ISSN 2515-8260 Volume 08, Issue 03, 2021

Prognostic significance of Procalcitonin, High sensitivity C-reactive protein and white blood cell count in comparison with blood culture in ICU patients with Sepsis and Septic shock in a tertiary care Hospital

Dr. Kondle Raghu[1]*, Dr. Krishnan Ramalingam[2]

[1]*Department of Medical Sciences, Lincoln University College, Malaysia.*

[2]*Department of Biochemistry, Narayana Medical College, Nellore, A.P, India.*

Abstract:

Background: *Sepsis is a life-threatening condition in ICU with high morbidity and mortality. Biomarkers which can act as a predictor for diagnosis, prognosis, and patient outcome in sepsis are needed.*

Aim: *Aim of the study is to compare the significance of hs-C-reactive Protein (CRP), Procalcitonin, White blood cell count, and blood culture in patients with bloodstream infections and compare their prognostic significance with blood cultures in sepsis.*

Materials and Methods: *This hospital based prospective observational study was conducted between July 2018 to July 2019 for one year with 216 cases of sepsis. Serial determination of Procalcitonin and CRP at admission and Day 6 was done. Data was analyzed check to compare the prognostic significance of the PCT, CRP, and WBC count.*

Results: *A blood culture positivity rate of 50.9% was reported with male preponderance. WBC count has significantly reduced after 72hrs of admission (p= 0.007). CRP levels have significantly reduced on day 6 (p = 0.043) in comparison to at the time of admission (p= 0.032). The serial determination of PCT levels at admission and on day 6 (p= 0.032) was found to be a better prognostic indicator in patients with sepsis than at the time of admission. The significant patient outcome in terms of mortality and reduction in length of hospital stay has been found (p= 0.018, p=0.002). The positive correlation of PCT and CRP and SOFA score has been reported.*

Conclusion: *Prognostic significance was found for the biomarkers PCT, CRP, and WBC count with significant patient outcomes in terms of mortality and hospital stay reduction.*

Keywords: Procalcitonin, C-reactive Protein, Blood culture, Sepsis, SOFA score.

1. Introduction:

The Word “sepsis” is derived from the Greek word “sips ‘meaning “to make rotten,” originally believed the product of blood putrefaction. Septicemia is defined as a condition in which bacteria reproduce in the blood, and the release of toxic products causes harm to the

host due to an infection [1]. Infections caused by the bloodstream are causes of morbidity and mortality in hospitalized patients. It is a leading cause of death with mortality rates ranging from 20% to 50%, especially in Intensive Care Units, prolonging the patients' hospital stay [2].

Sepsis is due to the exuberant response of inflammation pointing towards the role of proinflammatory mediators and cytokines in causing collateral damage further progression to multiorgan failure (MOF) [2].

Acute phase pentameric Protein of the pentraxin family of proteins found in blood plasma. Inflammatory mediators (IL-6, TGF-Beta, TNF-Alpha) act as stimuli.

CRP binds to the surface of the dying cells, including bacteria, and helps activate the complement system to facilitate cell removal. It is a Biomarker that can be elevated within two hours after triggering an event, helping diagnose and evaluate the prognosis of infection. Normal concentrations are 0.8 mg/l to 3.0 mg/l with a half-life of 19 hours [3].

PCT is the prohormone of calcitonin (CT). CT is produced by numerous cell types and organs after proinflammatory stimulation, especially when caused by bacterial challenge. Plasma PCT concentration in healthy people is below 0.05 ng/ml, and in Severe sepsis / septic shock is>2 - 10 ng/ml. Elevated PCT levels may indicate bacterial infection accompanied by a systemic inflammatory reaction.

With the increased mortality due to sepsis, the early detection of Blood Stream Infections by developments in blood culturing techniques is the need of the hour. Increased sensitivity of automated blood culture methods gives faster microbial recovery and earlier start of required antibiotic therapy.

Leukocyte counts have been evaluated as a diagnostic indicator, with <4000/mm or >11,000/mm is one of the SIRS criteria. Leukocyte shift aids in the diagnosis of infection and the degree of elevation may serve in detecting high risk for the depletion of marrow neutrophil reserves leading to death from sepsis. The specificity & sensitivity of WBC count in correlation with positive blood cultures can be used as a prognostic marker for sepsis [4].

This study aimed to compare the significance of hs-C-reactive Protein (CRP), Procalcitonin, White blood cell count, and blood culture in patients with bloodstream infections and compare the prognostic significance of Procalcitonin, hs-CRP, and WBC count with blood cultures in sepsis cases.

2. MATERIALS AND METHODS:

Study design: Hospital based prospective observational study was conducted at Intensive Care Unit, Department of Emergency Medicine, Narayana Medical College & Hospital, from July 2018 to July 2019 for one year duration with a sample size of 216 cases. The study protocol was approved by Institutional Ethics Committee, Narayana Medical College, Nellore.

Inclusion criteria were patients >18yrs with sepsis and septic shock.

Exclusion criteria is patients of <18yrs of age.

Method: Patients were assessed clinically by recording vital signs, SOFA score, blood investigations, including blood culture, CRP, PCT, total WBC count on day 0, 72 hours of admission, and day 6 after initiating antibiotics.

Blood Collection: 20 ml of blood was collected under strict aseptic conditions: Ipsilaterally, one from the peripheral line, and one from the central line before administering antibiotics and sent to the laboratory.

Culture and identification: Collected blood was kept in BacT / ALERT 3D system - Automated method. Plating was done on Blood agar, Nutrient agar, MacConkey's agar, Chocolate Agar and incubated at 37 ^{0} C aerobically for 18 -24hrs. Organisms were isolated, and antibiotic susceptibility testing was done according to CLSI guidelines (VITEK 2 system).

hs-CRP, Procalcitonin: blood samples were sent on day 0 and day 6. Both were tested by the immunoturbidimetry method.

WBC count: Blood sample was sent on day 0, 24 hours, and 72 hours and the WBC count was done by Beckman Coulter analysis.

Statistical analysis performed using SPSS software ver 22.0. Different clinical and laboratory variables were assessed, and a significant p-value was determined. A correlation analysis between PCT, CRP, and SOFA score was done. $p<0.05$ considered as Statistical significance.

3. RESULTS

Table 1: Age, Gender distribution, Mechanical Ventilation, Diagnosis

Variables	Blood Culture		Total (n=216)	P-Value
	Positive (n=110)	Negative (n=106)		
Age (Years)	52.25 ± 16.97	55.12 ± 16.25	53.65 ± 16.55	0.376
Gender, n (%)				
Male	76 (69.09)	56 (52.83)	132 (61.11)	0.083
Female	34 (30.909)	50 (47.16)	84 (38.89)	
Mechanical Ventilation, n (%)	106 (96.36)	100 (94.33)	206 (95.37)	0.617
Diagnosis, n (%)				
GI/Biliary	46 (41.8)	20 (18.9)	66 (30.55)	
Pneumonia	22 (20.0)	24 (22.6)	46 (21.29)	
Primary Bacteremia	2 (1.8)	4 (3.8)	6 (2.77)	0.105
Urosepsis	12 (10.9)	12 (11.3)	24 (11.1)	
Others	28 (25.5)	46 (43.4)	74 (34.25)	

Table 2: Distribution of SOFA score, APACHI II score, and Lactate levels at admission at 24hrs

Variables	Blood Culture		Total (n=216)	P-Value
	Positive (n=110)	Negative (n=106)		
SOFA				
Admission	12.73 ± 3.83	10.62 ± 3.72	11.69 ± 3.90	0.005*
72 hrs	9.04 ± 3.51	8.50 ± 3.98	8.78 ± 3.74	0.461
APACHI II				
Admission	23.75 ± 8.71	24.75 ± 9.14	24.24 ± 8.90	0.558
24 hrs	22.00 ± 8.12	25.17 ± 9.56	23.56 ± 8.96	0.066
Lactate				
Admission	3.26 ± 3.04	3.43 ± 2.83	3.34 ± 2.93	0.766
24 hrs	3.47 ± 2.88	3.03 ± 1.92	3.25 ± 2.46	0.346

Table 3: Distribution of WBC count, PCT levels, and CRP levels at admission and at 24hrs

Variables	Blood Culture		Total (n=216)	P-Value
	Positive (n=110)	Negative (n=106)		
WBC Count				
Admission	20154.72 ± 8967.15	16649.67 ± 6782.46	18403.19 ± 7785.97	0.024*
72 hrs	17160 ± 14895.36	11113.21 ± 5702.13	21.266 ± 12309.10	0.007*
PCT				
Admission	16.34 ± 20.49	23.86 ± 16.34	23.0 ± 26.39	0.038*
Day 6	9.28 ± 13.51	16.04 ± 18.49	12.66 ± 25.79	0.032*
CRP				
Admission	158.03 ± 109.30	203.44 ± 108.31	216.0 ± 102.46	0.032*
Day 6	88.95 ± 75.42	121.51 ± 89.53	129.0 ± 105.46	0.043*

Table 4: Distribution of Outcome of the patients

Variables	Blood Culture		Total (n=216)	P-Value
	Positive (n=110)	Negative (n=106)		
Outcome				
Hospital Mortality, n (%)	10 (9.09)	28 (26.41)	38 (17.6)	0.018*
Hospital stay (Days)	15.20 ± 11.31	9.92 ± 4.82	12.34 ± 9.11	0.002*
ICU Stay (Days)	10.53 ± 9.52	7.15 ± 3.31	8.74 ± 7.52	0.016*

Table 5: Distribution of WBC count at admission and at 72hrs, PCT and CRP at admission and on day 6

Variables	Blood Culture			P Value
	Negative (n=106)	Positive Gram-positive (n=14)	Positive Gram-negative (n=96)	
WBC Count Admission 72 hrs	 16649.67 ± 6782.46 11113.21 ± 5702.13	 22410.42 ± 5367.45 21265.74 ± 3308.98	 20630.19 ± 6980.16 19188.68 ± 5333.81	 0.0002* <0.0001*
PCT Admission Day 6	23.86 ± 16.34 16.04 ± 18.49	17.88 ± 20.64 9.37 ± 11.58	15.16 ± 18.73 8.45 ± 10.09	0.987 0.037*
CRP Admission Day 6	203.44 ± 108.31 121.51 ± 89.53	161.67 ± 103.25 87.34 ± 73.16	136.21 ± 109.44 82.91 ± 63.27	0.009* 0.044*

4. DISCUSSION:

The present study shows a blood culture positivity rate of 50.9%. Such high positivity rates have been reported by Parikh Madhubala and Singh Nandon (47%), Surya Kirani and Sailaja (42%) and Jaslyn et al. (42%), Shabnum et al (24.66%), Joshi et al. (25%) and Iregbu et al (22%)[1,5-9].

The average age of sepsis group in our study was 52yrs, in comparison to that reported by Qinhao Li et al. (56.6yrs), Zhang et al. (92yrs) and Arif et al. (43.45yrs). Male preponderance (69.1%) among the cases was reported in our study with similar results reported by Qinhao Li et al. (70%), Zhang et al. (81.6%), B. Suberviola et al. (63.6%), Arif et al. (53.2%) and Fatih Aygun (54.1%)[10-14].

Infections and sepsis are leading causes of morbidity and mortality in an Intensive Care Unit, making early diagnosis accompanied with proper treatment the need of the hour to reduce mortality [14]. With the body's resistance to sepsis-induced tissue damage and the inflammatory response further causing organ failure, certain biomarkers for predicting the occurrence of sepsis and having a prognostic value need to be evaluated to utilize their role in improving the clinical management of patients with sepsis[4, 10, 13, 15].

In our study, we have noted that the WBC count has significantly reduced after 72hrs of admission ($p = 0.007$) in comparison to at admission. Zhang et al. and Abedni et al. have reported WBC count has no prognostic significance ($p= 0.282$ and 0.29 respectively). This contrast in the reported findings makes this a marker to be further evaluated. WBC count has been an integral part of diagnosing sepsis and septic shock. Many patients present with leukocytosis in a delayed fashion, making WBC count one of the critical parameters to predict delayed abnormal host response [16,17].

CRP is one of the biomarkers for differentiating inflammatory from non-inflammatory conditions and assessing the severity of sepsis. CRP levels have significantly reduced on day 6 ($p = 0.043$) in comparison to at the time of admission ($p= 0.032$). Zhang et al. ($p= 0.003$) and Asadi et al. ($p= 0.001$) reported a significant reduction of CRP levels. CRP levels have been significantly reduced by the end of 1 week in a study reported by Qinhao et al.[10,11,18].

PCT has been reported to be a better biomarker in predicting the patients' outcome, but the serial determination of PCT levels at admission and on day 6 ($p= 0.032$) has been found to be a better prognostic indicator in patients with sepsis than at the time of admission. Such significant reduction in PCT has been reported by Qinhao et al., Zhang et al. ($p = 0.009$), Asadi et al. ($p= 0.005$), B. Suberviola et al.($p =<0.01$).

PCT rises faster than CRP in response to an infectious trigger and decreases faster once infection subsides, making PCT a reliable marker. Descending PCT values have been found to be a predictor for survival. The significant patient outcome in terms of mortality and reduction in length of hospital stay has been found in our study ($p= 0.018$, 0.002 respectively). Similar improvements in outcome have been reported by Asadi et al. ($p= 0.001$), Fatih Aygun ($p= <0.001$). Arif et al. have reported higher mortality in patients with higher CRP levels making a positive correlation between CRP levels and the patient's outcome.

The positive correlation of PCT and CRP and SOFA score has been reported in our study. Similar findings have been reported by Arif et al. Increased PCT, CRP, and WBC levels at admission and their decrease by day 6 with significant correlation with the patients' outcome make PCT, CRP, and WBC, good prognostic indicators of sepsis.

5. CONCLUSION

Current study shows significant correlation between serum PCT with blood cultures. Serum procalcitonin can be used as a diagnostic marker for sepsis in bacterial infections. Combined serum procalcitonin with hs-CRP and WBC count can strengthen the diagnosis of bacterial infections. Serial monitoring of CRP, PCT, and WBC count in patients with sepsis can help the clinician to decide whether to modify or continue the antibiotic treatment basing on the fact that decreasing levels of CRP and PCT denote indication of resolving sepsis and better patient outcome

REFERENCES

1. Shabnum M, Sreenivasulu Reddy P, Vasundhara P. Common isolates among Suspected cases of Septicemia with a special emphasis on Multidrug Resistant Strains. Int J Curr Microbiol App Sci 2018; 7(03): 711 – 721.

2. Kondle Raghu, M Shabnum. Emerging resistance in cases of septicemia with special reference to Vancomycin. Ind J Emerg Med 2018; 4(2): 125-130.

3. Anush MM, Ashok VK, Sarma RIN, Pillai SK. Role of C – Reactive Protein as an Indicator for Determining the Outcome of sepsis. Indian Journal of Critical Care Medicine, January 2019; 23(1), 11-14.
4. Nasimfar A, Sadeghi E, Karamyyar M, Manesh LJ. Comparison of serum procalcitonin level with erythrocytes sedimentation rate, C- reactive Protein, white blood cell count and blood culture in the diagnosis of bacterial infections in patients hospitalized in Motahhari hospital of Urmia (2016). J Adv Pharm Technol Res 2018; 9: 147-52.
5. Parikh Madhubala and Singh Nandon. Rapid Diagnosis of neonatal Bacteremia. Indian Journal of Microbiology 1995; 13: 37- 40.
6. Surya Kirani K.R.L and B.S.G Sailaja. Microbiological and Epidemiological Study of Neonatal Septicemia, International Journal of Scientific Research. 2015; 4(8): 118-121
7. Jaslyn M. Maurer, Janice M. Burns, Mary R. Godfrey, Carl M Urban, Sorana Segal – Maurer. Frequency of Blood cultures performed in a Community Hospital; Open Journal of Medical Microbiology, 2013; 3: 130-134
8. Joshi S. G et al., Neonatal Gram Negative Bacteremia. Indian J Pediatric 2000; 67: 27- 32.
9. Iregbu KC, Elegba OY, Babaniyi IB. Bacteriological profile of neonatal septicaemia in a tertiary hospital in Nigeria. African health sciences. 2006;6(3):151-4.
10. Qinhao Li and Xiaono Gong. Clinical Significnace of the detection of Procalcitonin and C-Reactive Protein in the Intensive Care Unit. Experimental and Therapeutic Medicine; 2018; 15: 4265- 4270
11. Zhang et al. Comparison of Procalcitonin and high sensitivity C- Reactive Protein for the diagnosis of sepsis and septic shock in the oldest old patients. BMC Geriatrics; 2017; 17: 173
12. Syafri Kamsul Arif, Maya P Suyata, Syafruddin Gaus, Muhammad Ramli Ahmad. Procalcitonin and C – Reactive Protein as a predictor of Organ Dysfunction and outcome of Sepsis and Septic shock patients in Intensive Care Unit. Global Journal of Health Science; 2017; 9 (12): 169-174.
13. B. Suberviola, A. Castellanos – Ortego, A. Gonzalez – Castro, L.A. Garcia – Asttudillo, B. Fernandez – Miret. Prognositic value of Procalcitonin, C – reactive Protein and leukocytosis in septic shock. Med Intensiva, 2012; 36 (3): 177-184.
14. Fatih Aygun. Procalcitonin Value is an early prognostic factor related to mortality in admission to pediatric intensive care unit. Critical Care Research and Practice; 2018; 1-5.
15. Yeh CF, Wu CC, Liu SH, Chen KF. Comparison of the accuracy of neutrophil CD64, procalcitonin, and C-reactive protein for sepsis identification: a systematic review and meta-analysis. Annals of intensive care. 2019;9(1):1-2.
16. Abedni M, Delpisheh A, Nikkhu B, Vahabi A, Afkhazadeh A. Procalcitonin and White Blood cell count (WBC), Erythrocyte sedimentation rate (ESR) and serum C- Reactive Protein (CRP) alterations in children with systemic inflammatory response syndrome before and after treatment. Afr J Biotechnol, 2012; 11: 0989-10993.
17. Seigel TA, Cocchi MN, Salciccioli J, et al. Inadequacy of temperature and white blood cell count in predicting Bacteremia in patients with suspected infection. J Emerg Med 2012;42:254-9.

18. Fardin Asadi, Hasan Pourmoshtagh, Saeideh Mazloomzadeh, Ali Koosha. Procalcitonin levels compared with CRP and ESR levels in septicemic children aged 3 months to 13 years in the paediatric and PICU wards of Ayatollah Mousavi Hospital, Zanjan. Arch Pediatr Infect Dis. 2016; 4 (4): 1- 5.