatal complication other than EONS admitted in NICU

Statistical analysis: The data was collected using MS excel sheet and analyzed. Summarization of the data was presented using basic tables. Categorical variables were presented as frequency and percentage. *p value* < 0.05 were considered as statistically significant.

Results

During the study period, total 150 babies were admitted in NICU with a diagnosis of EONS, with maternal history of PROM**.** Out of 150**,** The preterm babies were 86 (57.33%) in comparison to 64(42.66%) term with sex distribution as 78(52%) male and 72(48%) female(Table 1).

Table 1: Distribution of cases according to GA and sex

Neonate		No of Cases (n)	Percentage (%)
Gestational Age	Pre Term	86	57.33
	Term	64	42.66
Sex	Male	78	52
	Female	72	48

Table 2: Distribution of cases according to CRP

C – Reactive Protein	No of Cases (n = 150)
Positive (>5 mg/dl)	77 (51.33%)
Negative (≤5 mg/dl)	73 (48.67%)

In our study, CRP level above 5 mg/dl were taken as positive while a level below and equal to 5 mg/dl was taken as negative. Out of 150 cases CRP was positive in 77 cases (51.33%) while it was negative in 73 cases (48.67%).

Table 3: Incidence of Early onset Neonatal Sepsis

Early onset Neonatal Sepsis	No of Cases (n=150)	% of cases
Confirmed and suspected	117	78
Absent	33	22

The **confirmed** (Blood culture + but CRP –ve) and **suspected cases**(CRP positive ± clinical feature suggestive of EONS) in our study was 117(78%) while **absent** cases (CRP negative but clinical feature suggestive of EONS) were 33(22%).

Table 4: Distribution of cases according to relationship between Duration of PROM and CRP

Duration of PROM (hr)	Total	CRP	
		Positive (+)	Percentage (%)
0 - 6	105 (70.0%)	43	40.95
6 - 12	26 (17.33%)	15	57.69
12 - 24	16(10.66%)	16	100
24 - 48	03 (2.0%)	03	100
	150	77	
P value		0.000001	

When the duration of PROM was considered, majority of EONS 105(70%) were associated with 6 hr of rupture of membrane. Out of 105 cases of EONS, 43(40.95%) were CRP positive cases. Whereas 15(57.69%) cases out of 26 with 6 to 12 hr duration, 16(100%) out of 16 with 12 to 24 hr duration and 3 cases out of 3 were associated with 24 to 48 hr duration of PROM .In the remaining 33 CRP positive cases associated with more than 6 hr of PROM, may be due to antibiotic one or two doses received by some mother. Statistical significance was calculated between duration of rupture of membrane and CRP after dividing the

duration of rupture of membrane into two groups ≤ 12 hr (58/77) and > 12 hours(19/77).

Table 5: Distribution of cases according to relationship between PROM delivery Interval (PDI) and CRP

PROM delivery Interval(PDI) (hr)	Total	CRP	
		Positive (+)	Percentage (%)
0 - 12	36 (24.0%)	23	63.88
12 - 24	88 (58.67%)	32	36.36
24 - 48	25(16.67%)	21	84
> 48	01 (0.66%)	01	100
	150	77	
P value		0.0001	

In our present study, When the duration of PDI was considered, majority of EONS 88(58.67%) were associated with 12 to 24 hr interval of premature rupture of membrane to delivery. Out of 88 cases of EONS, 32(36.36%) were CRP positive cases. Whereas 23(63.88%) cases out of 36 with 0 to 12 hr duration, 21(84%) out of 25 with 24 to 48 hr duration and 3(100%) cases out of 1 were associated with 24 to 48 hr interval of PROM to delivery. Statistical significance was calculated between PROM – delivery interval and CRP after dividing the duration into two groups ≤ 24 hr(55/77) and > 24 hours(22/77).

Discussion

Majority of the cases (70%) in the present study were associated with 6 hour of rupture of membrane, whereas very few cases (2%) presented beyond 24hour. When the CRP values were analysed in relation to duration of rupture of membrane, CRP was positive in all cases that presented beyond 24 hour. In the remaining cases CRP positivity rate varied from 40.95% in those associated with 0-6 hours to 57.69% with 6-12 hours rupture of membrane, which is also statistically significant. It is comparable to one study by **Van de Laae et al**[2] assessed the accuracy of CRP in predicting neonatal sepsis in women with preterm PROM. Even though early presentation to the hospital, prompt identification of PROM and initiation of antibiotic in mother within 12 hours, may help to reduce EONS in babies. We should be cautious, as majority of mother in 6 hour duration of PROM led to CRP positive EONS in 40% of neonate. The risk of infection increases as the longer the membranes remain open and baby undelivered.[3,4]

When the relationship between PDI and CRP was analysed in the present study, the risk of developing EONS was higher (100%) in cases that delivered beyond 24 hours of rupture of membrane compared to the cases that delivered within 24 hours. Majority of EONS 88(58.67%) were associated with 12 to 24 hr of PDI, whereas 63.88% CRP positive case with 0-2hr of PDI. PDI was a significant risk factor for the development of EONS (p value <0.05). This is comparable to the studies done by **Soper et al and Newton et al**[5]. The chance of sepsis will be more in cases with PDI as compare to same duration of PROM. So we should start antibiotic even in small hour PDI compared to PROM in term babies. In PROM associated cases, where we can wait for sepsis screen to come positive. But for preterm babies, in both cases, we can start antibiotic in treatment to prevent need for neonatal intensive care without increase in perinatal morbidity and mortality.

Conclusion

In our study, we want to present the, percentage of chance of infection in newborn, in relation to duration of PROM and the interval between PROM and delivery. We concluded that even if 6 hour PROM is high risk for EONS, PDI should be considered first before PROM. So that, we will be more cautious and supportive and use of antibiotics in treatment to prevent need for neonatal intensive care without increase in perinatal morbidity and mortality.

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