Original Research Article

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Diagnostic utility of serum procalcitonin as a biomarker of sepsis and infection in post-operative patients at tertiary care centre

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ABSTRACT

Background: Procalcitonin (PCT), the precursor peptide of calcitonin, a hormone involved in calcium homeostasis, is present in normal subjects in extremely low serum levels (0.1 to 0.5 ng/ml). In response to bacterial infectious stimulation serum procalcitonin rises substantially and its role in inflammatory response includes chemotactic function modulation of inducible nitric oxide synthase and induction of cytokines, among other. The objective of this study to assess serum procalcitonin as a biomarker of sepsis and infection in post op patients.

Methods: The present descriptive observational study was conducted at Department of Surgery, Aarupadai Veedu Medical College and Hospital, Puducherry from September 2018 to June 2020. Total 48 patients who had undergone surgery and presented with post-surgical sepsis were included. Data entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA.

Results: Out of 48 cases, majority of cases i.e. 18 (37.5%) were from 36-50 years age group followed by 11 (22.9%) from 51-60 years age group. Prevalence of sepsis was 20.8%, septic shock 25%, severe sepsis 33.3% and SIRS 14.6%. Procalcitonin (PCT) assay shows positive in 47 (97.9%) cases. *E. coli* were isolated from 5 (45.5%) cases with PCT 2-10 as compared to 6 (16.7%) cases with PCT >10.

Conclusions: PCT shares remarkable promise as a marker of sepsis and can be used as a routine lab parameter. It was also found to be an accurate diagnostic parameter for differentiating various stages of sepsis and predicting the outcome.

Keywords: Procalcitonin, Post-operative sepsis, E. coli

INTRODUCTION

Worldwide, sepsis and its sequelae are still most common cause of acute illness and death in patients with community acquired and nosocomial infections.^{1,2} The American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference defined sepsis as systemic inflammatory response caused by infection.³ However, there is no gold standard exists for proof of infection. Bacteraemia is identified in about 30% of patients with sepsis, depending on previous antibiotic

treatment.^{4,5} Furthermore, early clinical signs of sepsis like fever, tachycardia, and leucocytosis, are non-specific and overlap with signs of systemic inflammatory response syndromes of non-infectious origin, especially in patients who have undergone surgery.⁵

Procalcitonin (PCT), the precursor peptide of calcitonin, a hormone involved in calcium homeostasis, is present in normal subjects in extremely low serum levels (0.1 to 0.5 ng/ml). In response to bacterial infectious stimulation serum procalcitonin rises substantially and its role in

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inflammatory response includes chemotactic function modulation of inducible nitric oxide synthase and induction of cytokines, among other.⁶⁻¹¹

The identification of a prognostic marker that may predict the outcome at the end of 24 to 48 hours of treatment of severe sepsis and septic shock could be very useful in order to provide a reassessment of the patient, identifying perpetuators of gravity, permitting interventions and conduct reorientation. The addition of this marker for the routine evaluation of patients with severe sepsis and septic shock treated according to the surviving sepsis campaign strategies might bring additional contribution towards reducing morbidity and mortality.¹²

So, the present study was carried out with the objective to assess the role of procalcitonin as a marker for sepsis and infection in post-operative patients.

METHODS

The present descriptive observational study was conducted at Department of Surgery, Aarupadai Veedu Medical College and Hospital assess with the objective to assess the role of serum procalcitonin as a biomarker of sepsis and infection in post-operative patients.

Patients who had undergone surgery and presented with post-surgical sepsis in surgery ward and surgical ICU of AVMC and H were included in the study. The calculated sample size for the study was 48. Duration of the study was 2 years during the period from September 2018 to 2020.

Inclusion criteria

Inclusion criteria were patients of both sexes and all age groups who had undergone surgery and presented with post-surgical sepsis in surgery ward and surgical ICU of AVMC and H. Those willing to participate in study after written consent.

Exclusion criteria

Exclusion criteria were patients receiving therapy with steroids, high biotin doses (i.e. >5 mg/day). Neonates <48 h of life (physiological elevation). Those who are not willing to participate in study.

Post op patients of AVMCH fulfilling the inclusion/exclusion criteria will be recruited for the study after obtaining written informed consent. Demographic data, history, clinical examinations and details of basic investigations will be recorded in a pre-structured proforma. Serum procalcitonin will be measured by immunochromatographic assay using a commercially available test kit and interpreted as per manufacturers recommendations.

The BRAHMS PCT-Q is an immuno-chromatographic test for the semi-quantitative detection of PCT

(procalcitonin), which is used for diagnosing and controlling the treatment of severe, bacterial infection and sepsis.¹³

Statistical analysis

Data was collected by using a structure proforma. Data entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of proportions. Quantitative data was expressed in terms of mean and standard deviation. Association between two qualitative variables was seen by using Chi square/Fischer's exact test. Descriptive statistics of each variable was presented in terms of mean, standard deviation, standard error of mean. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

RESULTS

We included total 48 cases in our study. Out of 48 cases, majority of cases i.e. 18 (37.5%) were from 36-50 years age group followed by 11 (22.9%) from 51-60 years age group. Least patients were seen from above 65 years age i.e. 3 (6.3%). Mean age of the study population was 41.73±15.26 (Table1).

Table 1: Distribution according to age and gender.

Variables		Frequency	Percent
Age (in years)	< 20	7	14.6
	21-35	9	18.8
	36-50	18	37.5
	51-65	11	22.9
	>65	3	6.3
Gender	Male	31	64.6
	Female	17	35.4
	Total	48	100

Table 2: AACP guideline results.

Variable		Frequency	Percent		
	Sepsis	13	20.8		
Result obtained as	Septic shock	12	25.0		
per AACP guidelines/d	Severe sepsis	17	33.3		
efinition	SIRS	6	14.6		
	Total	48	100.0		

Table 3: Results obtained as per PCT assay.

Variable		Frequency	Percent
Sepsis result	Present	47	97.9
obtained as	Absent	1	2.1
per procalcitonin assay	Total	48	100.0

We found sepsis cases as 20.8%, septic shock 25%, severe sepsis 33.3% and SIRS 14.6% (Table 2). Sepsis result obtained as per procalcitonin assay shows positive in 47 i.e. 97.9% cases (Table 3). Serum PCT was above 10 in 36 i.e. 75% of cases and between 2 to 10 in 11 (22.9%) cases (Table 4).

E. coli were isolated from 5 (45.5%) cases with PCT 2-10 as compared to 6 (16.7%) cases with PCT >10. *Pseudomonas spp.* were isolated from 2 (18.2%) cases with PCT 2-10 as compared to 7 (19.4%) cases with PCT >10. *Staph aureus* was isolated from 2 (18.2%) cases each with as compared to 4 (11.1%) cases with PCT >10.

The difference in the proportion was found to be not significant (>0.05) (Table 5).

Table 4: Distribution according to serum PCT.

Variable		Frequency	Percent
	< 0.5	1	2.1
Serum	0.5-2	0	0.0
PCT value	2-10	11	22.9
(ng/ml)	>10	36	75.0
	Total	48	100.0

Table 5: Serum PCT and type of organism detected in blood culture.

Ouganiam	<0.5 ng/ml		0.5 to 2 ng/ml		2 to 10 ng/ml		>10 ng/ml		Total
Organism	N	%	N	%	N	%	N	%	Total
E. coli	0	0.0	0	0.0	5	45.5	6	16.7	11
Enterobacter	1	100.0	0	0.0	0	0.0	0	0.0	1
Neisseria spp.	0	0.0	0	0.0	1	9.1	0	0.0	1
Proteus spp.	0	0.0	0	0.0	0	0.0	1	2.8	1
Pseudomonas spp.	0	0.0	0	0.0	2	18.2	7	19.4	9
Enterococcus	0	0.0	0	0.0	0	0.0	1	2.8	1
S. aureus	1	100.0	0	0.0	2	18.2	4	11.1	7
Streptococcus spp.	0	0.0	0	0.0	1	9.1	2	5.6	3

Fischer's exact test - 39.19, p 0.0001 (<0.001), highly significant.

DISCUSSION

Age and gender

We included total 48 cases in our study. Out of 48 cases, majority of cases i.e. 18 (37.5%) were from 36-50 years age group followed by 11 (22.9%) from 51-60 years age group. Least patients were seen from above 65 years age i.e. 3 (6.3%). Mean age of subjects was 41.73±15.26 years. Majority of them were males i.e. 31 (64.6%) and remaining 17 (35.4%) were females (Table 1).

Sinha et al in 2011 included 40 patients from the intensive care unit with suspected sepsis. ¹⁴ Sepsis was confirmed clinically and/or by positive blood culture. Study included 40 ICU patients with suspected sepsis. Patient ages ranged from 18 to 84 years male female ratio 28:12.

There was a slightly higher incidence in males affected with sepsis in our study which is similar to other studies. Based on the study by Martin et al from the United States, 48.1% of men had sepsis. A multi central trial from 12 medical centers in India by Todi et al reported that sepsis was common in males. Our findings are almost comparable with the findings of above-mentioned authors.

Sepsis based on AACP criteria¹⁷

We found sepsis cases as 20.8%, septic shock 25%, severe sepsis 33.3% and SIRS 14.6% (Table 2).

Velayuthannair et al in 2017 conducted prospective observational study. ¹⁸ Out of total 100 patients, 56, 20 and 24 patients were grouped based on the diagnosis of sepsis, severe sepsis and septic shock respectively.

Serum PCT assay and its utility as biomarker in sepsis

In our study, serum PCT was above 10 in 36 i.e. 75% of cases and between 2 to 10 in 11 (22.9%) cases (Table 3). Results obtained as per AACP guidelines/definition revealed that severe sepsis was seen in majority of the patients i.e. 17 (35.4%), sepsis in 13 (27.1%), septic shock in 17 i.e. 35.4% and SIRS in 6 i.e. 12.5% cases.

Sinha et al found in his study that PCT above 10 ng/ml was seen in 12 patients; 2-10 ng/ml, in 7 patients; 0.5-2 ng/ml, in 3 patients; and <0.5 ng/ml, in 18 patients. Among the 12 patients with PCT >10 ng/ml, 1 patient in shock did not have any signs of sepsis or infection and recovered with inotropic support only (no antibiotics were required; cardiogenic shock).

Vaziri et al reported that the procalcitonin value in 59 patients was less than 0.5 ng/ml and hence considered negative. ¹⁹ In the remaining 41 patients, 27 had a serum PCT value between 0.5-2 ng/ml, 9 between 2-10 ng/ml and 5 more than 10 ng/ml. Among nine patients with peritonitis, five patients had a PCT value more than 10 ng/ml and this value was between 2-10 ng/ml in four patients. In six cases of surgical site infection, one patient had a PCT value more than 10 ng/ml, four between 2-10

ng/ml and one patient had a negative PCT value. Our findings are consistent with the above-mentioned authors.

Many studies have demonstrated that serum PCT levels are increased in patients with sepsis, and the high levels of PCT correlate with the outcome of the disease. PCT can be used for differential diagnosis, prognosis, and follow-up of critically sick patients. ²⁰ Serum PCT levels have been noted to increase with increasing severity of sepsis. In addition, a rising PCT level might be used as an indicator that an infectious process is not under control and that better source control is required. ²¹

Blood culture and organisms detected

Blood culture was found positive in 34 cases i.e. 70.8%. Blood culture showed *E. coli* as predominant organism in 11 (22.9%) cases followed by *Pseudomonas spp.* in 9 i.e. 18.8% cases. *S. aureus* found in 7 cases i.e. 14.6% (Table 5). Sensitivity of our study using PCT was 97.43%.

Sinha et al found in his study that of the 11 patients with clinically diagnosed sepsis, 8 yielded positive blood cultures subsequently (2 patients with septic shock had *Staphylococcus aureus* bacteraemia). ¹⁴ All 7 patients with PCT of 2-10 ng/ml had some form of sepsis (sepsis, 4 patients; severe sepsis, 2; and septic shock, 1 patient). Four of them yielded positive blood cultures; 1 patient had parasitaemia; and 2 malignancy patients with febrile neutropenia who were on empiric antimicrobial therapy had negative blood cultures.

CONCLUSION

PCT shares remarkable promise as a marker of sepsis and can be used as a routine lab parameter. It was also found to be an accurate diagnostic parameter for differentiating various stages of sepsis and predicting the outcome.

Biomarkers may play an important role in the management of patients with sepsis in emergency rooms. PCT is considered a relatively innovative and highly specific biomarker for the diagnosis of clinically relevant bacterial infections and sepsis; therefore, it is increasingly recognized as an important diagnostic tool in clinical practice of emergency room.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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