International Journal of Advances in Medicine
Konyak N et al. Int J Adv Med. 2021 Oct;8(10):1494-1498
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20213704

Original Research Article

Serum procalcitonin as a biomarker of sepsis

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Received: 14 July 2021
Revised: 28 August 2021
Accepted: 29 August 2021

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ABSTRACT

Background: The overlap of clinical presentation between sepsis and SIRS has presented diagnostic difficulty in these two close common scenarios. Blood culture remains the gold standard for detection of specific micro-organism, the non-availability of culture report early and difficulty in culture of many organisms is a challenge in differentiation of sepsis from its mimickers. Keeping this background, a simple tool is needed to guide sepsis management while awaiting the culture report. Therefore, the present study is conducted to determine the procalcitonin level in the setting suspicious of sepsis and to differentiate it from SIRS. The objective of the study was to determine Serum procalcitonin level as a biomarker of early diagnosis of sepsis and also to differentiate sepsis from severe inflammatory response syndrome.
Methods: Cross sectional study on 79 patients aged above 18 years with suspected sepsis admitted in medicine ward. Serum procalcitonin levels were measured and analysed to look for any association with sepsis.
Results: Culture was positive in 41 patients and 38 patients were procalcitonin positive. The sensitivity, specificity, positive predictive value and negative predictive values of serum procalcitonin were found as 96.68%, 94.74%, 95% and 92.30% respectively.
Conclusions: There was a significant association between serum procalcitonin and culture positivity. Procalcitonin levels was found to have high sensitivity and high positive predictive value which may aid in the early diagnosis and guide initiation of anti-microbial therapy in sepsis.

Keywords: Procalcitonin, Sepsis, SIRS, Positive culture

INTRODUCTION

Sepsis is a common clinical condition seen in critically ill patients. No definite test distinguishes it from systemic inflammatory response syndrome (SIRS). Many consider microbiologically confirmed culture as gold standard for this. Sepsis-related inflammatory response arises when the body attempts to neutralize infection which leads to the activation of immune cells to secrete inflammatory protein which in turn damage tissues and organs of the host.[1] Severe sepsis is accompanied with hypoperfusion or dysfunction of at least one organ. In a number of patients sepsis is diagnosed on taking medical history and completing physical examination, but when non-infectious insults are responsible for SIRS or in comatose patients, sepsis diagnosis remains difficult.[2]

Prompt diagnosis and treatment with appropriate antimicrobial therapy is needed in reducing morbidity and mortality associated with sepsis. The lack of specific early marker of infection may be responsible for withholding or delaying or unnecessary administration of antimicrobial treatment in critically ill patients.[3] There is an unmet need for clinical or laboratory tools for this distinction though various markers of sepsis including Procalcitonin, C-reactive protein (CRP), tumor necrosis factor (TNF)-α,

IL-1β, IL-6 and IL-8, have all been studied to differentiate SIRS from sepsis.[4]

This study was undertaken to determine the serum procalcitonin level as a biomarker of early diagnosis of sepsis and also to differentiate sepsis from severe inflammatory response syndrome.

METHODS

A cross sectional study done in the department of Medicine, Regional Institute of Medical Sciences, Imphal in collaboration with Department of Biochemistry over a period of 2 years from September 2018 to August 2020.

Study design

The study was hospital based cross sectional study.

Study duration

The study was conducted from September 2018 to August 2020.

Inclusion criteria

Age more than 18 years of both genders. Those with features suggestive of sepsis with culture positivity.

Exclusion criteria

Those with history of malignancy, trauma or recent surgery. Those not willing to take part in the study.

Sample size

Sample size was calculated by using the formula n=-$4PQ/L^2$ with a calculated sample size of 79 cases as per the inclusion and exclusion criteria.

Methodology

The study subjects were 79 patients of both sex admitted with features of sepsis in Medicine wards. They were assessed by a detailed history, clinical examination and were subjected to investigations of Serum procalcitonin, complete haemogram, liver function test, kidney function test, blood sugar, urine RE, CRP, culture of blood, sputum and urine along with Chest X-ray.

Statistical analysis

Statistical analysis was done using Statistical package for social sciences (SPSS) Version 21. Results were reported as number of cases along with percentages for the categorical variables, Chi-square test was performed for determination of correlation and to find the significance of the study. A $p<0.05$ was considered as statistically significant.

RESULTS

The study had 79 clinically suspected sepsis patients aged 18 to 70 years. The age distribution showed majority in 40-60 years bracket, which constituted for 39.2% followed by <40 years with 26 (33%) and 22 (27.8%) in >60 years of age.

Table 1: Age distribution among the 79 patients.

Age in years	No. of patients n (%)
<40	26 (33)
40-60	31 (39.2)
>60	22 (27.8)

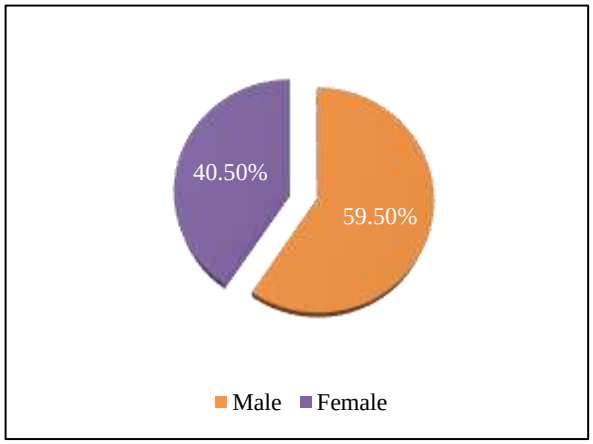

Figure 1: Gender distribution among the 79 patients.

Among the 79 patients gender distribution was 47 (59.50%) males while female constituted 32 (40.50%) of the study population.

The vitals recorded in the study showed 32 (40.5%) patients had hypotension, 68.4% of patients had tachycardia as defined by SIRS criteria.

Among the 79 patients' temperature distribution showed 44 had temperature more than 38˚C and 35 patients had temperature within 36˚C to 38˚ C.

Amongst the various infectious causes, the most common was urinary tract infection followed by respiratory tract infection. 41 patients were culture positive while 38 remained culture negatives. Urine culture was positive for 20 (48.78%) of the study population while Sputum culture was positive for microorganism in 8 (19.51%) and blood culture was positive in only 4 (9.75%) of the total 41 culture positive patient.

The association of culture positivity and the need of life supportive measures shows significant p value, as 23 (56.1%) required oxygen and 31 (75.6%) inotropic support in those culture positive while only 5 and 3 patients required oxygen and inotropes among the culture negative.

Table 2: Blood pressure and pulse rate distribution among the 79 patients.

Vitals	No. of patients, N (%)
SBP (mm Hg)	
<90	32 (40.5)
90-100	20 (25.3)
100-120	17 (21.5)
>120	10 (12.7)
DBP (mm Hg)	
<60	31 (39.2)
60-80	45 (57.0)
>80	3 (3.8)
Pulse per min	
<90	25 (31.6)
>90	54 (68.4)

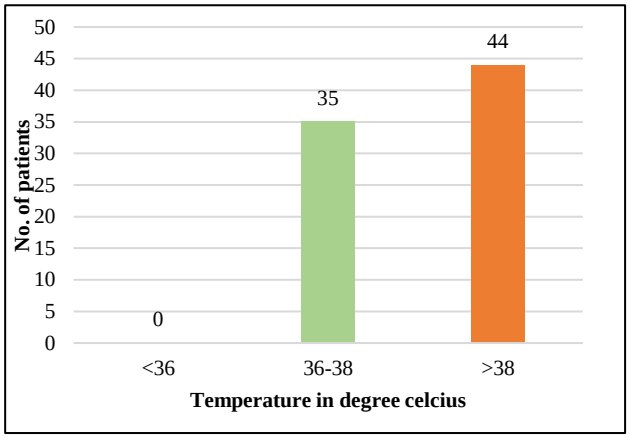

Figure 2: Temperature distribution in degrees among the 79 patients.

Table 3: Microbial culture in specimen collected from 79 patients.

Culture positive	No. of patients n=41
Urine	20
Sputum	8
Blood	4
Blood and urine	3
Blood and sputum	6

The p values were significant for the levels of procalcitonin, total leucocyte count, and the levels of creatinine.

Table 6 shows the association between culture positivity and clinical parameters. It shows significant p value findings in Systolic and diastolic blood pressures, respiratory rate and temperature.

Table 7 shows that neither the positivity nor the values of CRP were found significant with p values more than 0.05.

Table 4: Association between culture positivity and need of life supportive measures.

Oxygen Support	Presence of culture growth		P value
	Positive, n=41	**Negative, n=38**	
Yes	23 (56.1%)	5 (13.2%)	0.001
No	18 (43.9%)	33 (86.8%)	
Inotrope support			
Yes	31 (75.6%)	3 (7.9%)	0.001
No	10 (24.4%)	35 (92.1%)	

Table 5: Association between culture positivity and laboratory parameters (n=79).

Laboratory parameters	Presence of culture growth		P value
	Positive, n=41	**Negative, n =38**	
Procalcitonin (ng/ml)			
<0.5	3 (7.32%)	36 (94.73%)	0.001
0.5-2	9 (21.95%)	2 (5.26%)	
>2	29 (70.73%)	0 (0%)	
Urea (mg/dl)	90.46±81.46	42.29±37.07	0.001
Creatinine (mg/dl)	2.15±1.39	1.12±0.79	0.001
Total leukocyte count/mm^3	20095.93±5650.61	14002.08±3702.03	0.001

Table 6: Association between culture positivity and clinical parameters.

	Presence of culture growth		P value
	Positive n=41	**Negative n=38**	
Age in years	45.51±18.31	52.18±15.57	0.086
SBP (mm Hg)	79.51±15.49	113.63±18.15	0.001
DBP (mm Hg)	51.41±13.15	72.11±10.94	0.001
Pulse per min	111.78±16.17	92.11±16.29	0.001
Respiratory rate per minute			
<20	22 (53.7%)	36 (94.7%)	0.001
>20	18 (43.9%)	2 (5.3%)	
Temperature	38.87±0.93	37.92±0.98	0.001

Table 7: Association between culture positivity and CRP values in sepsis (n=79).

CRP test	Presence of culture growth		P value
	Positive, n=41	Negative, n =38	
CRP card test			
Positive	31 (75.6%)	26 (68.4%)	0.476
Negative	10 (24.4%)	12 (31.6%)	
Quantification of CRP in mg/l			
<30	24 (75%)	20 (76.9%)	0.865
>30	8 (25%)	6 (23.1%)	

Table 8: Diagnostic value of procalcitonin in sepsis (n=79).

Procalcitonin level in ng/ml	Presence of culture growth		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	Positive, n=41	Negative, n=38				
≥0.5	38	2	92.68	94.74	95	92.30
<0.5	3	36				

PPV=Positive predictive value, NPV=Negative predictive value.

Table 8 shows the diagnostic values of procalcitonin taking 0.5 as cut-off. 38 patients were found to be procalcitonin positive.

DISCUSSION

Sepsis and systemic inflammatory response syndrome (SIRS) are two common clinical scenarios in critically ill patients. Sepsis is the body's systemic response to proven or suspected infection plus some degree of organ hypo function while non-infectious insults are responsible for SIRS.

The study showed that affected age is less in those below 40 years, similar to Khan et al study. Fever was the most common presenting symptom in 37(46.83%) patients similar to a study by Lai et al followed by burning micturition in 24 (30.37%).[5,6]

In all 79 patients TLC was raised (>12000 cells/mm3) with accompanying neutrophilia. Culture positive group had a mean total leucocyte count of 20095.93±5650.61/mm3 while the mean in negative was 14002.08±3702.03/mm3 indicating a correlation between infection and WBC counts. Sepsis-induced acute kidney injury is characterized by healthy or reversible injured renal tubular epithelial cells. Serum creatinine was 2.15±1.39 mg/ml and 1.12±0.79 mg/ml in the culture positive and culture negative groups respectively, comparable to the findings of Lopes et al.[7]

Liver function derangement comprised of hyperbilirubinemia, mild to moderate increase in alkaline phosphatase and SGOT with SGPT elevation seen only in more severely ill patients and those with a prolonged shock episode. This pattern is similar to findings by Banks et al.[8]

During sepsis not only the infection itself is responsible for liver dysfunction, but also hyperreactivity of the inflammatory response, microcirculatory failure, and side effects of the therapy as stated by Woźnica et al.[9]

Culture positivity from urine, blood and sputum was seen in only 41 patients. The most frequently isolated bacteria from blood cultures were coagulase-negative staphylococci which accounted for 38.0% of the total isolates similar to the study by Karlowsky et al.[10] Urine culture had Escherichia coli strains as the most common isolate found in 68% of urine samples among the urinary tract infected patients, concurrent with the finding of Vranic et al.[11] Sputum culture grew Streptococcus pneumoniae as the most common bacteria in a similar finding to Cukic et al.[12]

The procalcitonin level in culture positive was elevated as compared to their negative counterparts. Only 3 culture positive patients and 38 culture negative patients had procalcitonin levels <0.5 ng/ml, just 2 culture negative and 9 culture positive patients had procalcitonin level in 0.5-2 ng/ml range, while 29 (70.73%) out of 41 culture positive had procalcitonin level more than 2 ng/ml. The p-value was found to be significant (<0.001). The total leucocyte count and serum creatinine were also elevated in the culture positive group. This findings were also significant with p<0.001 in both.

Considering the culture positive group as sepsis group and the negative ones as SIRS, levels of serum procalcitonin were significantly higher in the sepsis group. The finding is in concurrence with the study done by Ahmadinejad et al.[13] In our study CRP considered as one of the early markers of sepsis showed no positive co-relation between the culture positivity with either the CRP positivity or its levels. Procalcitonin is thus a better predictor of sepsis than

CRP. This finding is also supported by Patil et al in a comparative study of procalcitonin and CRP in sepsis patients.[14]

Limitation of the study

The limitation of the study can be attributed to the small sample size because of which the study result may not be generalized as a whole.

CONCLUSION

There was a significant association between serum procalcitonin and culture positivity. It has high sensitivity and high positive predictive value which may aid in early diagnosis and guide early initiation of anti-microbial therapy. Procalcitonin test should be established in a tertiary hospital to distinguish SIRS from SEPSIS in order to make decisions on initiation of antibiotics.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Rimmelé T, Leli C, Payen D, Cantaluppi V, Marshall J, Gomez H, et al. Immune cell phenotype and function in sepsis. Shock. 2016;45(3):282-91.
2. Bates DW, Cook EF, Goldman L, Lee TH. Predicting bacteremia in hospitalized patients: a prospectively validated model. Ann Intern Med. 1990;113:495-500.
3. Muller B, Becker KL, Schachinger H, Rickenbacher PR, Huber PR, Zimmerli W, et al. Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit. Crit Care Med. 2000;28:977-83.
4. Oberhoffer M, Rubwurm S, Bredle D, Chatzinicolau K, Reinhart K. Discriminative power of inflammatory markers for prediction of tumor necrosis factor-alpha and interleukin-6 in patients with systemic inflammatory response syndrome (SIRS) or sepsis at arbitrary time points. Intensive Care Med. 2000;26:170-4.
5. Khan AA, Singh R, Singh PK. Diagnostic and prognostic significance of procalcitonin in septicemia. Int J Adv Med. 2017;4(3):630-4.
6. Lai C, Chen S, Wang C. Diagnostic Value of Procalcitonin for Bacterial Infection in Elderly Patients in the Emergency Department. J Am Geriatric Society. 2010;58:518-22.
7. Lopes JA, Jorge S, Resina C, Santos C, Pereira A, Neves J et al. Acute kidney injury in patients with sepsis. A contemporary analysis: Int J Infect Dis. 2009;13(2):176-81.
8. Banks JG, Foulis AK, Ledingham IA, Macsween RN. Liver function in septic shock. J Clin Pathol. 1982;35:1249-52.
9. Woźnica E A, Inglot M, Woźnica KR. Liver dysfunction in sepsis: Adv Clin Exp Med. 2018;27(4):547-51.
10. Karlowsky JA, Jones ME, Draghi DC. Thornsberry C,Sahm DF,Volturo GA .Prevalence and antimicrobial susceptibilities of bacteria isolate from blood cultures .Ann Clin Microbiol Antimicrob. 2004;3:7.
11. Vranic SM, Zatric N, Rebic V, Aljicevic M. The most frequent isolates from outpatients with urinary tract infection. Mater Sociomed. 2017;29(1):17-20.
12. Cukic V, Hadzic A. The most common detected bacteria in sputum of patients with community acquired pneumonia (CAP) treated in hospital. Med Arch. 2016;70(5):354-8.
13. Ahmadinejad Z, Dadsetan B, Jalili M, Soudbakhsh A, Rasolinejad M. Evaluation of Serum Procalcitonin in Patients with Systemic Inflammatory Response Syndrome with and without Infection. Acta Medica Iranica. 2009;47(5):383-5.
14. Patil HV, Patil VC. Comparative study of procalcitonin and C Reactive Protein in patients with sepsis. J Nat ScBiol Med. 2020;11(1):93-9.

Cite this article as: Konyak N, Marangmei L, Kuotsu MM, Singh LC, Devi LS, Devi SB. Serum procalcitonin as a biomarker of sepsis. Int J Adv Med 2021;8:1494-8.