ORIGINAL RESEARCH PAPER

General Surgery

PROCALCITONIN AS A DIAGNOSTIC MARKER FOR SEPSIS AND ANTIBIOTIC THERAPY IN SURGICAL CARE PATIENTS

KEY WORDS:

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ABSTRACT

Background: Sepsis is becoming a frequent complication in hospitalized patients. Early and differential diagnosis of sepsis is needed critically. Procalcitonin is useful for the diagnosis of sepsis but its prognostic value regarding mortality is unclear. **Aim:** To study about the utility of procalcitonin as a diagnostic biomarker for bacterial infections and its efficient use as a marker for antibiotic therapy. **Materials and methods:**This prospective observational study was conducted among patients admitted with Septicemia in a tertiary care hospital from January 2019 to May 2020. In Sixty consecutive patients of sepsis, Procalcitonin (PCT), C-reactive protein (CRP) measurements were recorded in addition to their demographic, laboratory values and treatment outcomes. **Results:**Mortality rates were 6.5%, 28.6% and 62.5% respectively in the three groups of sepsis, severe sepsis, and septic shock, respectively. It was inferred that more the severity of sepsis, more is the positivity rate of serum procalcitonin levels. Similarly, the serum PCT values were higher among non-survivors [13.1ng/dl]. Procalcitonin value was a better predictor of all-cause short-term mortality than C-reactive protein as denoted by ROC analysis. **Conclusions:** PCT done once at the time of admission was proven to be very good, cost effective biomarker for the early identification of sepsis better than CRP levels and cultures.

INTRODUCTION:

Septic response is a leading contributary factor for morbidity and mortality especially in surgical patients despite the ongoing advances in the management of sepsis. [1]. Accurate identification of sepsis etiology in patients is often unattainable, largely because their infections can have minimal or even no symptoms or signs [2]. The established biological markers of inflammation (leukocytes, C-reactive protein) may often be influenced by parameters other than infection and may only be slowly released during progression of an infection [3]. Positive bacteriological results may be caused by contamination and negative results do not exclude sepsis. Since these common clinical and lab measurements lack sensitivity and specificity, other tests are needed to give an early marker of the infectious cause [4].

One such marker of sepsis is serum Procalcitonin (PCT), which is abnormally elevated in sepsis and can provide valuable and early information before culture results were available. It has also been evaluated to shorten the course of antibiotic therapy in septic patients [5]. However, the correlation between the level of PCT and the prognosis of sepsis is still unclear.

Hence, the present study was done to ascertain the possible diagnostic role of procalcitonin as a marker in septicemia. In addition, the serum PCT was compared with C-Reactive Protein (CRP) levels to identify the more sensitive and specific indicator.

METHODOLOGY

This prospective observational study design was done from January 2019 to May 2020 among patients admitted with probable diagnosis of septicemia in the Department of General Surgery of a tertiary care teaching hospital located in Kancheepuram district of Tamilnadu. A minimum sample of 60 was required, considering 10% prevalence of septicemia among surgical care patients, 5% absolute precision and 95% confidence.

Recorded data included demographic characteristics (age and sex), laboratory findings, microbiological culture results, length of stay and outcome of patients. Infection was diagnosed by standard clinical, laboratorial and microbiological parameters. All patients were treated according to the standard institutional protocol for management of sepsis and septic shock. A written informed consent from patients or surrogates and Institute Ethics Committee approval were obtained. PCT and high sensitivity CRP were measured in serum samples using enzyme linked immunosorbent assay (ELISA). Data was analyzed using SPSS v16. The statistical analysis was done using analysis of variance, Kruskal-Wallis, student t tests and ROC analysis, wherever appropriate. A $p < 0.05$ was considered statistically significant.

RESULTS:

A total of 60 patients were enrolled. Most of the patients were in the age group of 16-30 years (28.3%) and males (55%). Nearly one-third of the patients (31.7%) had diabetes and 16.7% of the patients had hypertension. (Table 1) The top three sources for sepsis were respiratory infections (31.7%), urinary tract infections (21.7%) and cellulitis (21.7%). (Table 2)

Table 1: Socio-demographic and morbidity characteristics of the sepsis patients

	Number	Percentage
Age		
16-30 years	17	28.3
31-45 years	15	25.0
46-60 years	16	26.7
>60 years	12	20.0
Gender		
Male	33	55
Female	27	45
Comorbidities		
Hypertension	10	16.7
Diabetes	19	31.7
Bronchial asthma	4	6.7
Heart Disease	3	5
Stroke	5	8.3

Table 2: Source of sepsis among the patients

Focus of sepsis	Number	Percentage
Respiratory	19	31.7
Urinary tract infection	13	21.7
Gastrointestinal tract	5	8.2
Cellulitis	13	21.7
Neuro-infection	2	3.3
Puerperal	4	6.7

Table 3: The type of sepsis and outcome among the patients

Sepsis type	Death	Survived	Total	p value*
Sepsis	2 (6.5)	29 (93.5)	31 (51.7)	0.001
Severe Sepsis	6 (28.6)	15 (71.4)	21 (35)	
Septic shock	5 (62.5)	3 (37.5)	8 (13.3)	
Total	13 (21.7)	47 (78.3)	60 (100)	

p value by chi-square test

More than half of the patients (52%) had sepsis, 35% had severe sepsis while 13% of the patients were in septic shock. Among the patients, 21.7% died and 78.3% survived. There were significantly higher deaths among patients with septic shock (62.5%) when compared to those with severe sepsis (28.6%) and sepsis (6.5%). (Table 3) Acinetobacter spp. was the most common microorganism isolated from tracheal aspirates (50%). Klebsiella spp. (41.7%), Acinetobacter spp (25%). and Escherchia coli (25%) were the most common microorganisms isolated from blood culture. (Figure 1)

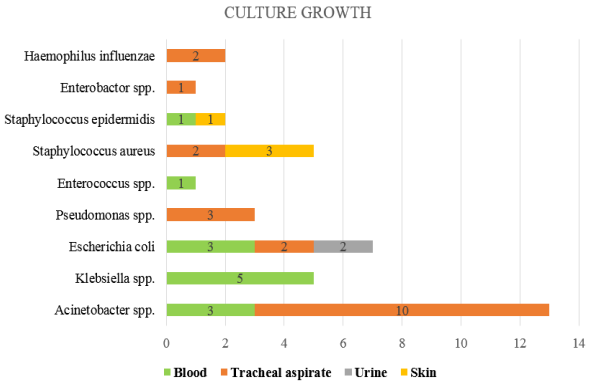

Figure 1: Graphical representation of the microbiological characteristics of the patients

Table 4: Comparison of procalcitonin and CRP levels among the sepsis types

		Sepsis	Severe sepsis	Septic Shock	P value
Procalcitonin, n(%)	**Positive (≥ 0.5 ng/ml)**	16 (51.6)	17 (81)	8 (100)	0.009*
	Negative (<0.5ng/ml)	15 (48.4)	4 (19)	0	
Procalcitonin, Median (IQR)		0.5 (0.3-1.8)	7.2 (1.7-13.9)	10.6 (4.7-20.8)	< 0.001#
CRP, mean (±SD)		17.6 (±7.3)	20.1 (±7.4)	21 (±7.4)	0.76^

p value by chi-square test; #p value by kruskal-wallis test; ^p value by one-way ANOVA

Higher number of procalcitonin positive values were significantly found in patients with severe sepsis (81%) and septic shock (100%). Similarly, the PCT values were significantly higher in patients with septic shock and severe sepsis. However, there was no significant difference in the CRP values among the sepsis types. (Table 4)

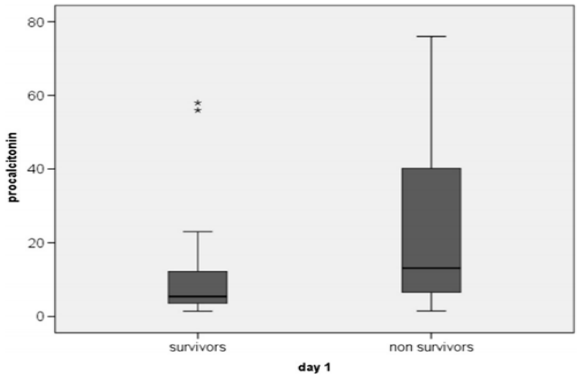

Figure 2: Procalcitonin values among the outcome types

Levels of serum procalcitonin were significantly higher in non-survivors compared to that of survivors [13.1 (6.3-42) vs. 5.38 (3.48-12.8) ng/mL; p < 0.01]. (Figure 2) The level of Procalcitonin predicted both sepsis and mortality with an Area Under the Curve value of 0.729 which was statistically significant (p<0.001). (Figure 3) The C-Reactive Protein value had an AUC value of 0.477 and hence did not predict mortality in sepsis (p=0.56). (Figure 4)

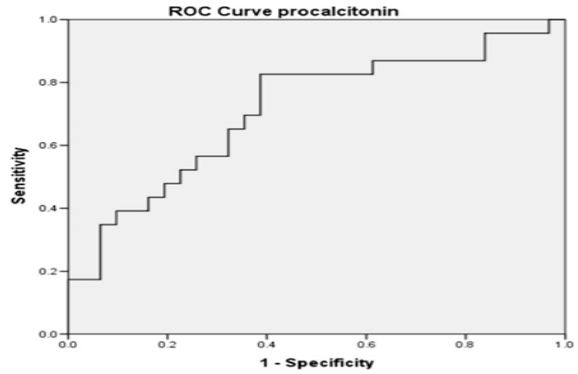

Figure 3: ROC curve analysis for Procalcitonin

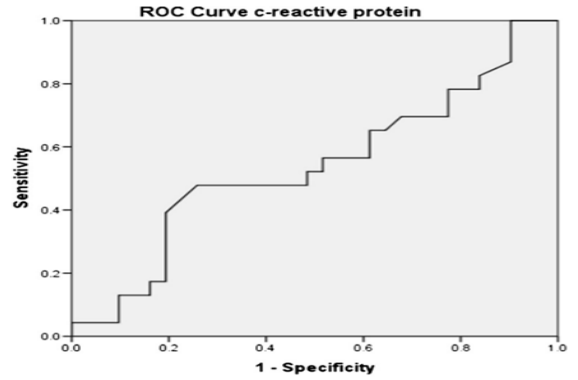

Figure 4: ROC curve analysis for Procalcitonin

DISCUSSION

Despite advances in medical science and antibiotic therapy, sepsis remains a major cause of morbidity and mortality in ICU. In our study, the mortality rate was 22%. Mortality rates were 6.5%, 28.6% and 62.5% respectively in the three groups of sepsis, severe sepsis, and septic shock, respectively. Thus, with the increasing severity of sepsis, mortality rate increased. There was significant association between severity of outcome and study population. In the study by Sudhir U *et al* [6] mortality was seen in 23 patients (23%). A study by Martin *et al* [7] showed that mortality in patients with sepsis from various centers varied between 16.8 and 31.8%. Sands *et al* [8] who studied sepsis in eight academic medical centers reported a mortality rate of 34%.

In our study, median value of serum procalcitonin in the group

of patients with sepsis was 0.5 ng/ml. It was 7.2 ng/ml and 10.6 ng/ml in patients with severe sepsis and septic shock respectively. Thus, inferring that higher median levels of serum procalcitonin were noticed in the groups with more severe forms of sepsis. Thus, quantitative correlation of higher values of serum procalcitonin with worse prognosis was established.

In the study by Sudhir U *et al* [6], 26.9% of patients in the group of sepsis, 40% in the group of severe sepsis and 47.8% of patients in the group of septic shock had high serum procalcitonin levels of more than 10 ng/ml. This is similar to the results obtained in our study. This was comparable to various studies done previously Meisner *et al* [9], Stucker *et al* [10] in which there was significant statistical association between serum procalcitonin levels and categories of sepsis. On the contrary, no significant differences between levels of hsCRP were observed in two groups and hsCRP did not predict mortality in sepsis. This finding is supported by previous studies. It was also found that the level of hsCRP fell over the course of in hospital stay in survivors which might be since CRP is an acute inflammatory reactant, and its levels improve with time [11].

Some of the limitations of this study include this being a single centre study with a relatively small sample size and majority of patients were receiving course of antibiotics prior to admission. The levels of procalcitonin were measured using an ELISA based assay which is relatively less sensitive than time-resolved amplified cryptate emission (TRACE) technology in which the duration of assay is rapid (19 min) but expensive [12].

CONCLUSION

Serum procalcitonin done once at the time of admission was proven to be very good, cost effective biomarker for the early identification of sepsis better than CRP values and cultures. Serum PCT can reduce the antibiotic exposure in septic patients. Estimation of serum procalcitonin for identification and prognostication of sepsis should be practiced for patients since it is definitely accurate and not a compromise with the other costlier biomarkers. Markers are recommended to be considered only in conjunction with clinical history and physical examination and in the light of experience.

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