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ORIGINAL ARTICLE

CORRELATION BETWEEN PCT LEVELS AND STAGE OF SEPSIS AMONGST PATIENTS PRESENTING IN A TERTIARY CARE HOSPITAL- A PROSPECTIVE STUDY

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ABSTRACT:

Background: Sepsis is a common and serious disease with substantial morbidity and mortality despite recent advances in supportive care and disease-specific treatments. There is no specific diagnostic test for the septic response. Even the bacteriological evidence of infection is not sensitive enough. The initial phase of the care of patients with sepsis (the so called "golden hours") is considered critical; timely hemodynamic support, along with administration of appropriate antibiotic treatment has been demonstrated to improve survival and significant clinical end points. The first mention of Procalcitonin in sepsis appeared in the report of 1983 mentioning its elevated levels in toxic shock syndrome (TSS) caused by staphylococcal aureus. The aim of the present study is to determine PCT levels amongst patients with sepsis, severe sepsis and septic shock presenting in a tertiary care hospital. **Materials and methods:** The present prospective study was conducted in the Department of Medicine Dayanand Medical College and Hospital Ludhiana during a period from 1st January 2013 to 1 February 2014.Details of the patients including: name, age, sex, admission number, data of admission, central record number etc were noted and all the symptoms were recorded. Relevant past history like diabetes, hypertension, COPD, recent surgery etc. was noted. Specimen of blood (10ml) was obtained from each patient by aseptic technique and was inoculated into commercially prepared Bactec/ Bac-T/Alert vials at the bedside. Procalcitonin was measured with VIDAS (ELFA) technique. The detection limit of the assay is 0.1 ng/ml and procalcitonin levels of healthy subjects are usually <0.1 ng/ml. Data were analysed using SPSS software version 18. p value <0.05 was considered as statistically significant. Chi square test was used to compare these variables. Procalcitonin values were analysed and presented in terms of Median with interquartile range since the data were not uniformly distributed. Kruscal Wallies test was used to compare median procalcitonin between the three groups of sepsis. Mann Whitney U test was used were two variables are present. **Result:** A total of 102 consecutive patients who satisfied the inclusion criteria were enrolled in the study. There were 39 patients (38.2%) had sepsis, 43 patients (42.2%) had severe sepsis and 20 patients (19.6%) were in septic shock. Out of the total 102 patients, 45 patients (44.11%) were categorized as having severe bacterial SIRS, 31 patients (30.39%) had severe SIRS, while 15 patients (14.70%) had moderate SIRS. Out of the total number of patients, in normal group there were 7 males (63.63%) & 4 females (36.36%), in the moderate SIRS group there were 12 males (80%) & 3 females (20%), in the severe SIRS group there were 21 males (67.64%) & 10 females (32.25%) and in the severe Bacterial SIRS there were 30 males (66.66%) & 15 females (33.33%).The median PCT value in the sepsis group was 2.56 ng/ml, in the severe sepsis group was 9.3 ng/ml and in the septic shock group was 17.5 ng/ml. p value was significant. The PCT value was more in the septic shock group (68.18%) and the severe sepsis group (45.45%) as compared to the sepsis group (27.77%). p value is 0.015 which was significant suggesting that rising level of PCT correlated with the severity of sepsis. **Conclusion:** Median value of serum procalcitonin in the group of patients with sepsis was 2.56 ng/ml, in the group of severe sepsis was 9.3 ng/ml and in the group of patients with septic shock it was 17.5 ng/ml. 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 the traditional system of blood or body fluid cultures.

Keywords: Bacteriological, Golden Hours, Procalcitonin, Sepsis.

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INTRODUCTION

Sepsis and severe sepsis causes significant morbidity and mortality among populations worldwide. It is the most common cause of morbidity and mortality in ICU patients. Approximately 20-35% of patients with severe sepsis and 40-60% of patients with septic shock dies within 30 days[1] Sepsis is a common and serious disease with substantial morbidity and mortality despite recent advances in supportive care and disease-specific treatments. Sepsis is defined as an infection with concurrent systemic manifestations that are the result of the host response. This response, known as systemic inflammatory response syndrome (SIRS), can be measured biologically but measurement is cumbersome and not routinely clinically available. Therefore, clinical features have been selected as surrogate markers of this host immunologic response. These features were modified in a joint consensus statement by the ACCP (American college of chest Physician) and the Society of Critical Care Medicine (SCCM) in 1992. It included clinical and microbiological evidence of infection along with two out of four of the following criteria to demonstrate evidence of systemic inflammatory immune response syndrome (SIRS).There is no specific diagnostic test for the septic response. Even the bacteriological evidence of infection is not sensitive enough. The initial phase of the care of patients with sepsis (the so called "golden hours") is considered critical; timely hemodynamic support, along with administration of appropriate antibiotic treatment has been demonstrated to improve survival and significant clinical end points.In view of this diagnostic and therapeutic dilemma, an effective and specific marker is needed that can support or exclude the diagnosis of infection [2]

Procalcitonin (PCT) is a recently rediscovered biomarker that fulfills many of the requirements, especially in comparison to "older" and commonly used biomarkers, and that has demonstrated superior diagnostic accuracy for a variety of infections, including sepsis. While blood cultures are still considered the "gold standard" for the diagnosis of bacteremia and sepsis, and are perhaps one of the most important functions of the clinical microbiology laboratory, PCT provides important information in early stages of sepsis as well as during antimicrobial treatment. Calcitonin is produced by the thyroid C-cells and has an important role in calcium homeostasis[3].The first mention of Procalcitonin in sepsis appeared in the report of 1983 mentioning its elevated levels in toxic shock syndrome (TSS) caused by staphylococcal aureus [4]. However, it was Assicot et al who in 1993 first described PCT as a new marker for infection [5]. The aim of the present study is to determine PCT levels amongst patients with sepsis, severe sepsis and septic shock presenting in a tertiary care hospital.

MATERIALS AND METHODS

The present prospective study was conducted in the Department of Medicine Dayanand Medical College and Hospital Ludhiana during a period from 1st January 2013 to 1 February 2014.Patients admitted in emergency or Intensive Care Unit (ICU) and clinically suspected to have sepsis were included in the study. All the patients were informed about the study and a written informed consent was obtained from all patients. Details of the patients including: name, age, sex, admission number, data of admission, central record number etc were noted and all the symptoms were recorded. Relevant past history like diabetes, hypertension, COPD, recent surgery etc. was noted. Findings of general physical examination and specific systemic examination were recorded in detail.

Specimen of blood (10ml) was obtained from each patient by aseptic technique and was inoculated into commercially prepared Bactec/ Bac-T/Alert vials at the bedside. Procalcitonin was measured with VIDAS (ELFA) technique. The detection limit of the assay is 0.1 ng/ml and procalcitonin levels of healthy subjects are usually <0.1 ng/ml. According to the value of procalcitonin, patients were divided into following groups:

1. 0.05 to < 0.5 ng/ml---Normal value (no bacterial infection)
2. ≥0.5 to < 2.0 ng/ml (Local infection) , Moderate SIRS
3. ≥2 to <10 ng/ml, Severe SIRS
4. ≥ 10 ng/ ml, Severe bacterial sepsis or septic shock.

Data were analysed using SPSS software version 18. p value <0.05 was considered as statistically significant. Descriptive statistics of variables such as age, sex, groups of sepsis etc, were analysed and presented in terms of percentage. Chi square test was used to compare these variables. Procalcitonin values were analysed and presented in terms of Median with interquartile range since the data were not uniformaly distributed. Kruscal Wallies test was used to compare median procalcitonin between the three groups of sepsis. Mann Whitney U test was used were two variables are present.

RESULTS

A total of 102 consecutive patients who satisfied the inclusion criteria were enrolled in the study.

Table 1 shows the number of patients categorized into sepsis, severe sepsis and septic shock according to the American college of chest Physician (ACCP)/Society of critical care medicine (SCCM). There were 39 patients (38.2%) had sepsis, 43 patients (42.2%) had severe sepsis and 20 patients (19.6%) were in septic shock.

Graph 1 shows the levels of PCT amongst patients.Out of the total 102 patients, 45 patients (44.11%) were categorized as having severe bacterial SIRS, 31 patients (30.39%) had severe SIRS, while 15 patients (14.70%) had moderate SIRS. It is worthwhile to note that out of these 102 patients; 11 patients had normal PCT level.

Table 2 shows Age wise distribution of patients according to PCT levels.In our study, in the normal (<0.5) group most patients (41.66%) were aged between 41-50 years, in the Moderate SIRS (≥0.5 to < 2.0) group most patients were aged between 41-80 years, in the Severe SIRS (≥2 to <10) group most patients (32.25%) were aged between

61-70 years whereas in the Severe Bacterial SIRS (≥ 10) group most patients (33.33%) were aged between 51-60 years.

Graph 2 shows Gender wise distribution of patients according to PCT levels.Out of the total number of patients, in normal group there were 7 males (63.63%) & 4 females (36.36%), in the moderate SIRS group there were 12 males (80%) & 3 females (20%), in the severe SIRS group there were 21 males (67.64%) & 10 females (32.25%) and in the severe Bacterial SIRS there were 30 males (66.66%) & 15 females (33.33%).

Table 3 shows Gender wise distribution of all patients in sepsis groups.In the sepsis group, there were 27 males (69.23%) & 12 females (30.77%). In the severe sepsis group there were 32 males (74.42%) & 11 females (25.58%). In the septic shock group there were 11 males (55%) & 32 females (45%).

Table 4 shows Median procalcitonin value in three goups of sepsis**.** The median PCT value in the sepsis group was 2.56 ng/ml, in the severe sepsis group was 9.3 ng/ml and in the septic shock group was 17.5 ng/ml. p value was significant suggesting that a rising PCT level in sepsis corresponded to the severity of sepsis i.e the level rises as we analyse the data from the sepsis group to the group with septic shock.

Table 5 shows Procalcitonin value in three groups of sepsis.The PCT value was more in the septic shock group (68.18%) and the severe sepsis group (45.45%) as compared to the sepsis group (27.77%). p value is 0.015 which was significant suggesting that rising level of PCT correlated with the severity of sepsis.

Table 1: CAtegarywise wise distribution of patients according to PCT levels

Category	Number	Percentage (%)
Sepsis	39	38.2
Severe Sepsis	43	42.2
Septic shock	20	19.6
Total	102	100.0

Graph 1: Levels of PCT amongst patients

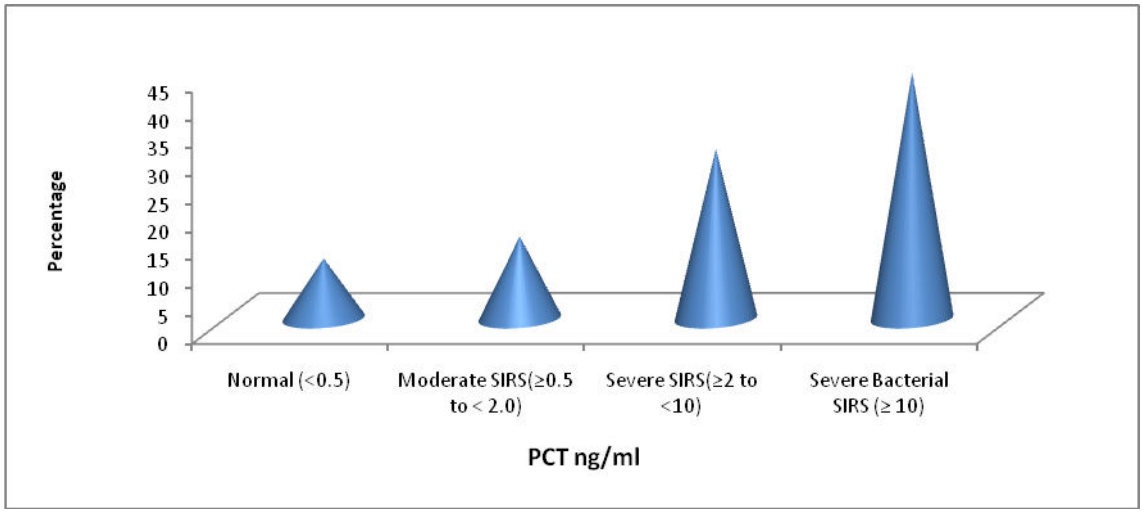

Table 2: Age wise distribution of patients according to PCT levels

Age (yrs) (Decade wise)	Normal (<0.5)		Moderate SIRS(≥0.5 to < 2.0)		Severe SIRS(≥2 to <10)		Severe Bacterial SIRS (≥ 10)		Total	
	n	%	n	%	n	%	n	%	n	%
10-20	0	0	1	5.88	2	6.45	2	4.76	5	4.90
21-30	1	0.69	3	17.64	3	9.67	2	4.76	9	8.82
31-40	0	0	2	11.76	2	6.45	1	2.38	5	4.90
41-50	5	41.66	3	17.64	6	19.35	9	21.42	23	22.54
51-60	3	25.00	2	11.76	8	25.80	14	33.33	27	26.47
61-70	1	0.69	3	17.64	10	32.25	12	28.57	26	25.49
71-80	1	0.69	3	17.64	0	0	2	4.76	6	5.88
More than 80	1	0.69	0	0	0	0	0	0	1	0.98
Total	12		17		31		42		102	

Graph 2: Gender wise distribution of patients according to PCT levels

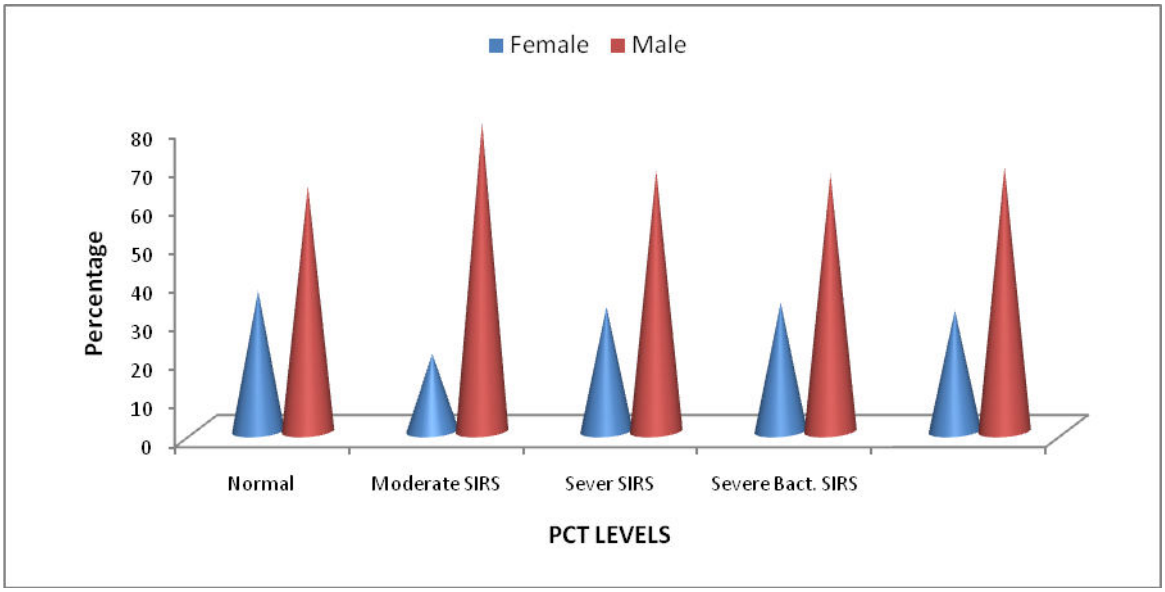

Table 3: Gender wise distribution of all patients in sepsis groups

Gender	Category of sepsis						Total		
	Sepsis		Severe Sepsis		Septic Shock				
Female	12	30.77%	11	25.58%	9	45.00%	32	31.37%	
Male	27	69.23%	32	74.42%	11	55.00%	70	68.63%	p-value
TOTAL	39	100.00%	43	100.00%	20	100.00%	102	100.00%	0.301

Table 4: Median procalcitonin value in three goups of sepsis

PCT levels (ng/ml)	Sepsis		Severe Sepsis		Septic Shock		p value
	MEAN	**SD**	**MEAN**	**SD**	**MEAN**	**SD**	
PCT levels (ng/ml) MEDIAN	14.4026	26.15518	18.5790	25.64607	22.7155	24.47024	0.003 Sig.
	2.56		9.3		17.5		

Table 5: Procalcitonin value in three groups of sepsis

PCT Value	Category of sepsis						Total	
	Sepsis		Severe Sepsis		Septic Shock			
Normal	8	22.22%	2	4.5%	1	4.5%	11	10.78%
Mod. SIRS	8	22.22%	6	13.63%	1	4.5%	15	14.70%
Sever SIRS	10	27.77%	16	36.36%	5	22.72%	31	30.39%
Severe Bact. SIRS	10	27.77%	20	45.45%	15	68.18%	45	44.11%
Total	36	100.00%	44	100.00%	22	100.00%	102	100.00%

DISCUSSION

Procalcitonin, normally produced in the C-cells of the thyroid gland, is the precursor of calcitonin, under the control of calcitonin gene related peptide (CALC -1) gene [6]. Procalcitonin (PCT) is a 116 amino acid long peptide having a molecular weight of 13 KDa [7]. A specific protease cleaves procalcitonin to calcitonin, catacalcin, and an N-terminal residue. The pathophysiological role of procalcitonin in sepsis is imperfectly understood [8]. It has been proposed that in inflammation, the release of procalcitonin may be a two way process: direct and indirect [9,10]**.** The toxins and lipopolysaccharides released by microbes can induce the release of procalcitonin in a direct manner ; or alternately the inflammatory cytokines like interleukin (IL) 1ß, IL-6, tumor necrosis factor –α (TNF- α) etc may indirectly influence procalcitonin production.

The study was conducted in 102 patients admitted in Dayanand Medical College and Hospital, Ludhiana. Patients who were suspected to have sepsis and were admitted in the emergency or intensive care units were included in the study. Patients fulfilling the inclusion criteria were enrolled in the study and their serum procalcitonin levels were measured.

Most of the patients in our study population were in the age group of 51-60 years (26.5%). In sepsis group most of the patients were in the age group of 51-60 yrs

(28.21%), in severe sepsis group 51-60 yrs (30.23%) and in septic shock group 61-70 yrs (35%).

In the severe bacterial SIRS group most patients were in the 51-60 years (33.33%), in the severe SIRS group it was 61-70 years and in the moderate SIRS group it was evenly distributed in the age group of 41-50 years, 61-70 years and 71-80 years. The mean age of males was 52.8 And females was 53.7. This infers the occurrence of sepsis mostly in the older agegroup in this study. In a similar study conducted by Sudhir U et al , the highest number of patients were in the age group of 50 to 59 years [(11)].In another study by Meynaar IA, mean age of patients with sepsis was 65 and those with SIRS were 62 years [(12)].

We found a slightly higher percentage of males affected with sepsis compared to females in the present study. Studies by previous workers also indicated a higher incident among men. Todi and group reported from a multicenter trial done at 12 centers in India that sepsis was more common in males [(13)].

In our study, median value of serum procalcitonin in the group of patients with sepsis was 2.56 ng/ml, in the group of severe sepsis was 9.3 ng/ml and in the group of patients with septic shock it was 17.5 ng/ml. Thus inferring that higher median levels of serum procalcitonin were noticed in the groups with more severe forms of sepsis. In our study, the comparison between the two group i.e. the patients categorized according to PCT levels and according to ACCP/SCCM was found to have p value of 0.015 which was statistically significant that rising level of PCT correlates with the severity of sepsis.

Similarly study was done by Sudhir U et al, in which 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 [(11)]. This is similar to the results obtained in our study. This was comparable to various studies done previously such as Meisner et al[(14)], in which there was significant statistical association between serum procalcitonin levels and categories of sepsis with p value = 0.001.

CONCLUSION

Sepsis is a major cause of admissions to ICU and emergency wards in any tertiary care centre with a significant mortality and morbidity. 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 the traditional system of blood or body fluid cultures. It was in addition proven to be a simple prognostic marker when quantitatively estimated. This would warrant early initiation of effective treatment strategies.

Thus, estimation of serum procalcitonin for identification and prognostication of sepsis should be practiced since it is definitely accurate. Median value of serum procalcitonin in the group of patients with sepsis was 2.56 ng/ml, in the group of severe sepsis was 9.3 ng/ml and in the group of patients with septic shock it was 17.5 ng/ml.

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