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Comparison of procalcitonin and C-reactive protein as markers of neonatal sepsis

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Abstract
Objective: To compare the clinical informative value of procalcitonin (PCT) and C-reactive protein (CRP) plasma concentrations in the detection of infection and sepsis and in the assessment of severity of sepsis.
Study Design: This prospective study was conducted in Neonatology unit of department of pediatrics SKIMS, Srinagar. Study was conducted on 100 patient including preterm and term both.
Results: In our study Sensitivity of CRP in detecting sepsis was found to be 77.78%, specificity 78.08%. In the present study Sensitivity of Procalcitonin in detecting sepsis was found to be 96.30%, specificity 69.86%.
Conclusion: PCT is a better marker of sepsis than CRP.

Keywords: Procalcitonin, C-reactive protein, infection, sepsis

Introduction
Neonatal Sepsis is defined as invasive bacterial infection which occurs in first four weeks of life [1]. Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries [2, 3]. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes [3]. Neonatal sepsis can be classified into two sub-types depending upon whether the onset of symptoms is before 72 hours of life (early onset) or later (late onset) [5].
A number of acute proteins serve to indicate the presence of infection in neonate.

A. Those which increase with inflammation are: Procalcitonin, CRP, Acid Glycoprotein, Haptoglobin, Antitrypsin, Fibrinogen.

B. Those decreasing with inflammation are: Prealbumin, Transferrin.
The sensitivity of CRP is known to be the lowest during the early stages of infection. Thus, a single normal value at the initial sepsis work-up is not sufficient to rule out an infection [6-8].
On the other hand a raised CRP is not necessarily diagnostic for sepsis, as elevations may as well occur due to the physiologic rise after birth or non infection associated conditions, e.g stressful delivery, prolonged rupture of membranes and/or prolonged labor, asphyxia, meconium aspiration syndrome, in intraventricular hemorrhage, pneumothorax, and tissue injury [9].
Normally plasma PCT concentrations are found to be below 0.05 ng/ml. PCT concentrations can increase up to 1.0 ng/ml in patients with sepsis, severe sepsis or septic shock. Concentrations above 10 ng/ml are almost exclusively found in patients with severe sepsis or septic shock [10]. PCT concentration increases in the serum within 2-3 hours of beginning of infection peaking by 6-12 hours and returning to normal concentrations in 2 days [11].

Materials & Methodology
This prospective study was conducted in Neonatology unit of department of pediatrics SKIMS, Srinagar. Study was conducted on 100 patient including preterm and term both. All were informed regarding the study and their written consent was obtained. Data such as name, age, gender etc. was recorded. Procalcitonin and CRP were measured using QDx Instacheck Reader.

Procalcitonin: principle of test: The test uses a sandwich immunodetection method, such that the detector antibody in buffer binds to PCT in serum sample and antigen-antibody complexes are captured to another PCT antibody that has been immobilized on test strip as sample mixture migrates nitrocelluose matrix. Thus the more PCT antigen in serum, the more antigen-antibody complexes accumulated on the test strip. Signal intensity of fluorescence on detector antibody reflects the amount of antigen captured and is processed by QDx Instacheck Reader to show PCT concentration in specimen. The working range of QDx Instacheck PCT test is 0.25 ~ 100ng/mL. Procalcitonin > 0.5ng/ml was considered as positive test report in present study.

Sample type: Serum or plasma not older than 24 hours

CRP: Principle of Test: QDx Instacheck CRP is an immunoassay system based on antigen- antibody reaction and fluorescence technology. When a test sample (human serum, plasma, or whole blood) is processed with the detection buffer in the detection buffer tube, the fluorochrome-labeled detector antibodies (anti-CRP) in the detection buffer binds with CRP in the test sample. When this processed test sample is loaded into the sample well on the test cartridge as per the prescribed test procedure, it migrates through the nitrocellulose matrix of the test strip. The fluorochrome-labeled detector antibody-analyte (CRP) complexes get captured on to the capture antibodies (anti-CRP) which have been immobilized at the test line on the test strip. As a result, the complexes of the capture antibody-analyte (CRP)- detector antibody get accumulated at the test line on test cartridge membrane. Thus, more the CRP in the test sample, more the complexes that get accumulated at the test line on the test cartridge membrane. Upon inserting the sample-loaded test cartridge in the QDx Instacheck Reader, the laser light illuminates the test cartridge membrane thereby triggering fluorescence from the fluorochrome-labeled complexes of CRP. Intensity of the fluorescence is scanned and converted into an electric signal. The on-board microprocessor computes the CRP concentration based on a pre-programmed calibration. The computed and converted result is displayed by the QDx Instacheck Reader quantitatively in terms of mg/L. CRP level >6mg/L was considered as positive test report in present study.

Results

Table 1: PCT VS CRP

	CRP		Total
	> 6mg/L	< 6mg/L	
> 0.5ng/ml	32	16	48
PCT < 0.5ng/ml	5	47	52
Total	37	63	100

Table 2: Correlation of PCT and CRP

	Procalcitonin positive	CRP positive	P value
All cases (100)	48	37	0.115
Blood culture positive (27)	26	21	0.113
Blood culture negative (73)	22	16	0.346

Out of 100 patients Procalcitonin was positive in 48patients and CRP was positive in 37 patients. Out of 27 blood culture positive patients Procalcitonin was positive in 26 patients and CRP was positive in 21 patients.

Study of Sensitivity & Specificity of Procalcitonin test (with cut-off value 0.5 ng/ml) for diagnosis of Neonatal Sepsis

	Test Report (Procalcitonin test)		
Actual Outcome of Sepsis (Disease)	Positive Test Report (Procal> 0.5 ng/ml)	Negative Test Report (Procal ≤ 0.5 ng/ml)	Total
Present	26	1	27
Absent	22	51	73
Total	48	52	100
		P value < 0.001	

Procalcitonin was positive in 26 out of 27 culture positive cases and 22 out of 73 culture negative patient with a statistical significant p value of .001. Procalcitonin was negative in 1 patient out of 27 culture positive patients and 52 out of 73 culture negative patients.

Procalcitonin Test (> 0.5)	Estimated Value	95% Confidence Interval	
		LCL	UCL
Sensitivity	96.3	81.03	99.91
Specificity	69.86	58	80.06

Sensitivity of Procalcitonin in detecting sepsis was found to be 96.30%, specificity 69.86%, positive predictive value (PPV) 54.17% and Negative predictive value (NPV) 98.08 %, positive test likelihood ratio 3.2, negative test likelihood ratio 0.05 and Odds ratio 60.273.

Study of Sensitivity & Specificity of CRP test (with cut-off value 6 mg/l) for diagnosis of Neonatal Sepsis

	Test Report (CRP test)		
Actual Outcome of Sepsis (Disease)	Positive Test Report	Negative Test Report	Total
Present	21	6	27
Absent	26	57	73
Total	37	63	100

CRP Test (> 6)	Estimated Value	95% Confidence Interval	
		LCL	UCL
Sensitivity	77.78%	57.74	91.38
Specificity	78.08%	66.86	86.92

CRP was positive in 21 cases out of 27 culture positive cases and 16 cases out of 73 culture negative patient with a statistical significant p value of .001. CRP was negative in 6 cases out of 27 culture positive cases. Sensitivity of CRP in detecting sepsis was found to be 77.78%, specificity 78.08%, positive predictive value (PPV) 56.76% and Negative predictive value (NPV) 90.48.

Discussion

Neonatal sepsis is one of the most important cause of morbidity and mortality in newborns throughout the world. Early detection of neonatal sepsis is difficult because the first signs of disease may be minimal and are often non-specific being similar to those of various non infectious processes. In the present study a total of 100 neonates

meeting the inclusion criteria were enrolled. Out of 100 neonates males were 59% and females 41% which is comparable to the results of Swarankar *et al*. [12] and close to results of Mathai *et al*. [13] which showed male incidence of 58% and 56.8% respectively. In our study Sensitivity of CRP in detecting sepsis was found to be 77.78%, specificity 78.08%, Gerdes *et al*. [14] reported sensitivity of CRP as 47-100%, specificity 83-94%. In the present study Sensitivity of Procalcitonin in detecting sepsis was found to be 96.30%, specificity 69.86%, Boo *et al*. [15] reported sensitivity 88.9%, specificity 65.2%, Adib *et al*. [16] reported sensitivity 75%, specificity 80%.

Conclusion

In conclusion CRP has higher specificity for neonatal sepsis as compared to Procalcitonin, but Procalcitonin has higher Sensitivity than CRP making it is a better diagnostic marker for neonatal sepsis as compared to CRP.

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