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## The Value of C- Reactive Protein in Neonatal Sepsis

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### Abstract:

**Background:** Neonatal sepsis occur 1-8 per 1000 live birth. It is mandatory to have a high index of suspicion for the possibility of sepsis since the signs and symptoms are non specific. (C-Reactive Protein) CRP an acute phase protein used as a screening test for inflammation and disease activity and diagnostic adjuvant.

**Objective:** To evaluate the importance of CRP in the diagnosis of neonatal sepsis, sensitivity, specificity and the predictive value of it.

**Patients & methods:** One hundred neonates with suspected sepsis were admitted to the Central Teaching Hospital for Children / Baghdad, between 1<sup>st</sup> of April and 1<sup>st</sup> of October 2005, were selected for diagnosis of sepsis by CRP and blood culture. The clinical presentations of these neonates were studied to find the most common signs and symptoms.

**Results:** there were 76% of total cases with positive CRP . 53% of cases had positive blood culture and CRP, and the sensitivity was 96.36%, specificity was 48.8% and the negative predictive value was 91.6% and the positive predictive value was 69.7%

**Conclusions:** CRP show high sensitivity and negative predictivevalue which are helpful in the diagnosis of sepsis. A single normal value cant exclude infection and serial measurements will enhance the sensitivity of the test. CRP is not recommended as a sole indicator of neonatal sepsis but may be one of a septic work up.

**Key Words:** CRP, Neonatal Sepsis, Blood Culture

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### Introduction:

Infection is one of the major problems in neonates. The diagnosis is difficult to establish based on clinical criteria alone since the clinical signs of neonatal sepsis are non specific and are associated with characteristics of the causative microorganism and the body response to the invasion. The accuracy of most of the laboratory tests have yielded variable results, these variations might be attributable to differences in population baseline, severity and risk status<sup>[1]</sup>.

However the illness severity and risk status are unlikely to interfere with the use of CRP(C-Reactive Protein) for the detection of neonatal sepsis<sup>[2]</sup>.

CRP was identified in 1930 and subsequently considered to be one of an acute phase proteins which were used as a non specific indicators of bacterial sepsis and an early indicator of infections or inflammatory conditions , a marker for activity, and diagnostic adjuvant<sup>[3]</sup>.

The highest concentrations of CRP have been reported in bacterial infections. CRP is raised in 85%of sepsis cases with a specificity of 90%.It can be normal in cases of true sepsis and should be used in conjunction with clinical signs and culture results<sup>[4]</sup>. However, CRP alone has no role in the diagnosis of

Clinical entities, and a normal CRP level should never delay antibiotics coverage<sup>[3]</sup>.

### Aim of the Study:

To evaluate the significance of the usually used infections marker (CRP)for the diagnosis of neonatal sepsis and to determine the sensitivity, specificity and

predictive values of it as an early indicator of neonatal sepsis.

### Patients & Methods:

The study was done in the Central Teaching Hospital For Children in Baghdad , over a 6- month period, between 1<sup>st</sup> of April and 1<sup>st</sup> of October 2005. The samples were collected randomly from 100 neonates who were admitted for evaluation of sepsis if the clinical manifestation of sepsis were present. The principle clinical features were reluctant to feed , lethargy, poor reflexes and sucking , temperature instability, respiratory distress, irritability, apnea, cyanosis, skin changes ,abdominal distension, vomiting and diarrhea, jaundice and organomegaly.

CRP (by latex agglutination which is easy to perform at the bedside, it is a qualitative test), as a screening test was performed along with blood culture from peripheral venepuncture the golden standard for diagnosis of sepsis.

The diagnosis of sepsis was made when there were positive results of cultures. Neonates with a negative blood culture may have sepsis but this study was designed to asses the role of CRP in culture positive cases.

The sensitivity, specificity, positive predictive and negative predictive values were calculated in culture positive cases only.

### Results:

The main clinical presentations in those neonates were reluctant to feed ( 86% ), and lethargy ( 50% ) as shown in table (1)

Table (1) :Main clinical signs and symptoms in the study sample

Clinical manifestation	No. &%
1-Reluctant to feed	86(86%)
2- Lethargy	50 (50%)
3- Respiratory distress	35(35%)
4- Cyanosis	32(32%)
5- Fit	30(30%)
6- Jaundice	28(28%)
7- Umbilical infection	26(26%)
8- Temperature instability	22(22%)
9- Apnea	20(20%)
10- Vomiting	17(17%)
11- Diarrhea	15(15%)
12- Abdominal distension	15(15%)
13- Irritability	15(15%)
14- Hepatomegaly	12(12%)
15- Sclerema	11(11%)
16- Pallor and mottling	10(10%)

**Note:** Some of the neonates had more than one sign & symptom.

Of the collected 100 blood samples from these neonates, the results were 76 neonates (76%) with a positive CRP and (24%) with negative CRP, while (55%) of cases had positive blood culture and (45%) had negative blood culture. Fifty three neonates (53%) had positive blood culture and CRP, while (23%) of those with a positive CRP had a negative blood culture as shown in table(2).

There were two cases (2/24) with negative CRP and positive culture, the rest of the cases (22/24) were with negative CRP and blood culture as shown in table (2).

The sensitivity of CRP in sepsis proven cases was 96.36%, the specificity was 48.8%, the positive predictive value was 69.7% and the negative predictive value was 91.6%, as shown in table (3).

Table (2): The distribution of the results of CRP and blood culture

CRP	Blood culture		Total
	No. of positive	No. of negative	
No. of positive	53	23	76
No. of negative	2	22	24
Total	55	45	100

**Table (3): Sensitivity, specificity and the predictive values in culture positive cases.**

Values	%
<b>Sensitivity</b>	<b>96.36</b>
<b>Specificity</b>	<b>48.8</b>
<b>Positive predictive value</b>	<b>69.7</b>
<b>Negative predictive value</b>	<b>91.6</b>

**Discussion:**

Infection in the neonatal period is an extremely serious condition and the diagnosis is difficult to establish based on clinical criteria alone, but requires microbiological and clinical correlation<sup>[5]</sup>.

Forty five infants classified as having probable sepsis have clinical evidence but they lacked the microbiological proof of infection. This may be due to preadmission use of antibiotics which influence the results of culture<sup>[5]</sup>. Laboratory tests used to support the diagnosis have shown variable predictive values, so CRP (acute phase protein) is widely used as a marker of infection<sup>[6]</sup>, and it has been found to be high in culture proven sepsis<sup>[7]</sup>, in agreement with our study.

In our study (53/55) cases with proven sepsis by blood culture had positive CRP, similar results observed in one study done by Wietkamp and Aschner on 100 neonates having clinical features of sepsis of which the CRP was positive in 24/28 (85.7%) of the sepsis proven cases., the test found to be highly sensitive test with high negative predictive value<sup>[8]</sup>.

In this study raised CRP were found in 76% of cases, this figure was similar to that reported by Pepsys MB, he noted that raised CRP are found in 50-90% of neonates, but the raised level are non specific for bacterial infection<sup>[9]</sup>. The frequent occurrence of raised CRP in sera of uninfected newborn infants eliminates it as a useful indicator of infection but may suggest an acute tissue damaging process<sup>[10]</sup>.

Recently many investigators considered CRP estimation to be of value in the early diagnosis and monitoring of neonatal sepsis. However, in a large study from New York, CRP value found to be moderately raised in sepsis but the serum level found to be high in asphyxia, shock and other conditions not related to infections<sup>[11,12]</sup>.

For a test to be useful in establishing the diagnosis of sepsis it should be of maximum sensitivity so as not to miss a case of sepsis and maximum negative predictive value to exclude sepsis when the test is

negative<sup>[13]</sup>.

In our study the CRP show high sensitivity 96.36% and high negative predictive value 91.6%, high sensitivity (68.97%) were noted in a study done on culture proven septic neonates<sup>[14]</sup>.

Other study done on 50 cases of suspected sepsis the over all sensitivity and specificity are equal to negative and positive predictive value respectively i.e. 66.66% and 48.27% in all culture positive and negative cases<sup>[13]</sup>.

The loss of specificity and positive predictive value is acceptable since the risk of over treatment with antibiotics is much lower than the risk associated with sepsis<sup>[15]</sup>.

The sensitivity, specificity and the predictive values can be enhanced by serial rather than single measurements and serial CRP show very high predictive values for the diagnosis of sepsis as shown in one study which show the sensitivity, specificity, positive predictive and negative predictive values were 100%, 94%, 91.6% and 100% respectively<sup>[16]</sup>.

**Conclusions & Recommendations:**

CRP show high sensitivity and negative predictive value which are important in more accurate diagnosis of sepsis and early treatment.

Estimation of CRP have some value in the diagnosis of neonatal sepsis but the frequent occurrence of raised CRP in the sera of uninfected neonates eliminates it as a useful indicator of sepsis but may suggest an active damaging process. We advocate not to rely on the result of single test, even with the combination of test, we still stress the importance of correlating the clinical and laboratory data.

Current methods to detect signs of sepsis and to identify the causative microorganisms are not 100% sensitive and accurate, and continued research is necessary to identify the most sensitive markers for diagnosis and therapy in the future.

**References:**

- 1-eMedicine 2003 Linda Bellig .Neonatal Sepsis .
- 2-Chiesa, Pellegrini, Panero et al .CRP ,IL-6 , Procalcitonin in the immediate postnatal period : influence of illness severity , risk status ,antenatal and perinatal complication and infection. Clin. Chem.2003.Jan.: 49(1):60-8.
- 3-Clyne-B;Olshaker-Js.TheCRP.J-Emerg-Med. 1999Nov.-Dec;17(6):1019-25.
- 4-Isaacs D,Moxon ER. Handbook of neonatal infections-a practical guide. WB Saunders, London.1999: 9-11.
- 5-Squire E, Favara B, Todd J. Diagnosis of bacterial infections hematological and pathological findings in fatal and non fatal cases . Pediatrics 1979;64:60-8.
- 6-Apostola,Dimitriou,Kaleyias,et al .Levels of soluble ICAM-1 in the preterm and full term neonates with infection .Mediators – Inflamm. 2002.Apr;11(2):95-8.
- 7-Ixagasioglu,Caksen,Sutcu,etal.Serum CRP and IL-6 levels in neonatal sepsis . Acta- Medica. 2002; 45(3):111-3.
- 8-Wietkamp and Aschner. Diagnostic value of CRP and hematological parameters in neonatal sepsis. J-Coll-Physcian-Surg-Pak.March 2005;15(3):152-6.
- 9-Pepsys MB; CRP fifty year on, Lancet, 1981; 1: 653-7.
- 10-Stoll BG, Weisman LE. Infections in perinatology. Clin. Perinato l.1997; 24(1): 1070-79.
- 11-Ainbender E, Cabata EE, Guzman DM, ET al. Serum CRP and problems of newborn infants . J.Pediatr 1982; 101:438-40.
- 12- Stoll BJ et al :late in very onset sepsis low birth weight neonates report from the National Institute of Child Health and Human Development National Research Network .J pediatr 1996; 129:63.
- 13- Mustafa S, Farooqui S ,Waheed S,et al. evaluation of CRP as early indicator of blood culture positive in neonate. Pak.J.Med.Sci. 2005, 21(1):69-73.
- 14-Krishna , Nadgir, Tallur et al . IgM estimation and CRP detection in neonatal septicemia. Indian – J- Pathol- Microbiol. 2000 Jan; 43(1):35-40.
- 15-Amarican Family Physicain,Review of tests for diagnosis of neonatal sepsis. Ped. Infectious disease journal, May1995, vol 14 :p 362.
- 16-Nuptnarumit , pinkaew, Kitiwan wanich et al . predictive value of serial CRP in neonatal sepsis. J-Med- Assoc-Thia. 2002 Nov ; 85 Suppl 4 :S1151-8.

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