ORIGINAL ARTICLE

Role of Procalcitonin Levels in Patients with Sepsis in Medical Intensive Care Unit

Dattatreya Sarkar[1*], Rajeev Chatterji[2]

Authors' Affiliations: [1,2]KPC Medical College and Hospital, Jadavpur, WB, India
***Correspondence:** Dr. Dattatreya V Sarkar[1], **Email**: sarkardv_ms@gmail.com

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ABSTRACT

Introduction: Sepsis has a death rate of ~25% globally and its clinical treatment presents an important clinical challenge. The Acute Physiology and Chronic Health Evaluation II (APACHE II) is the standard method for assessing sepsis. Serum PCT level can be increase in case of sepsis. With this background, the present research is aimed to study the survival among the sepsis cases and correlate them with serum procalcitonin levels, APACHE II Score and other risk factors.

Methodology: The study was conducted among 75 cases diagnosed having sepsis admitted in medical ICU. APACHE II score, serum procalcitonin (PCT) and other investigation were carried out along with clinical history and examination. Data were analysed using epi-info software.

Results: The cases fatality rate of sepsis cases in medical intensive care unit in our hospital was 37.3%. The mortality rate was significantly higher patients with comorbidities, especially cases with respiratory or CNS involvement. The serum PCT levels were significantly higher in the group of non survivors as compared to group of survivors. Higher APACHE II score associated with higher mortality. Serum PCT levels go on increasing along the spectrum of sepsis. A PCT level was significantly hire in culture positive cases compare to sterile cases.

Conclusion: From this study we conclude that serum PCT level is useful investigation in sepsis cases to predict mortality.

Keywords: Sepsis, ICU, APACHE II, serum procalcitonin, PCT, mortality rate

INTRODUCTION

Sepsis has a death rate of ~25% globally and its clinical treatment presents an important clinical challenge. The rapid progression of sepsis requires correspondingly swift adjustments in therapy, and accurate identification of disease severity is therefore vitally important for predicting prognosis, treatment, preventing complications, reducing complication and mortality.[1]

Mortality rate in ICUs' rely on severity of the disease and worsening of health condition of critically ill cases. The condition that has shown to raise the in-hospital mortality rates are increasing age of case, severity of disease, certain pre-existing clinical conditions such as malignancy, immune suppressive and renal replacement therapy. Assessment of outcome of clinical treatment was first considered as an issue by Florence nightingale in 1863.[2]

Initially the treatment outcome prediction of severely ill cases was based on judgments made by the physician's but today the rapid development of ICUs, demand quantitative measurement and review of the outcomes to enhance practices largely based on evidence. The original initial outcome prediction scores were developed more than 25 years before to get an indication or prediction of risk of mortality critically ill cases. Since then, many situation-based ICU scoring systems were developed though only a few of them are practically put into practice. Therefore, assessment of prognosis is a vital part of management of any critically ill cases.[3]

Multiple scoring systems are available for assessment and study prognosis of the severity of morbidity in critical care units. The scoring systems classify the severity of critically ill cases based on clinic-biochemical values and classify the case in a specific risk category. Hence scoring systems have been developed and it is critical to use them in ICUs to improve standards of care and outcome.[4]

Acute Physiology and Chronic Health Evaluation II (APACHE II) is a severity score and mortality estimation tool developed for ICU cases in the US by Knaus et al in 1985.[5] The critical care severity scores are calculated from the data obtained on the first day of ICU admission e.g., APACHE, SAPS (Simplified Acute Physiology Score), and Mortality Probability Model (MPM). The Scoring system contains of two divisions: a severity score which is a digit (generally higher the score more is the severity of the condition) and a calculated probability of mortality. [6,7] In addition to clinical observation and advance treatments in health care, practicing clinicians need to realize and utilize scoring systems in their day today practice.[8]

The Acute Physiology and Chronic Health Evaluation II (APACHE II) is the standard method for assessing sepsis, but along with that other diagnostic and prognostic biomarkers are also investigated.[5]

Procalcitonin is a 116 amino acid precursor of calcitonin. Serum procalcitonin concentrations are below the detectable level in healthy persons (0.5 ng/ml), and however, it can increase to 1000 ng/ml in severe bacterial infection or

sepsis. [9] Procalcitonin has a half-life of 15–20 h in the blood, and its plasma concentration is correlated with severity of infection in cases in the intensive care unit (ICU).[10]

With this background, the present research is aimed to study the survival among the sepsis cases and correlate them with serum procalcitonin levels, APACHE II Score and other risk factors.

MATERIAL AND METHODS

This was a prospective observational non interventional cohort study was conducted in the Clinic of Intensive Care unit of a tertiary care centre in western India during December 2017 to May 2019. The approval of the Ethics Committee of the institute was obtained prior to the initiation of the study. Written informed consent was taken from all participants or their relatives before including them into the study.

Eligibility criteria: All patients above the age of 18 years who have been admitted to medicine ICU with sepsis were included in the study. Patient with major trauma, Burns or surgery; patients who have received massive blood transfusions; patient having chronic infections necessitating chronic antibiotic usage and patients with immunosuppression were excluded from the study. Patients meeting the inclusion criteria were enrolled in this study.

Patients were diagnosed and classified into following 3 groups namely using Criteria for SIRS (Systemic Inflammatory Response Syndrome), sepsis, severe sepsis, and septic shock based on the 1991 ACCP/SCCM Consensus Conference.

Table 1: Criteria for SIRS, sepsis, severe sepsis, and septic shock

Term	Criteria
SIRS	2 out of the 4 following criteria:
	Temperature >38 °C or <36 °C
	Heart rate >90/min
	Hyperventilation evidenced by respiratory rate >20/min or arterial CO2 < 32 mmHg
	White blood cell count >12 000 cells/μl or <4000 cells/μl
Sepsis	SIRS criteria with presumed or proven infection
Severe Sepsis	Sepsis with organ dysfunction
Septic shock	Sepsis with hypotension despite adequate fluid Resuscitation

After obtaining written informed consent, subjects aged 18 and older were included in the study. A detailed history was elicited from the patients, and general physical examination and systemic examination of the patients was done.

Routine complete blood counts, routine urine analysis and microscopy, renal function tests, random blood sugar, liver function tests, serum electrolytes, C-reactive protein, chest X-ray, ECG, sputum Gram's stain/AFB, cultures-blood/sputum/urine etc will be done wherever indicated and serum Procalcitonin will be done for all patients.

The APACHE II (Acute Physiology and Chronic Health Evaluation) severity score was calculated on the day of admission. ELECSYS B·R·A·H·M·SPCT assay which is an electrochemiluminescence assay was used to determine serum PCT levels. The measuring range was 0.5-100 ng/ml.

Statistical analysis: 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 as percentage. Chi square test was used to compare the categorical variables.

Procalcitonin values were analysed presented in terms of Mean with standard deviation Median with Interquartile range since data were not normally distributed. The unpaired student t test was used to evaluate the association between serum PCT values of two groups namely: sepsis and severe sepsis, sepsis and septic shock, septic shock, and severe sepsis. The APACHE II score was presented as Mean with Standard deviation, Median with interquartile range. The unpaired t test was also used to evaluate the significance of difference between the Mean and standard deviation of APACHE II scores of groups of survivors and non survivors

Serum PCT level of 2 ng/mL was considered as a cut off point for diagnosis of sepsis. The association between Serum PCT and APACHE II score was studied using Spearman rank correlation coefficient test. The *rho* value was calculated. The specificity and false positivity rate of various serum PCT levels for predicting mortality were calculated plotted and receiver operating characteristic curve was plotted for the same. The area under the receiver operating characteristic curve (AUROC) was calculated with AUROC closer to 1.0 being significant. Similarly, sensitivity and false positivity rate of various APACHE II scores were calculated and ROC for evaluation the association between mortality and the severity score. The AUROC for APACHE II was calculated with value closer to 1.0 being considered significant. The association between the serum PCT level and various categorical variable such as outcome, culture growth, APACHE II score was evaluated with Chi square test.

RESULTS

Total 75 patients diagnosed with sepsis were included in this prospective observational study. Of the total 75 patients, 47 patients were survivors, and 28 patients were non-survivors. The mean age in the group of survivors was 55.17±16.61 and the mean age in the group of non survivors is 50.67±14.27. Total 47 (62.7%) patients were males of which, 31 (65.9%) survived and 16 (34.1%) died. Total 28 (37.3%) patients were females, of which 16 (57.1%) survived and 12 (42.9%) died. There was presence of comorbidity in 48 (64%) patients whereas 27(36%) patients didn't have any history of comorbidities. There was no difference in mortality rate according to age and gender (p value >0.05), however, mortality rate was significantly higher in patients with comorbidities (p value <0.001).

Table 2: Comparison of age, gender, and comorbidities with survival in sepsis cases

	Outcome		P value
	Survivors (n=47) (%)	Non survivors (n=28) (%)	
Age groups (in years)			
25-39	10 (55.6)	8 (44.4)	
40-49	7 (70.0)	3 (30.0)	
50-59	7 (58.3.0)	5 (41.7)	
60-69	13 (54.2)	11 (45.8)	
70-79	10 (90.9)	1 (9.1)	
Total	47 (62.7)	28 (37.3)	
Age (mean ± SD)	55.17 ± 16.61	50.67 ± 14.27	0.890
Gender			
Male (n=46)	31 (65.9)	16 (34.1)	0.445
Female (n=26)	16 (53.8)	12 (46.2)	
Comorbidity			
Present (n=48)	24 (50.0)	24 (50.0)	<0.001
Absent (n=22)	23 (85.2)	4 (14.8)	

Table 3: Comparison of clinical and biochemical variables with survival in sepsis cases

Indicators	Outcome		P value
	Survivors (n=47) (%)	Non survivors (n=28) (%)	
System Involved			
Respiratory system	27 (72.9)	10 (27.1)	0.153
Renal system	11 (55.0)	9 (45.0)	
Gastrointestinal system	7 (47.0)	8 (53.0)	
Cellulitis	2 (100)	0 (0.0)	
CNS	0 (0)	1 (100)	
Serum PCT			
>2 ng/mL	34 (55.7)	27 (44.3)	<0.009
<2 ng/mL	13 (92.8)	1 (7.2)	
Mean ± SD	3.7 ± 2.18	8.8 ± 3.8	<0.001
APACHE II Score			
Mean ± SD	28.95 ± 4.07)	41.25 ± 12.75	<0.001
<30	20 (90.9	2 (9.1)	0.0011
>=30	27 (50.9	26 (49.1	
APACHE II >30			
PCT <2 ng/mL	5 (18.5)	1 (13.8)	0.092
PCT >2 ng/mL	22 (81.5)	25 (96.2)	
APACHE II <30			
PCT <2 ng/mL	8 (40.0)	0 (0)	0.262
PCT >2 ng/mL	12 (60.0)	2 (100)	
Severity of disease			
Sepsis (n=26)	24 (92.3)	2 (7.7)	<0.001
Severe Sepsis (n=26)	14 (53.9)	12 (46.1)	
Septic Shock (n=23)	9 (39)	14 (61)	
Culture			
Infected	29 (54.7)	24 (45.3)	0.027
Sterile	18 (81.8)	4 (18.2)	
Total	47 (62.7)	28 (37.3)	
Culture growth			
Gram positive	7 (63.6)	4 (36.4)	0.048
Gram negative	21 (56.8)	16 (43.2)	
Fungus	1 (20.0)	4 (80	
Sterile	18 (81.8)	4 (18.8)	

Table 4: Comparison of APACHE II score with procalcitonin level

Indicators	Procalcitonin level		P value
	>2.0 ng/mL (%)	0.5-2.0 ng/mL (%)	
APACHE II Score			
<30	14 (58.3)	10 (41.7)	<0.001
≥30	47 (92.2)	4 (7.8)	
Survivor			
<30	12 (54.5)	10 (45.5)	0.010
>30	22 (88.0)	3 (12.0)	
Non Survivor			
<30	2 (100.0)	0 (0.0)	0.777

>30	25 (96.2)	1 (3.8)	
Culture			
Infected	47 (88.7	6 (11.3	0.011
Sterile	14 (63.6	8 (36.4	

The mortality rate in patients with respiratory system as the focus of sepsis was 13.3%, the mortality rate in renal patients was 12%, mortality rate in GI system patients was 10.7%, and the mortality rate in the patients with CNS as the focus of sepsis was 100%. The difference was statistically insignificant (p value >0.05).

Serum procalcitonin in study population

In the total study population of 70 patients, 61(87.1%) patients had serum PCT levels >2ng/ mL and 9(12.9%) patients had serum PCT levels <2ng/ml.

Amongst the 75 patients, mortality rate amongst the group of patients with PCT>2 was 44.3% and that in the group with PCT level <2 was 7.2%. The sensitivity is 96.4% and specificity is 27.7%. The PPV is 44.2% and NPV is 92.9%. The mortality rate in patients with serum PCT level >2ng/mL was higher than that of the group with serum PCT level <2ng/mL is statistically significant (p value <0.01). The mean serum PCT level in the group of survivors was 3.72±2.18 with a median of 3.54 (2.3-4.35). The mean serum PCT level in the group of non survivors was 8.8±3.80 with a median of 8.75 (6.3-11.67). The serum PCT levels were significantly higher in the group of non survivors as compared to group of survivors (p value <0.001).

Distribution APACHE II score in study population

In the study population of 75(100%) patients, majority of the patients 37 (49.3%) had APACHE II score in the range of 35-100 followed by 14 (18.7%) patients had APACHE II score in the range of 30-34.

In the group of survivors, the mean APACHE II score was 28.95±4.07 with the median APACHE II score of 28 (26 - 32.5). Total 28 patients belonged to the group of non-survivors and the mean APACHE II Score in this group was 41.25±12.75. The median APACHE II score in the group of non survivors was 44 (29-52.25). The difference between the APACHE II score of the 2 groups is statistically significant (p value=0.0000).

The mortality rate of patients with APACHE II score <30 was 2.7% as compared to 34.6% in the group of patients APACHE II score >30. The sensitivity of cut off APACHE II score > 30 for predicting mortality was 92.9% and specificity was 42.6%. The PPV was 49.1% and NPV was 90.9%. The mortality rate in group of patients with APACHE II score >30 is significantly higher than those with APACHE II Score<30 (Df-1; X^2=10.61399; 'p' value=0.00112).

The relation between serum PCT and outcome in the group of patients with APACHE II score >30 was statistically insignificant (p value=0.0919). The relation between serum PCT and outcome in the group of patients with APACHE II score <30 was statistically insignificant (p value 0.262).

The mortality rate in patients diagnosed with sepsis, severe sepsis and septic shock was 2.7%, 16% and 18.7% respectively. The mortality rate was more in the patients diagnosed with septic shock and difference between the mortality rates of three groups is statistically significant (p value <0.001).

Adhering the ACCP guidelines the patients were classified to 3 categories of Sepsis, Severe Sepsis and Septic Shock. The mean serum PCT level in the group of patients diagnosed with sepsis was 2.58±0.92 ng/mL with a median of 2.45 (1.725-3.275). The mean serum PCT in severe sepsis was 3.87±0.99 ng/mL with a median of 5.21 (3.85-6.75). The mean serum PCT level in septic shock cases was 9.01±3.92 ng/mL and a median of 5.7 (5.4-9.31). Serum PCT levels go on increasing along the spectrum of sepsis, severe sepsis, and septic shock.

Total 53 (70.7%) patients' sample cultures showed growth whereas 22 (29.3%) patients' sample cultures were sterile. The mortality in group of patients with positive sample cultures was 32% as compared to 5.3% in the group of culture negative samples. The difference was statistically significant (p value <0.05).

The mortality rate in the group of Gram-positive induced disease is 36%, in the group of Gram-negative induced disease is 43.2 % and that of patients with fungal causative agent is 80%. The mortality the group of patients with sterile sample cultures was 18.8%. The difference was statistically significant (p value <0.05).

A PCT level was significantly hire in culture positive cases compare to sterile cases (p value <0.011).

DISCUSSION

The difference of mortality rates between male and female mortality rate is statistically not significant ('p' value=0.44524). The male preponderance in the study population was like previous studies. Jain et al[11] reported non-significant association between gender and outcome ('p' value >0.05). Not many studies have investigated the correlation between the outcomes. Rhee C et al[12] too reported male predominance in their study population of patients diagnosed with sepsis. However like observations of the present study no significant association was observed between gender and outcome by the previous study.

Total 48 (64%) of the 75 patients had pre-existing comorbidities. The prevalence of comorbidities in the study population is similar to that reported by Artero et al[13] (66%). Diabetes mellitus was found to be commoner comorbidity (41.7%) in the study population followed by hypertension (18.7%). The observation of this study was like that reported by A. Artero et al[14] in Spain which reported Diabetes mellitus to be a commoner comorbidity in their study population with prevalence of 32.7%. Rhee C et al[12] reported conducted a similar prospective observational cohort study in USA and reported solid cancer and other malignancies to be the most common underlying comorbidity. The above observation was in contrast the that of the present study. The difference in the prevalence can be attributed to more prevalence of Diabetes mellitus in Indian population

as well lack of awareness and screening for malignancies. However, none of the studies observed any significant association between comorbidities and gender.

It is observed that mortality was 5.3% amongst the group of patients with no comorbidities and mortality of 32% was observed in group of patients with history of comorbidities. The above observation was like that reported by Suarez De La Rica et al[15] which also reported increased mortality in subset of patients with comorbidities and diagnosed with sepsis.

Total 37 (49.3%) patients were reported to have respiratory system as the source of sepsis, therefore it being the commoner source of infection followed genitourinary system in 20 (26.7%) patients. A. Artero et al[13] also reported respiratory system (24.1%) as the commonest source of sepsis in their study population. However, the 2nd most common source of sepsis reported by them was gastrointestinal system in contrast to observations in this study population. Jain et al[11] reported respiratory system as the source of sepsis in 71% cases, however the study setting was predominantly a respiratory ICU. Clec'h.etal[16] also reported respiratory system to be the contributor to most of the cases (19%). Watanbe et al[17] also reported respiratory system to be commonest source of sepsis in their study. Rhee C et al[12] also observed pneumonia to be the most common presentation in their prospective cohort study. However, none of the studies found any association between system involvement and outcome.

The median serum PCT level observed in the study population is 3.7ng/mL (2.7-5.75) which was lower as compared to reported by Jain et al median serum PCT value of 6.9 (3.9-19.2). The median serum PCT level observed in the group of survivors in the present study population was 3.5 (2.25-4.35) and it was lower as compared to median 5.4 (3.5-12.8) in the survivor group reported by Jain et al [11]. Similarly median in the group of non survivors in the present study population 4.5 (3.67-6.3) was comparatively lower than that reported by Jain et al 13.1 (6.3-42). The mean serum PCT levels in survivors observed in present study 3.702±2.18 was significantly lower than that mean serum PCT value in group of non survivors 5.60±3.16 ('p' value =0.0026). this observation is like that reported by Karlsson et al[18] with mean serum PCT level in the group of survivors being 3.44±3.09 and that of non survivors was 10.04±2.89 (p value<0.05). Similar observations were made by Zhao et al[19] in their prospective study. They reported serum PCT levels of 8.15±12.74 among non survivors and 2.715±3.65 among survivors. Yangi et al[20] reported serum PCT levels of 10.1±18.0 ng/mL in the group of non survivors as compared to survivors 5.7±13.7ng/mL. thus, the serum PCT was higher among non survivors. However, the findings of the present study were in contrast to those of Anand et al [21], where they reported to lower PCT levels in non survivors as compared to survivors (11.56 vs 2.015). Huang P et al[22] in their study measured serum PCT levels on 1st, 3rd and 5th day of admission and recorded higher serum PCT values in the group of non survivors as compared to survivors. Mustafic et al[23] significant association between serum Procalcitonin levels and outcome ('p' vale <0.049). The study also reported serum PCT to be 50% sensitive and 98.53 % specific for predicting mortality in their study. Gupta S et al[24] had divided the study population in 3 groups namely control, culture positive and culture negative. Irrespective of the three groups, serum PCT levels was higher in non survivors as compared to survivors. The similarity between observations of the present study and those of previous studies helps us to conclude that serum procalcitonin can be used as prognostic marker in sepsis.

In the present study area under ROC for serum PCT for predicting mortality was 0.84. The serum PCT level of 5 ng/mL when used as cut off for predicting mortality had sensitivity of 92.6% and specificity of 70%. The serum PCT value of 6ng/mL had sensitivity of 89 % and specificity of 81% for predicting mortality.

Dolatabadi AA et al[25] evaluated procalcitonin serum levels in predicting sepsis patients' outcome (mortality vs survival) which found the highest sensitivity 24 hours after antibiotic administration. The area under curve for 6.5 ng/mL cut-off point for serum procalcitonin levels 24 hours after initiation of treatment was 0.789 (95% CI 0.717−0.862). It was able to do prediction with sensitivity of 67% and specificity of 80%

In a study by Mustafić et al[23] a cut off of 15.05 ng/mL PCT showed the best mortality prediction with AUC 0.92, with positive predictive value of 88.89%, negative predictive value of 89.33%, sensitivity 50%, specificity 98.53% and the accuracy of 89.29%.

Ryoo SM et al[26] found that the optimal cut-off values of PCT in receiver operating characteristic (ROC) curve was 17 ng/dL. The sensitivity, specificity, positive predictive value, and negative predictive value of PCT were 39.1%, 65.7%, 22.8%, and 80.5, respectively.

In the group of survivors, the mean APACHE II score was 29.09091±4.175 which was lower than the group of non-survivors and the mean APACHE II Score in this group was 35.34±8.67. Jain et al[11] reported mean APACHE II score in survivors as 21.9±7.1 which was lower than 28.6±7.1. Anand et al[21] reported higher APACHE II scores among non survivors a s compared to survivors (21.5 vs 29.28). Similarly, Mustafic et al[23] reported higher median APACHE II score in non survivors as compared to survivors (19 vs 11). In the present study median APACHE II Score in the group of non survivors was 37.5 (28.75-42.5) and in the group of survivors was 28 (25.75-33). The difference between the APACHE II score of the 2 groups is statistically significant (p value=0.0002). Similar difference was reported by Jain et al [11], and Artero et al [14]. Similarly, Dupleiss et al[27] noted mean APACHE II score of17.5±5.9 among non survivors which was higher as compared to 10.1±5.9 among survivors. Artero A et al[14] in their study observed APACHE II score to be significantly different between the two groups of survivors and non survivors. Similarity between findings of this study present study and the previous reports implies the significance of APACHE II score as an independent marker for prognosis in sepsis.

The mortality in group of patients with positive sample cultures was 45.3% as compared to 18.2% in the group of culture negative samples. Statistically significant association exists between culture positivity and outcome as observed in this study population. However, Jain et al[11] reported no significant association between culture and mortality. This spectrum of the sepsis needs to be investigated more to correlate and consider the association between the sample cultures and survival of patients diagnosed with sepsis

In the study the 70.7% patients had positive sample cultures as compared to 29.3% patients with negative sample cultures. Of the patients with positive sample cultures 88.7% patients had serum PCT values >2ng/mL as compares 11.3% patients with serum PCT values < 2 ng/mL. Of the patients with sterile sample cultures, 56% patients had serum PCT values > 2ng/mL and 44% patients had serum PCT values < 2ng/mL. A significant association was seen between serum PCT levels and sample culture growth. Sharma R et al[28] also reported higher serum PCT values in subjects with culture positive sepsis as compared to culture negative sepsis. Clec'h et al[16] also reported higher serum PCT values in patients with severe systemic infections as compared to patients with culture negative sepsis. Mustafic et al[23] also reported a strong relation between serum PCT and sample culture growth (p value<0.0001). The sensitivity of serum PCT for predicting infectious sepsis was 88.7% in this study as compared to 67% reported by Mustafic et al[26]. The Serum procalcitonin was found to be 44% specific for diagnosing a infectious as compared to 96% specificity reported in the above study. Huang P et al[22] also reported higher serum PCT levels in patients with culture positive sepsis as compared to culture negative sepsis (p ' value,<0.05). A systemic review and meta-analysis carried out on 30 studies by Wacker et al[29] (2013) reported that serum procalcitonin has a mean sensitivity of 0.77 and specificity of 0.79. According to Watanbe et al[17] the serum PCT was 74.5 % sensitive and 59% specific for detection of infection in sample cultures. The differences between values of sensitivity and specificity could be attributed to the difference in the sample size of the studies. However, we can conclude that serum PCT is significant indicator of infectious sepsis.

Total 26 (34.7%) patients were diagnosed with sepsis of which 21 (92.3%) patients survived and 2 (7.7%) patients died. Total 26 (36.2%) patients were diagnosed with severe sepsis, of which 14 (53.9%) patients survived and 12 (46.1%) died. Total 23 (31.9%) patients were diagnosed with septic shock of which 9 (39%) patients survived and 14 (61%) patients died. The mortality rate in patients diagnosed with sepsis, severe sepsis and septic shock was 2.7%,, 16% and 18.7% respectively. The mortality rate was more in the patients diagnosed with septic shock and difference between the mortality rates of three groups is statistically significant (p value=0.000323). The increasing trend of mortality was observed in an survey carried out by Mayr et al[30] in 2014 in USA where they recorded24% mortality in patients diagnosed with sepsis, 50% mortality in patients diagnosed with severe sepsis and septic shock respectively. Similar trends were seen in an retrospective study conducted by Kaukonen et al[31] in New Zealand and Australia over the period of 2000 to 2012. Similarities between observations of the present study and previous notable reports attach importance to association between the severity of disease and mortality and implies need of quicker management and intensive approach.

The serum PCT values found in patients severe sepsis were higher than those found in patients diagnosed with sepsis (3.6±0.99 vs 2.73±0.869; 'p' value=0.0002). The serum PCT values found in patients diagnosed with septic shock were significantly higher than the serum PCT levels found in patients diagnosed with severe sepsis (11.3±19.1 vs 3.6±0.99; 'p' value=0.031). The mean serum PCT level recorded in patients with septic shock was higher than that recorded in sepsis (11.3±19.1vs 2.73±0.869; p value<0.018). Thus, we conclude that serum PCT levels go on increasing along the spectrum of sepsis, severe sepsis and septic shock. Dupleiss et al[27] too reported similar trends of serum PCT in their study (0.4±0.4 vs 6.5±15.6 vs 20.7±34.4). Mustafic et al[23] also recorded higher serum procalcitonin levels as the severity of sepsis increased. Suarez Santamaria et al[32] in their study also concluded that positive correlation existed between the serum PCT levels and severity of the sepsis. Huang P et al[22] to reported increase in serum PCT levels in the patients as the sepsis became more severe. Yang Yi et al[20] observed higher values of serum PCT in patients with septic shock (14.29±22.36) as compared patients diagnosed with sepsis (3.55±6.39). Though they classified the study population in two groups instead of three according to present definition of sepsis, higher PCT values in patient with septic shock as compared to sepsis signify the importance of serum PCT in indicating the severity of the disease. Duplessis et al[27] in their study observed higher values of serum PCT in patients with septic shock as compared to those diagnosed with severe sepsis and sepsis.

Total 22 (32%) patients had APACHE II score <30, of which 14 (63.6%) patients had serum PCT level >2ng/mL and 8 (36.4%) patients had serum PCT level <2ng/ml. Total 53 (70.7%) patients had APACHE II score >30 of which 47 (88.7%) patients had serum PCT level>2ng/mL and 4 (7.8%) patients had serum PCT serum PCT level <2ng/ml. Of 61 patients with serum PCT>2ng/mL, 47 (77%) patients had APACHE II score >30 as compared to 14 (22.9%) patients who had APACHE II score <30. Significant association exists between APACHE II score and serums procalcitonin levels (p value <0.05). Thus 88.7% patients with APACHE II score >30 had serum PCT values > 2ng/mL. Similar results were reported by other studies. Khan et al[33] reported that 93.8% patients with APACHE II score had raised serum PCT levels. Corsino Ray et al [34], reported serum PCT was to be high in 92.6%. Szedejesi J et al[35] also recorded strong association between serum PCT and APACHE II score ('p' value<0.0001). Huang et al[36] also concluded that serum PCT was strongly associated with APACHE II for prediction of prognosis in patients with sepsis. Lopez et al[37] too reported a positive correlation between serum PCT and APACHE II score, higher values of serum PCT associated with high APACHE II scores ('p'value<0.001). Wang S et al[38] also recorded a strong association between serum PCT and APACHE II score ('p'value<0.001). Duplessis et al[27] recorded a modest correlation (0.41) between serum PCT and PAACHE II scoring system. Thus we can conclude that serum PCT combined with APACHE II score can be a better marker for predicting prognosis as well as diagnosis of the sepsis.

CONCLUSION

From this study we conclude that the cases fatality rate of sepsis cases in medical intensive care unit in our hospital was 37.3%. The mortality rate was significantly higher patients with comorbidities, especially cases with respiratory or CNS involvement. The serum PCT levels were significantly higher in the group of non survivors as compared to group of survivors. Higher APACHE II score associated with higher mortality. Serum PCT levels go on increasing along the spectrum of sepsis. A PCT level was significantly

hire in culture positive cases compare to sterile cases. Finally, this study conclude that serum PCT level is useful investigation in sepsis cases to predict mortality.

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