ORIGINAL ARTICLE

A Study of Procalcitonin as Biomarker in Sepsis Patients Admitted in Super Speciality Hospital

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Abstract

Aim: Sepsis, a systemic inflammation, mainly originated due to infectious viral, fungal, or parasitic infections. No long-term data are available which compare the procalcitonin (PCT) levels and C-reactive protein (CRP) levels in different emergency conditions as well as differentiating the PCT levels in males and females in sepsis or other related condition. The main objective of this study was to evaluate PCT, a reliable biomarker, and to compare the different parameters for the diagnosis of sepsis, severe sepsis, and septic shock conditions. **Materials and Methods:** For this study, the samples of 74 patients were taken which were admitted in Intensive Care Unit (ICU) in the Max Hospital, Mohali. All the candidates fall in the age group of 05–70 years. The parameters which were used for the diagnosis and differentiating the sepsis conditions were PCT levels, CRP levels, and total leukocyte count levels. The total number of 74 patients was grouped into different groups on the basis of their gender, age and *P*-value. After a period of 16 weeks, subjects from different groups had great difference in their PCT values in the sepsis condition. **Results and Discussion:** The Gram-negative bacteria are one of the most common causative agents associated with sepsis condition which was 54.3%, whereas remaining 45.7% was other Gram-positive bacteria, fungi, and yeast. From the study, it was appeared that the prevalence of sepsis condition is found to be more prominent in males as compared to females. It will be concluded that severity of sepsis increases as serum PCT increases and similarly mortality also increased. **Conclusion:** Sepsis is the most common cause of morbidity and mortality in ICU. Due to its low specificity of CRP in the sepsis condition and unable to differentiate between the severities of the infection, we need to look for another biomarker. Thus, PCT is more promising reliable biomarker for the diagnosis of sepsis and start to effective antibiotic and reducing the mortality.

Key words: Biomarker, C-reactive protein, intensive care unit, mortality, procalcitonin, sepsis

INTRODUCTION

Sepsis is the life-threating inflammatory response due to the bacterial infections which increase the severity to severe sepsis and septic shock. It is one of the most common problems in older age group including various causative agents such as *Staphylococcus aureus, Escherichia coli, Acinetobacter,* and *Klebsiella pneumonia*. In sepsis form, sepsis causes multiple organ dysfunctions, depression of heart, drop blood circulation, and abnormalities of metabolic rate. Outcomes in sepsis have greatly recovered on early diagnosis, fluid resuscitation, and administration of antibiotics.[1]

Bacterial infections are one the major causes of morbidity and motility. Diagnostic biomarkers such as D-dimers in pulmonary embolism, natriuretic peptides in acute heart failure, and troponin in myocardial infarction have been administrated in the medical field.[2] However, to timely differentiate infectious from non-infectious causes of

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inflammation and fever remains challenging. Besides, infectious causes include bacterial, viral, fungal, parasite, *Mycobacterium*, and rickettsial infections. Fever can also be caused by non-infectious causes such as autoimmune diseases, malignancy, drugs, venous thromboembolism, transplant rejection, gout, and myocardial and cerebral infarction.[3]

To control irrational use of antibiotics and the development of antibiotic resistance, in the early stage of diagnosis, there must be identified the bacterial and non-bacterial infection.[4] Various clinical markers are currently available for the differentiation of infectious and non-infectious disease and characterization of the immune response. Specific laboratory test accurately identifies the type and activity of on-going inflammation. In daily routine diagnosis, there are also few biomarkers such as C-reactive protein (CRP), total leukocyte count (TLC), and erythrocyte sedimentation rate which are not sufficient and sensitive due to uncertain clinical assessment.[1] Blood culture, which is also known as the gold standard for diagnosis has disadvantage in the form of a long turnaround time, inability to provide specific information on host response, and unable to identification between bacterial colonization and infection.[5] Procalcitonin (PCT) is an excellent biomarker for bacterial infection. It is not only helps in early diagnosis but also informs about the course and prognosis of the disease and drug monitoring. At present, evidence have been showed that PCTs promising marker for diagnosis of bacterial infection.[6]

PCT is a hormokines, prohormone of calcitonin, made up of 116 amino acids, and it is synthesized from the precursor pre-PCT.[6] Moreover, PCT is synthesized by the parafollicular cell or C-cell of the thyroid gland and helps to regulate of calcium level in a body. PCT level is increased along with calcitonin in the thyroid carcinoma. On the other hand, only PCT level increased in various conditions, for example, bacterial infection, sepsis, organ failure, and organ transplant rejection with normal level of calcitonin.[7,8] However, PCT level is highly increased in bacterial inflammation rather than other infection such as viral inflammation, autoimmune disease, and organs transplant rejection. This is very useful in clinical diagnosis for the deferential of bacterial inflammation and viral inflammation on the basis of the concentration of PCT level in serum.[9]

PCT's kinetics profile supports it a helpful monitoring tool, because its level promptly elevate continue 3–6 h of infection, peak at 12–48 h and rapidly down during improvement,[2,10,11] whereas CRP starts synthesis in between 4 and 6 h after stimulation. Its level becomes double every 8 h and then optimum in between 36 and 50 h of infection or acute inflammation occurs also take more time to falls down its to normal levels.[12-14] PCT can be used to differentiate between bacterial from viral infection because upregulation interferon-gamma which is stimulated by cytokine in response to viral infection.[9] Furthermore, the rapidity testing of PCT useful to diagnosis[15] and can facilitate to making clinical decision for the initiation or discontinuous of antibiotic therapy.[16,17] Thus, PCT would be a more reliable biomarker for optimizing the clinical diagnosis, monitoring, and antibiotic therapy in patient with systemic bacterial and viral infection.

The aim of this study was to evaluate the level of PCT in critically ill patients having bacterial infections such sepsis, severe sepsis, septic shock, and other surgery and viral infections, evaluate the PCT level on the basis of gender, age basis, and correlate with CRP and TLC.

MATERIALS AND METHODS

The prospective study was conducted at a multispecialty hospital, Mohali in Punjab region. This was carried out over 4 month's period from January 2, 2017, to April 29, 2017.

Data were collected from a total of 74 patients; of them, 46 were male patients, whereas 28 were female patients. The range for age was 52.37 ± 20.84 years for both male and female patients. In the data, ID, name, sex, level of PCT, CRP, and TLC were noted down along with report of blood culture. Then, the data differentiation was done on the basis of percentage, mean, SD, and Chi-square test.

RESULTS AND OBSERVATIONS

The study was carried out at Max Super Speciality Hospital, Mohali, from 2nd January to April 29, 2017. In my study, I had selected 74 patients who came for the treatment of inflammatory syndrome. Of 74 patients, the samples from 57 patients were selected; those who are having the PCT level >0.5 ng/dl and are considered as "study Group - 1" and 17 patients whose PCT level was <0.25 ng/dl are considered as "control group." PCT samples of the infected patients were obtained from the emergency department of Max Hospital. In data on-going treatment, patient's ID, name, age, gender, patient's diagnosis, patient's history, and treatment therapy were studied by CPRS. The patients whose PCT level was >0.5 ng/dl; of them, 77.2% were suffering from the sepsis condition and remaining 22.8% were cancer patients, autoimmune disease patients, and surgery patients, etc.

Age-wise Distribution

Of 57 patients studied in the test group (<14 and >65 years), maximum 28 (49.12%) were in Group C (35–64 years) followed by 17 (29.83%) in Group D (>65 years). Moreover, there were only 3 (5.26%) patients in Group A (<14 years). There were 3 times greater number in Group C (15–34 years) than Group A. A total of 17 individuals whose PCT level was <0.25 ng/dl included in the control group and out of the total 17 individuals, maximum, 9 (52.94%) were in the Group D. Whereas 0 patients

were in Group A and 4 (23.53%) each in the Group B and Group C. Hence, the data show that Group C category patients come in hospital for the treatment of inflammatory syndrome while Group A patients are found to be lowest.

Sex-wise Distribution

In this study, sepsis condition found more in male than in female. In contrast, numbers of female found more in control group. Therefore, of 57 patients, 40 (70.18%) patients were male, whereas 17 (29.82%) patients were female. In total infected population, 72.73% of male were in sepsis condition while 27.27% were female, and in control group, 11 (64.71%) were female and only 6 (35.29%) were male.

In a study by Sinha *et al*., females were less with female-male ratio of 12:28 in sepsis condition, which is similar to the result of this study (103).

Types of Sepsis

Based on the ACCP definition guidelines, patients were categorized as sepsis, severe sepsis, and septic shock accordingly; of 57 patients, 44 patients were in sepsis condition. Among 44 patients, 16 (36.4%) were in the group of sepsis, 7 (15.9%) patients were in the group of severe sepsis, and 21 (47.7%) patients were in the group of septic shock. In this study, a number of septic shock patients were more due to the sample which was selected in the patients who had PCT level >0.5 ng/dl [Table 1].

Table 1: Types of sepsis

Types of sepsis	Frequency (%)
Sepsis	16 (36.4)
Severe sepsis	7 (15.9)
Septic shock	21 (47.7)
Total	44 (100)

Table 2: Result of outcomes in population

Sex	Test		Control	
	Death (%)	Survive (%)	Death	Survive (%)
Male	17 (42.5)	23 (57.5)	0	6 (35.29)
Female	3 (17.6)	14 (82.4)	0	11 (61.71)
Total	20 (35.09)	37 (64.19)	0	17 (100)

In the study by Sudhir U *et al.,* patients in the group of sepsis were 26.9%, in the group of severe sepsis were 25.3%, and in the group of septic shock were 47.8%. Septic shock patient had serum PCT level of >10 ng/dl which is almost same to the results obtained in our study. Previously, comparison of various studies done by Meisner *et al*. and Stucker *et al*.[7, 18-21]

Result outcome in population

In our study, 42.5% of 40 male patients died and 57.5% of patients improved, whereas 82.4% of female patients survived while 17.60% of female patients died of 17 female patients. However, there was no one died in control group. 6 (35.29%) were male patient and 11 (61.71%) were female patients [Table 2].

The study shows that male patients died more than female patients infected by bacterial infections. PCT level was found more in male patients so mortality risk increases in males more than females.

Result outcome in sepsis patients

Our study shows that of 16 (18.8%) sepsis patients had died and 13 (81.2%) patients improved. Similarly, 3 (42.9%) patients died, whereas 4 (57.1%) patients were hemodynamically stable among seven patients who were in severe sepsis condition. In septic condition, most patients died. In this group, 14 (66.7%) patients died while only 7 (33.3%) patients improved. As the severity of the sepsis increased, the death also increased from 18.8% in sepsis to 66.7% in septic shock [Table 3].

Our study represents that as the PCT value is increased severity also increased. Due to the high value of PCT from sepsis to septic shock, high mortality in septic condition arises. Hence, high value of PCT indicates the high mortality and low PCT value represents low risk of mortality in sepsis condition.

There was significant association between the severity and prognostic of sepsis with *P* value being <0.05.

Mean value of sepsis condition

Mean value of serum PCT in 36.36% of patients with sepsis was 3.9 ± 4.8 ng/dl, 8.9 ± 5.3 ng/dl in 15.1% of patients with severe sepsis, and in 47.73% of patients with septic shock,

Table 3: Result outcome in sepsis patients

Types of sepsis	Death (%)	Survive (%)	Total (%)	*P*-value
Sepsis	3 (18.8)	13 (81.2)	16 (36.36)	0.015
Severe sepsis	3 (42.9)	4 (57.1)	7 (15.91)	
Septic shock	14 (66.7)	7 (33.3)	21 (47.73)	
Total	20	24	44	

it was 51.6 ± 37.1 ng/dl [Table 4]. Thus, higher mean value of serum PCT was noticed in the groups with more severe sepsis. Thus, quantitative correlation of higher values of serum PCT with worse prognosis was established.

In the study by Sudhir *et al*.,[20] 47.8% of patients in the group of septic shock had high serum PCT levels of >10 ng/dl. This is similar to the results found in our study. This was similar to several studies done earlier Meisner *et al*.[7,20,21]

PCT correlation with microbiology study

Of 44 sepsis patients, 35 cases found culture positive. Among them, 34.30% of cases had Gram-positive cases, 54.30% had Gram-negative cases, and remaining 11.4% had others yeast and fungus cases [Table 5]. The study represents that Gram-negative is main causative agents than Gram-positive and other fungus and yeast. Thus, PCT level is increased in sepsis patient due to Gram-negative bacteria.

In the study by Singer, approximately 50% of sepsis infectious condition is Gram-negative bacteria and slightly <50% are caused by Gram-positive bacteria. Other causes of sepsis include fungi and virus such as immune deficiency virus (HIV) and protozoa. This is almost same to our study.

PCT correlation with culture

Moreover, of 44 sepsis patients, 35 (79.50%) patients had culture-positive sepsis. Of eight patients, whereas 9 (21.50%) of 44 patients who had culture-negative sepsis had positive serum PCT level.

Blood culture is standard for the diagnosis of sepsis condition. Though, long turnaround time, inability to provide specific information on host response and unable to identification between bacterial colonization and infection are some common drawback of blood culture.[22] Thus, it can suggest that serum PCT can be used as a reliable diagnostic biomarker in the diagnosis of sepsis in addition to its utility in the prognosis of sepsis by quantitative correlation.

Table 4: Mean value of PCT in sepsis condition

Parameter	Sepsis mean (ng/dl)	Severe sepsis mean (ng/dl)	Septic mean (ng/dl)
PCT mean	3.9±4.8	8.9±5.3	51.6±37.1

PCT: Procalcitonin

Table 5: PCT correlation with microbiology study

Gram bacteria	*n* (%)
Gram-positive	12 (34.30)
Gram-negative	19 (54.30)
Yeast and fungus	4 (11.40)

PCT: Procalcitonin

Comparison of PCT with CRP and TLC

In our study, PCT level is continuously increased from patient 1 to 3 reached at 19.37 ng/dl which was 11.3 ng/dl in the patient no. 1. After then, it highly increased and peaked at >100 ng/dl from 19.37 ng/ml. However, PCT value is dropped down and maintained the lowest value of 6.8 ng/ml at patient no. 10.

In contrast, CRP value is 313.11 mg/L which is the highest value among the patients. CRP value is decreased from patient 1 to patient 4 while in case of PCT, it was in increased trend. Similarly, in patient no. 5, CRP value is lowest 2.97 mg/l which is normal level. After then, from patient no. 6–10, CRP level was fluctuating. TLC trend is similar to the PCT but no significance difference between high and low value of PCT.

Thus, we can highly recommend the PCT for the diagnosis of infectious patient and to initiate the microbial therapy immediately in intensive care unit and emergency ward.

CONCLUSION

In general, sepsis is life-threatening disease. It requires early and accurate diagnosis which can help to make appropriate treatment plane and save the patient life. However being efficient with the diagnosis is the most important criteria, as this will save the cost of antibiotic drugs because the prescription will be specific. It will also save time (duration of treatment) as it will reduce the development of drug resistance. Thus, for early diagnosis and immediate effective treatment strategies of sepsis, there is necessity of a reliable biomarker.

There are CRP and serum PCT most commonly used for the diagnosis of inflammatory disease. CRP is one of the infectious biomarkers which are applied for the diagnosis of infection. From my study, it was concluded that CRP level cannot be used as a reliable marker for the infectious condition detection. The main reason behind this conclusion is mainly due to the kinetic profile of CRP values in different conditions. The CRP kinetic profile takes more time to elevate in the initial stage of the infection. Once reached on its peak level, it remains high and takes enough time to reach to its normal value even after the improvement of the infectious condition. Due to its low specificity in the sepsis condition and unable to differentiate between the severities of the infection, we need to look for another biomarker.

TLC is another parameter which is used for the investigation of infectious disease, but it is unable to differentiate between the types and condition of infection during the medical process. It value can be easily effected by the antibiotics, cancer, malaria, etc., which is rapidly decreased <4,000/L. Moreover, TLC increased above the normal range due to

the infection such as bacterial infection, parasitic infection, bone marrow tumor, and other conditions. However, it cannot specify the types of infection due to the association of immune system.

Serum PCT is promising remarkable biomarker for the accurate diagnosis of patient with sepsis. Diagnosis of serum PCT was done at the time of admission, it was recognized to be the cost-effective biomarker for the early treatment of sepsis. Along with the diagnosis of infection, PCT helps to take decision initiation and discontinuous of antimicrobial therapy in the patient with critical stage. In addition, it is also verified better than culture from our study. Likewise, it also used to a prognostic marker by the quantitative estimation of PCT value. In the same way, we found severity increased on the aged and sepsis condition found more in male than female. This study also recognized as Gram-negative bacteria were main causative agent than other bacteria and fungi for the elevation PCT level in body. Thus, estimation of serum PCT for identification and prognostication of patient with sepsis should be applied.

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