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SERIAL CRP EVALUATION FOR THE DIAGNOSIS OF NEONATAL SEPSIS: A PROSPECTIVE OBSERVATIONAL STUDY.

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Abstract

Aim: to evaluate the role of serial CRP evaluation in the diagnosis of neonatal sepsis.

Materials and Methods: The present prospective observational study was conducted in the Department of Pediatrics, Darbhanga Medical College and Hospital, Bihar for the period of 1 year. A total of 97 neonates suspected of sepsis having birth-weight >1,500 g constituted the study population. CRP was measured from the serum by quantitative turbidimetric immunoassay. The CRP 1 level was measured at the time of clinical presentation; CRP 2 and CRP 3 were measured at 24 and 48 hours respectively.

Results: In the present study out of total 97 subjects, there were 59 (60.8%) males and 38 (39.2%) females. CRP was found positive in 60 cases. In the present study, lethargy (100%), decreased activity (100%), poor feeding (94.7%), poor cry (94.7%), tachypnea (89.5%), hypotonia (47.4%), hypothermia (31.6%), convulsion (26.5%), prolonged CFT (21.1%) and fever (10.5%) were the various symptoms observed.

Conclusion: Serial CRP measurements are useful in the diagnosis of neonatal sepsis. CRP 3 level may virtually rule out or rule in the diagnosis of neonatal sepsis, and has very good correlation with blood culture.

Keywords: CRP, Sepsis, Neonates

Introduction

Globally 2.5 million children died in the first month of life in 2018. The world has made substantial progress in child survival since 1990. Globally, the number of neonatal deaths declined from 5.0 million in 1990 to 2.5 million in 2018. However, the decline in neonatal mortality from 1990 to 2018 has been slower than that of post-neonatal under-5 mortality.[1]

Sub-Saharan Africa had the highest neonatal mortality rate in 2018 at 28 deaths per 1,000 live births, followed by Central and Southern Asia with 25 deaths per 1,000 live births. A child born in sub-Saharan Africa or in Southern Asia is 10 times more likely to die in the first month than a child born in a high-income country. Reducing neonatal mortality is therefore increasingly important for ongoing progress for child survival, and also because the health interventions needed to address the major causes of neonatal deaths generally differs from those needed to address other under-five deaths.[1]

Sepsis is the second major cause of mortality among neonates, killing more than one million neonates annually.[2] Neonatal sepsis, pneumonia and meningitis together result in up to a quarter of all newborn deaths.[3]

Though isolation of organism by culture of body fluids is the gold standard, there are problems associated with this method: result being influenced by prior antibiotic exposure, inadequate sample volume, and delay in getting the report (24 to 72).[4] Being exclusively produced in liver, CRP is an acute phase reactant whose level increases within six hours of acute inflammation, parallels the activity of inflammatory process, and then decreases faster than any other acute phase reactant. These characteristics make CRP very useful in monitoring response to antibiotics.[5] CRP value is reliable in the first 24-48 hours after the onset of infection.[6]

So, monitoring serial CRP level may help in early diagnosis and management of neonatal sepsis, initiation and adjustment of antibiotic therapy, thereby reducing the length and cost of hospital stay as well as the parental anxiety.

Materials and methods

Study design

The present prospective observational study was conducted in the Department of Pediatrics, Darbhanga Medical College and Hospital, Bihar for the period of 1 year. A total of 97 neonates suspected of sepsis having birth-weight >1,500 g constituted the study population.

Inclusion criteria

- Neonatal sepsis
- Neonatal Birth-weight >1,500 g
- Who give informed consent

Exclusion criteria

- Neonatal Birth-weight <1,500 g
- Neonate showing any underlying surgical condition

- Not willing to participate

The study protocol was reviewed by the Ethical Committee of the Hospital and granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained.

Methodology

Neonates were evaluated by thorough history from mother and detail clinical examinations. The findings were recorded in the predesigned proforma.

The laboratory and radiological evaluation done for the diagnosis and confirmation of infection were following: serial measurements of CRP, WBC count, IT ratio, toxic granules; blood culture and sensitivity, CSF analysis and culture, and chest X-ray.

A-15 CRP kit bio-system (Costa Brava, Barcelona, Spain) was used for quantitative measurement of CRP from the serum by turbidimetric immunoassay. The CRP 1 level was measured at the time of presentation; CRP 2 and CRP 3 were measured at 24 and 48 hours respectively. A CRP value of >1 mg/dl was taken as positive.

Statistical analysis

The recorded data was compiled entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations were calculated. The statistical tests applied were student t-test and chi-square test. The level of significance was set at 5%.

Table 1: gender distribution of the study population

Gender	N= (%)
Male	59 (60.8%)
Female	38 (39.2%)
Total	97 (100.0%)

Table 2: distribution of clinical symptoms

Symptoms	N (%)	
	Absent	Present
Poor Feeding	1	18
	5.3%	94.7%
Lethargy	0	19
	0.0%	100.0%
Poor Cry	1	18
	5.3%	94.7%
Prolonged CFT	15	4
	78.9%	21.1%
Hypotonia	10	9
	52.6%	47.4%
Tachyapnea	2	17
	10.5%	89.5%
Hypothermia	13	6
	68.4%	31.6%
Fever	17	2
	89.5%	10.5%
Convulsion	14	5
	73.5%	26.5%
Decreased activity	0	19
	0.0%	100.0%

Table 3: distribution of study population according serial CRP evaluation

Serial CRP	N=97 (%)
CRP 1	29 (29.9%)
CRP 2	41 (42.3%)
CRP 3	60 (61.9%)

Table 4: distribution of cases of neonatal sepsis in the study population

sepsis	N (%)
Probable sepsis	32 (53.3%)
Proven sepsis	15 (25.0%)
Clinical	13 (21.7%)
Total	60 (100.0%)

Table 5: distribution of cases according to type of sepsis

Type of sepsis	N (%)
Early onset	16 (26.7%)
Late onset	44 (73.3%)
Total	60 (100.0%)

Discussion

In the present study out of total 97 subjects, there were 59 (60.8%) males and 38 (39.2%) females. Gupta P et al.[7] and Sharma A et al.[8] in their investigations reported male predominance of 64.7% and 74% respectively.

A review of the articles showed that neonatal septicemia is more common in boys than in girls which can be due to genes related to the sex involved in the immune system.[9,10] The factors regulating the synthesis of gamma globulins are probably situated on the X chromosome. Presence of one X chromosome in the male infant thus confers less immunological protection compared to the female counterpart.[11]

In the present study, lethargy (100%), decreased activity (100%), poor feeding (94.7%), poor cry (94.7%), tachypnea (89.5%), hypotonia (47.4%), hypothermia (31.6%), convulsion (26.5%), prolonged CFT (21.1%) and fever (10.5%) were the various symptoms observed.

Khatua SP et al.[11] in his study observed that refusal of feeds, lethargy, diarrhea, hypothermia, abdominal distension, jaundice and vomiting were the most common presenting feature. Sharma A et al.[8] reported the common symptoms to be refusal of feeds (76%) lethargy (60%) and temperature changes (52%).

The statistical analysis showed that serial measurement of CRP 2 and CRP 3 had significantly high correlation compared to single measurement of CRP 2 only in cases of proven and probable sepsis of early as well as late onset ($p<0.05$). These findings are consistent with the findings of others. Another study concluded that predictive value of CRP could be enhanced by serial rather than a single measurement.[12-14]

Conclusion

CRP is the highest researched biomarker in relation to the diagnosis of neonatal sepsis. It is an acute phase protein that

rises in response to the body's inflammatory reaction. It is commonly used to monitor the progress and treatment of a disease in both the adult and pediatric population. The early evaluations of CRP provide indications of the response to the treatment. Serial measurement of CRP should be used for the diagnostic evaluation of the neonates with suspected sepsis as it is a very good screening test for the early detection of sepsis. Serial CRP negativity almost excludes neonatal sepsis and help guide the duration of antibiotic therapy.[68]

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