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Research Article

SIGNIFICANCE OF SERUM PROCALCITONIN AS A PROGNOSTIC INDICATOR IN PATIENTS WITH SIRS/SEPSIS

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A B S T R A C T

Objective: To study the significance of SerumProcalcitonin (PCT) in determining the prognosis in patients with systemic inflammatory response syndrome (SIRS)/ sepsis.
Introduction: Sepsis is defined as SIRS in the presence of an underlying infectious process, and is associated with high rates of morbidity and mortality particularly when initial therapy is delayed. PCT is currently the most studied infection biomarker and its blood levels seem to mirror the severity of illness and outcome. PCT may help in discriminating infections and can have prognostic value.
Methods: Total numbers of 200 cases of SIRS/ sepsis admitted in medical ICUs were included in the study. PCT levels were compared in moderate SIRS, severe sepsis and septic shock. PCT values andoutcome was analyzed.
Results: Out of total 200 cases, 182 had PCT value ≥0.5 ng/ml whereas 18 had PCT value of <0.5 ng/ml. As the PCT value increases mortality increases. In the PCT levels <0.5 ng/ml and ≥0.5-<2 ng/ml, mortality was 6.4% and 18.3% which was less as compared to patients who were discharged in satisfactory condition being 12.1% and 28.6% respectively.
Conclusion: PCT as a biological marker appears to have a significant value in determining the prognosis of the patient with SIRS/Sepsis

INTRODUCTION

Sepsis is a critical condition associated with death and mortality. The word, "sepsis" has a complete association with SIRS concept (systemic inflammatory response syndrome). Severe sepsis is the presence of sepsis with organ dysfunction, and septic shock is defined as sepsis with hypotension.[1] The definite diagnosis of sepsis is a positive blood culture and this test is time consuming, so other biochemical parameters have been introduced. Clinical history and routine laboratory investigation (WBC count, thrombocyte count, coagulation studies, ESR etc) aid in diagnosis of SIRS/ sepsis.[2] PCT is a biomarker which aids in diagnosis of sepsis. It is a prohormone of calcitonin synthesized by C cells of thyroid gland. It is encoded by the CALC 1 gene located on the short arm of the chromosome 11.[3,4] During microbial infections there is increased CALC-1 gene expression in various extra thyroid tissues and cells including kidneys, pancreas, liver, leucocytes, and adipose tissue with concomitant release of PCT throughout the body.[5]PCT becomes detectable within 2 to 4 hours after a triggering event and peaks by 12 to 24 hours.

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After reaching peak levels, the circulating PCT concentration declines with a 50% plasma-disappearance rate of roughly 1-1½ days. [2]
Elevated level of PCT at admission to the ICU was found to be a better predictor of mortality that helps in the stratification of patients and to identify patients at higher risk of adverse outcomes.[6]

High PCT levels have a high positive predictive value in the diagnosis of sepsis, severe sepsis, or septic shock. On the contrary, normal or very low PCT plasma concentrations have a high negative predictive value to rule out severe systemic inflammation or sepsis.[7-9]

PCT results should be correlated with clinical findings as false positive and false negative results can occur.[10] False positive results seen in newborns, massive stress like trauma, burns, cardiogenic shock, vasculitis, paraneoplastic syndromes. False negative results seen in empyema, osteomyelitis, steroid intake, early course of infection.[11] In comparison to commonly used biomarkers (CRP, lactate, IL-6, IL-8, strem-1) PCT has demonstrated superior diagnostic accuracy as it has specificity in diagnosing bacterial infections, rapidity of its rise and decline with immune control and antibiotic therapy, and excellent correlation with severity of illness.[12]

This study was planned to evaluate serum PCT as an early surrogate marker for prediction of sepsis and to determine its prognostic value.

MATERIAL AND METHODS

This was a prospective observational clinical study done in a tertiary care hospital of North India. A total number of 200 cases admitted in medical ICU's, satisfying two or more criteria's of SIRS/sepsis i.e. Temperature more than 38˚C or less than 36˚C, heart rate more than 90 beats/ minute, respiratory rate more than 20 times/ minute or PaCO2 less than 32mm Hg, WBC more than 12,000 cells/µL or less than 4,000 cells/µL (1992 ACCP/SCCM Sepsis definitions) were included. [13] Patients below the age of 18 years; with any malignancy or cardiogenic illness were excluded from the study. The demographic details, history of illness and outcome of the patients were taken into account.

Procalcitonin Assay

The PCT levels were measured using an automated system based on electrochemiluminescence (ECL) technique (Roche diagnostics Cobas e 411 analyzer).Interpretation of PCT concentrations for diagnosis of sepsis was: -0.05 - < 0.5ng/ml - no bacterial infection; ≥0.5 - < 2 ng/ml - local infection, moderate SIRS, severe trauma, surgery, cardiogenic shock ;≥ 2.0 - <10 ng/ml - severe SIRS (sepsis and organ dysfunction ; ≥ 10 ng/ml - severe bacterial sepsis/ septic shock (sepsis and hypotension).[14]

Blood and body Fluid Culture

Blood and body fluids samples were collected taking all aseptic precautions and were inoculated into blood culture bottles. The bottles were incubated in the BacT/Alert or BACTEC blood culture system till they were flagged positive or maximum for a period of 7 days. Gram's stained smears from the positive culture bottles were prepared. Simultaneously subcultures from positive bottles were done on blood agar and Mac Conkey's agar plates. The plates were incubated at 37°C for 18-24 hours. Growth was identified and antimicrobial sensitivity testing was done in VITEK 2 system. For each patient, only one bloodstream infection episode and, for each episode, only the first samples were considered. Coagulase- negative staphylococci and other skin commensals were considered contaminants when isolated from only one blood culture.

Other specimens (apart from blood and body fluids samples) were inoculated on blood agar and Mac Conkey's agar and incubated for 24-48 hours. The organisms were identified as per the standard protocols. [4]

Data Analysis

Patients with SIRS/Sepsis were included in the study. Infectious etiologies were correlated with PCT levels. Changes in PCT levels were analyzed. Fall/raise in the PCT levels was seen. Outcome of the patients and its role as a prognostic marker analyzed.

OBSERVATION AND RESULTS

This prospective study was conducted in the Department of Microbiology, DMCH, Ludhiana.

A total of 200 patients admitted in the medical ICUs (MICU, PCCU and STICU) satisfying two or more criteria's of Systemic Inflammatory Response syndrome (SIRS)/ Sepsis (Temperature more than 38˚C or less than 36˚C, heart rate more than 90 beats/ minute, respiratory rate more than 20 times/ minute or PaCO2 less than 32mm Hg, WBC more than 12,000 cells/µL or less than 4,000 cells/µL) were enrolled.
All the results are depicted in the tables and graphs that follow:

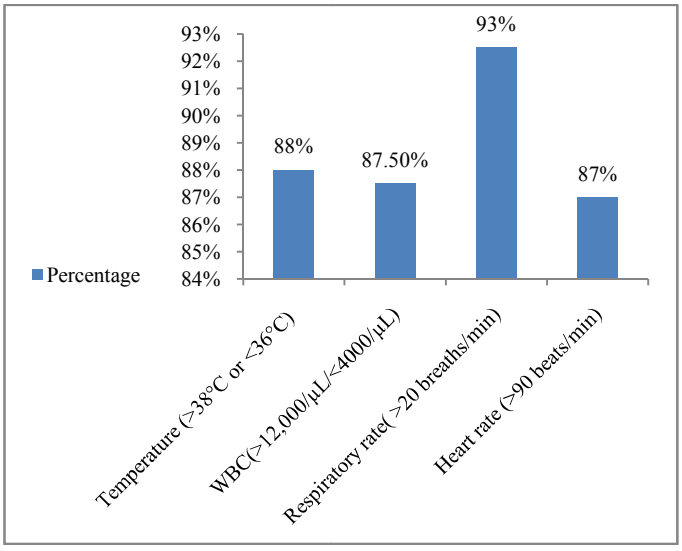

Figure 1 Distribution of SIRS criteria (n=200)

Most common SIRS criteria was tachypnea (respiratory rate >20 breaths/minute).

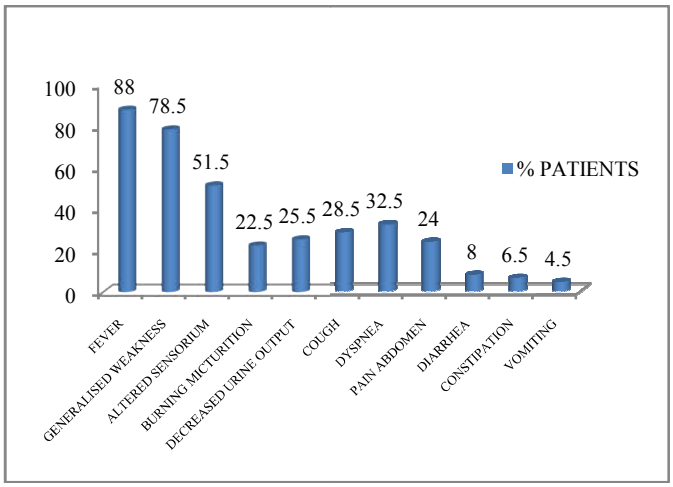

Figure 2 Clinical presentation of patients with SIRS/ Sepsis (n=200)

Fever (88%) was the most common presenting feature followed by generalized weakness (78.5%), and altered sensorium (51.5%) etc.

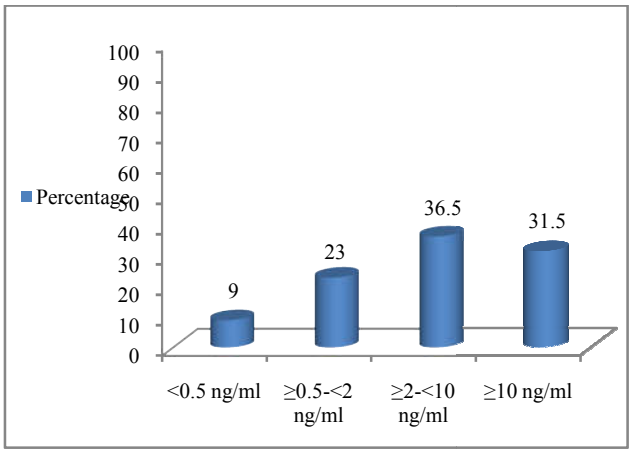

Figure 3 Distribution of SIRS/ sepsis cases (n=200) according to the PCT levels

Out of 200 cases of SIRS/ Sepsis, 182 (91%) had PCT values ≥ 0.5 ng/ml. Out of 182 patients with PCT values ≥ 0.5 ng/ml, 63 (31.5%) patients had PCT values ≥10 ng/ml indicative of septic shock; 73 (36.5%) patients had PCT values in the range of ≥2-<10 ng/ml suggestive of severe sepsis and 46 (23%) patients had PCT values between ≥0.5-<2 ng/ml indicating moderate SIRS. Only 18 (9%) of the patients had normal PCT values i.e. <0.5 ng/ml suggestive of no bacterial infection.

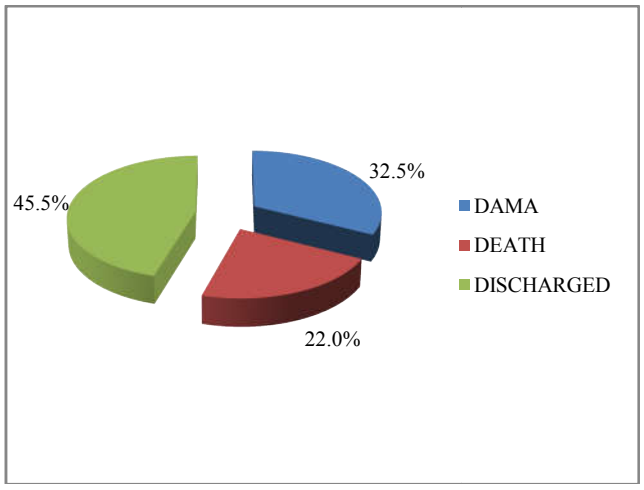

Figure 4 Outcome of patients with SIRS/ sepsis (n=200)

Out of 200 cases of SIRS/ Sepsis, 91 (45.5%) patients were discharged in satisfactory condition. Patients discharged against medical advice and patients who died were 32.5% and 22% respectively.

Out of 200 cases of SIRS/Sepsis, 91 patients were discharged in satisfactory condition and 109 patients either died or were discharged against medical advice. PCT has a role as a prognostic marker ($p < 0.05$).

Table 2 Outcome of patients with septic shock (n=63)

PCT (ng/ml)		Outcome	
		Death	Discharged
≥10 ng/ml	≥10-<25 (n=32)	22	10
	≥25-50 (n=13)	8	5
	51-<75 (n=5)	4	1
	≥75 (n=13)	9	4
Total		43	20

Maximum number of deaths were seen in the PCT range of ≥10-<25 ng/ml.

DISCUSSION

Severe sepsis with septic shock is a major cause of morbidity and mortality in the ICU. Mortality increases with the severity of sepsis. Clinically, once the diagnosis of sepsis is made, the prediction of survival is important for the risk stratification of patients and in indicating the potential success or failure of treatment. The incidence of sepsis is increasing in all areas of the world.[3,15] Biomarkers to diagnose sepsis may allow early intervention which, although primarily supportive, can reduce the risk of death. It has become the mostly widely used biomarker in the management of sepsis. The ambiguous conclusions of different studies regarding the diagnostic accuracy of PCT and CRP are mainly due to the lack of a gold standard for infection, the propagation and misuse of an insensitive assay in the wrong clinical setting (e.g. early infection or immune-compromised patients), and the negligence of the fact that, as for all hormones, different cut-off levels have to be used according to the clinical questions asked.[16] In our study, 200 patients satisfying the criteria of SIRS/sepsis (ACCP) were included and 182 (91%) patients had PCT value of ≥0.5 ng/ml. Infective foci were seen in 74.7% (136/182) of patients with PCT levels of ≥0.5ng/ml as demonstrated by positive cultures (bacterial and fungal) or serological evidence. In a study of a group of 40 patients statistically significant correlation between the presence of sepsis and a PCT levels was found. The study concluded that PCT levels above 2 ng/ml are effective markers of sepsis.[17] In the study by Sudhir *et al*, PCT proved to be an excellent indicator of sepsis with sensitivity of 94 %.[18]

Clinically once the diagnosis of sepsis is made, the prediction of survival is important for the risk stratification of the patients and in indicating the potential success or failure of treatment.

Table 1 PCT as a prognostic marker (n=200)

		Outcome				Total	Chi-square value	p-value
		DEATH		DISCHARGED				
PCT	<0.5	7	6.4%	11	12.1%	18	0.170	0.680
	≥0.5-2	20	18.3%	26	28.6%	46	1.067	0.302
	≥2-10	39	35.8%	34	37.4%	73	0.102	0.749
	≥10	43	39.4%	20	22.0%	63	0.617	0.432
Total		109	100.0%	91	100.0%	200	8.863	0.031

We evaluated the predictive value of PCT for survival of patients with PCT value ≥0.5 - <2 ng/ml (moderate SIRS), ≥2 - <10 ng/ml (severe sepsis), and ≥10 ng/ml (septic shock).The mortality was higher in 43 patients with septic shock (PCT≥10 ng/ml) as compared to moderate SIRS and severe sepsis. Severe sepsis with septic shock is a major cause of morbidity and mortality in the ICU's. Mortality increases with the severity of sepsis. Studies have reported mortality rates for severe sepsis and septic shock ranging between 18% and 50%.[19-21] The 28-day mortality was 56% in patients with severe sepsis, and 60% in those with culture-negative severe sepsis. [20]In the study by Min Yi Huang, the mortality because of severe sepsis and septic shock was 22.9 %.[22]

Serial measurement of biomarkers may be helpful because of the large variability of biomarker secretion at different times during the progression of critical illness. PCT values of 420 consecutive patients during hospitalization were observed.Of the 420 patients, 63 (15%) died in the ICU, 12 (2.86%) died 1 month after ICU discharge and 16 (3.80%) died 1 year after ICU discharge. In patients who died, PCT values were higher on last day as compared to other patients.[23]

In the present study, a mortality of 43.4% (20/46), 53.4% (39/73) and 68.2% (43/63) were observed in patients with moderate SIRS, severe sepsis and septic shock respectively.
PCT has a role as a prognostic marker. As the PCT value increases mortality increases. In the PCT levels <0.5 ng/ml and ≥0.5-<2 ng/ml, mortality was 6.4% and 18.3% which was less as compared to patients who were discharged in satisfactory condition being 12.1% and 28.6% respectively.In patients with PCT values ≥2-<10 ng/ml and ≥10 ng/ml, mortality was 35.8% and 39.4% as compared to discharged patients being 37.4% and 22 % respectively.

Biomarkers have been effective at reducing mortality; existing supportive measures alone will probably not be enough to finally bring sepsis under control. Since most of the new innovative approaches to treating sepsis target specific biomarkers, more robust ways to measure them will help support the success of these new modes of treatment. Although, measurement of biomarkers at a single time point may be of limited value because of the large variability of biomarker secretion at different times during the progression of critical illness and needs to be further evaluated.

References

1. American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med. 1992;20:864-74.
2. Meisner M. Update on Procalcitonin Measurements. Ann Lab Med. 2014;34:263-73.
3. Christ-Crain M, Müller B. Procalcitonin in bacterial infections--hype, hope, more or less? Swiss Med Wkly. 2005;135:451–60.
4. Choudhary R, Maisel AS. Procalcitonin use to identify the infected heart failure patient. In: Vincent JL, editor. Annual Update in Intensive Care and Emergency Medicine. Berlin-Heidelberg: Springer-Verlag, Berlin Heidelberg; 2013. pp. 77–83.
5. Muller B, White JC, Nylen E, Snider R, Becker K, Hebner JF. Ubiquitous expression of the calcitonin- 1 gene in multiple tissues in response to sepsis. J ClinEndocrinolMetab. 2001;86:396-04.
6. Jain S, Sinha S, Sharma SK, Samantaray JC, Aggrawal P, Vikram NK, *et al*. Procalcitonin as a prognostic marker for sepsis: a prospective observational study. BMC Res Notes. 2014;7:458.
7. Pfister R, Kochanek M, Leygeber T, Brun-Buisson C, Cuquemelle E, Paiva Machado MB, *et al*. Procalcitonin for diagnosis of bacterial pneumonia in critically illpatients during 2009 H1N1 influenza pandemic: a prospective cohort study, systematic review and individual patient data meta-analysis. Crit Care. 2014;18:R44.
8. Gendrel D, Raymond J, Assicot M, Moulin F, Iniguez JL, Lebon P, *et al*. Measurement of procalcitonin levels in children with bacterial and viral meningitis. Clin Infect Dis. 1997;24:1240-2.
9. Moulin F, Raymond J, Lorrot M, Marc E, Coste J, Iniguez JL, *et al*. Procalcitonin in children admitted to hospital with community acquired pneumonia. Arch Dis Child. 2001;84:332-6.
10. Müller B, Becker KL.Procalcitonin: how a hormone became a markerand mediator of sepsis. Swiss Med Wkly. 2001;131:595-602.
11. Azeem A,Hamdy G, SarayaM,Fawzy E, Anwar E, AbdulattifS.The role of procalcitonin as a guide for the diagnosis, prognosis, and decision for antibiotic therapy in lower respiratory tract infection.Egyptian J of chest diseases and tuberculosis. 2013;62:687-95.
12. Rune A, Ulrik J. Procalcitonin guided antibiotic treatment of respiratory tract infections in a primary care setting: are we there yet?. Prim care Respir J. 2011;20(4);360-7.
13. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, *et al*. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41:580-637.
14. Jain S, Sinha S, Sharma SK, Samantaray JC, Aggrawal P, Vikram NK, *et al*. Procalcitonin as a prognostic marker for sepsis: a prospective observational study. BMC Res Notes. 2014;7:458.
15. Nelson GE, Mave V, Gupta A. Biomarkers for sepsis: a review with special attention to India. Biomed Res Int. 2014;2014:264351.
16. Castelli GP, Pognani C, Meisner M, Stuani A, Bellomi D, Sgarbi L. Procalcitonin and C-reactive protein during systemic inflammatory response syndrome, sepsis and organ dysfunction. Crit Care. 2004;8:R234-42.
17. Sinha M, Desai S, Mantri S, Kulkarni A. Procalcitonin as an adjunctive biomarker in sepsis. Indian J Anaesth. 2011;55:266-70.
18. Sudhir U, Venkatachalaiah RK, Kumar TA, Rao MY, Kempegowda P. Significance of serum

procalcitonin in sepsis. Indian J Crit Care Med. 2011;15:1-5.
19. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000.N Engl J Med. 2003;348:1546–54.
20. Brun-Buisson C, Doyon F, Carlet J, Dellamonica P, Gouin F, Lepoutre A, *et al*. Incidence, risk factors, and outcome of severe sepsis and septic shock in adults: a multicenter prospective study in intensive care units. Journal of the American Medical Association. 1995;274:968– 74.
21. Heffner AC, Horton JM, Marchick MR, Jones AE. Etiology of illness in patients with severe sepsis admitted to the hospital from the emergency department. Clin Infect Dis. 2010;50:814–20.
22. Huang MY, Chen CY, Chien JH, Wu KH, Chang YJ, *et al*. Serum procalcitonin and procalcitonin clearance as a prognostic biomarker in patients with severe sepsis and septic shock. Biomed Res Int. 2016;2016:1758501.
23. Zampieri S, Bettonte P, Ortolani M, Frison G, Schweiger V, Gottin L, *et al*. Procalcitonin as prognostic marker of mortality. Crit Care. 2013;17:29.

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