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Role of Serum Pro-Calcitonin Levels and Sequential Organ Failure Assessment Score (Sofa Score) in Assessing the Sepsis

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SUMMARY

Introduction: Serum pro-calcitonin is a biomarker that specifically increases in response to bacterial infections, providing a valuable diagnostic indicator in the context of sepsis. Pro-calcitonin is ubiquitously and uniformly expressed in multiple tissues throughout the body in response to sepsis. In healthy conditions, its level in circulation is barely detectable. PCT concentration start to rise from 3-4 hrs after an endotoxins challenge, peak about 6 hrs and remain increased for over 24 hours.

Materials and Methods: The present prospective interventional study was conducted at the department of Internal Medicine Tirath Ram Shah Hospital, Delhi, over a period of 2 years from July 2022- July 2024 among patients transferred to ICU after initial qSOFA assessment (>2) to study the correlation of pro-calcitonin level with severity of sepsis and septic shock by using SOFA score. Eight- seven consecutive patients admitted to the ICU with sepsis between 18 years and below 70 years fulfilling the inclusion and exclusion criteria were included in the study. m PCT levels and sepsis outcome variables. A Predesigned and pretested schedule to collect data on sociodemographic variables, laboratory parameters, and follow up data till discharge. Telephonic interviews of patients or relatives/ caregivers were used to collected data on prognosis 3 months following discharge. Collected data were entered into MS Excel (Microsoft Corp.), cleaned and analyzed using SPSS version 20, and presented using the principles of descriptive and inferential statistics.

Results: The commonest age group in the study population were between 50-59 years of age (35.6%) while the least common age group were 60-69 years (20.7%).The mean age of the study population was 50.4 years with a standard deviation of 9 years. The minimum and maximum age of patients included in the study were 34 and 65 years. Almost half (49.4%) of the study population were female and 50.6% male.The most common comorbidity in the study was diabetes (36.8%) followed by liver disease(27.6%) and hypertension(9.2%). Asthma was seen in only 2.3% of the study population.64.4% population had serum lactate < 4 mmol/L and the rest had a value more than equal to 4 mmol/L.After 72 hours of incubation there was growth in blood culture in 73.6% of cases and 26.4% had no growth.57.8% of the cultures revealed a gram-positive organism with staphylococcus hominis as the predominant organism (25%) and 42.1% of cultures revealed Gram-negative organisms with Escherichia coli being the most commonly cultured Gram-negative organism (14.1%)The mean SOFA score of the present cohort was 7.0 (4.5) The mean pro-calcitonin levels in the present cohort was 22.6(29.6) mg/dl.Pro-calcitonin levels in patients revealed a strong positive correlation with their SOFA score55.2% of the study population survived and were discharged and 44.8% patients died during admission.At 3-month follow-up among the patients who were discharged from the hospital 50% of the patients were alive and 50% were not.The mean (SD) pro-calcitonin value was higher in patients with death [37.7 (36.4)] than in patients that were discharged [10.4 (13.8], the differences being statistically significant. The mean SOFA score of patients that died was significantly higher [9.9(3.8)] than those that were discharged [4.6 (3.5)].

Conclusion: The present study shows that there is a strong positive correlation of pro-calcitonin level with the SOFA scores. Higher SOFA scores are associated with higher Pro-calcitonin levels. The positive correlation is seen in both survivors and non-survivors of the episode. The mean pro-calcitonin levels and SOFA scores are significantly higher in patents than that of patients that were discharged after the episode of admission to the ICU.

I. INTRODUCTION

Sepsis is common and deadly disease, defined as a “systemic inflammatory response to infection” is one of the leading causes of morbidity and mortality. The global impact of sepsis is twice that of previous estimate with an estimated 48.9million incident cases reported worldwide. Sepsis related deaths represent 19.7% of all global deaths, of which 85% occur in low- and moderate-income countries. India currently tackles approximately 11 million cases of sepsis every year claiming to more than 3 million lives every year.

Sepsis is a multifactorial host response to pathogen enhanced by endogenous factors. Pro-inflammatory reactions directed at eliminating pathogen are responsible for "collateral" tissue damage in sepsis, whereas anti-inflammatory responses are implicated in enhanced susceptibility to secondary infections that occurs later in course. Mortality rates as a result of sepsis are associated with a pattern characterized by progressive dysfunction or failure of non-pulmonary organ systems, including neurologic, coagulation, and renal functions. Early diagnosis and prompt management can reduce mobility and mortality. The wide and variable presentation of sepsis makes the diagnosis very difficult. Thus, precise clinical assessment and diagnostic approach for earlier identification and quantification of sepsis is much needed. The SOFA score, developed to assess the extent of a patient's organ function or rate of failure, is an essential tool in monitoring sepsis progression. SOFA score i.e. Sepsis related Organ Failure Assessment score, has been predominantly used now days. Six organ systems are evaluated on a scale of 1-4 each. This score assesses the functions of respiratory, cardiovascular, neurological, renal coagulation and hepatic systems. According to dysfunctions of these organs it is graded between 0 to 24.[3] An increase in the SOFA score over time is associated with higher mortality, making it an effective tool for prognostication in septic patients. The score's dynamic nature allows clinicians to track the progression of sepsis and make necessary adjustments to therapeutic strategies, ultimately guiding the intensity and type of interventions required.[3,]Various biomarkers such as, C-reactive protein (CRP), neutrophils, macrophage migration inhibitory factor (MMIF) soluble urokinase-type plasminogen activator receptor(suPAR), interleukin-6 (IL-6), and triggering receptor expressed on myeloid cells-1 (TREM-1), have been studied as a biomarker of sepsis, but none has been shown reliability to diagnose sepsis.

Pro-calcitonin is a 116 amino acid polypeptide which is produced by Para follicular cells of thyroid and by neuroendocrine cells of lung and intestine in normal healthy individuals.[5] It is a biologically active precursor of the calcium-modulating hormone calcitonin. Serum pro-calcitonin is a biomarker that specifically increases in response to bacterial infections, providing a valuable diagnostic indicator in the context of sepsis. Pro-calcitonin is ubiquitously and uniformly expressed in multiple tissues throughout the body in response to sepsis. In healthy conditions, its level in circulation is barely detectable. PCT concentration start to rise from 3-4 hrs after an endotoxins challenge, peak about 6 hrs and remain increased for over 24 hours. PCT can be used for early detection of sepsis and prediction of outcome.

The present study used Pro-calcitonin (PCT) and sequential organ failure assessment (SOFA) as a bedside investigation to identify patients who were likely to develop or who were already in sepsis, as defined by SOFA score

Pro-calcitonin

Pro-calcitonin (PCT), a protein consisting of 116 amino acids, is the peptide precursor of calcitonin. Calcitonin is a hormone that is synthesized by the para-follicular C cells of the thyroid gland It is involved in calcium homeostasis in the body. Pro-calcitonin is formed from endopeptidase-cleaved pre-pro-calcitonin. The reference value for pro-calcitonin in adults is less than 0.1 ng/mL, and levels greater than 0.25 ng/mL can indicate the presence of an infection.

Laboratory estimation of pro-calcitonin helps in the diagnosis of sepsis and is also used to guide and monitor antibiotic therapy. Pro-calcitonin (PCT) is frequently said to be superior to C- Reactive Protein (CRP) because it is more specific for sepsis and bacterial infection. PCT rises earlier and returns to normal concentrations faster than CRP, enabling for earlier identification and better monitoring of disease progression. Patients with localized infection have lesser increases of pro-calcitonin in comparison to those with generalized sepsis, severe sepsis and septic shock. A declining concentration of pro-calcitonin usually reflects resolution of sepsis.

Aims and objective

To study the correlation of pro-calcitonin level with severity of sepsis and septic shock by using SOFA score.

II. MATERIALS AND METHODS

Study type and design: The present study was a prospective interventional study.

Study setting: The study was conducted at the department of Internal Medicine Tirath Ram Shah Hospital, Delhi.

Study duration: The study was conducted over a period of 2 years from July 2022- July 2024.

Study population: Study population consisted of in-patient subjects admitted to hospital and transferred to ICU after initial qSOFA assessment (>2).

International Journal Dental and Medical Sciences Research
Volume 7, Issue 2, Mar - Apr 2025 pp 288-302 www.ijdmsrjournal.com ISSN: 2582-6018

Inclusion criteria:
1. Age above 18 years and below 70 years.
2. Patients with suspicion of sepsis with qSOFA score of 2 or more

Exclusion criteria:
1. History of recent surgeries
2. Trauma
3. Burns
4. Cancer patients.
5. People living with HIV
6. Patients who didn't give consent

Sample size: the sample size was calculated based on the formula for sample size for a single proportion

$$n = (Z_{\alpha/2})^2 * p(1-p)/ E^2$$

where Zα/2= value of standard normal deviate, p= proportion of patients with expected outcome, E = margin of error.
Using anticipated proportion of in-hospital mortality among ICU admissions with sepsis (p)= 35%, margin of error (E)=10%, alpha error =5%, the minimum calculated sample size was 87.

Sampling techniques: All consecutive patients admitted to the ICU with sepsis were screened and all patients fulfilling the inclusion and exclusion criteria were included in the study.
Study tools and variables

- Predesigned and pretested schedule to collect data
- Outpatient records
- Bed Head tickets
- Discharge summary/ Death certificates
- Pathological and microbiological investigation reports
- Mobile phone

Study variables

Age	Sex	Co-morbidities
Serum lactate	Growth on culture	Organism
Hemoglobin	WBC	Hospital stay (in days)
Pro-calcitonin	PaO2/FiO2	Platelets (X10^3)
Liver Bilirubin mg/dl	SBP (mmHg)	DBP (mmHg)
MAP (mmHg)	GCS Score	Creatinine mg/dl
SOFA Total score	Outcome at discharge	Outcome at 3 months

Study technique: All adult patients admitted in intensive care unit of Tirath Ram Shah hospital Delhi, India who were detected to have sepsis at admission and those who satisfy the inclusion and exclusion criteria were included in study after written informed consent.Demographic data, chief complaint on presentation and vital data were recorded.A complete laboratory investigation were carried out. Serum pro-calcitonin was measured by Immunometric assay method. Blood culture on admission from 2 different sites before administration of antibiotics, culture from the suspected source of infection such as urine, sputum, and cerebrospinal fluid (in suspected cases) on admission were done to establish the organism responsible. SOFA were done on day 1, 4 and 7 and/or at time of discharge. All patients were treated according to the standard institutional protocol for management of sepsis and septic shock. All patients included in the study were followed up during their course in the hospital and patients that are discharged were be followed up at 3 months through telephonic interview with them/ their caregivers to record outcome.

Operational definition Patient were assessed for sepsis by the presence of Organ Dysfunction which were defined as an acute change in total SOFA score ≥ 2 point.

International Journal Dental and Medical Sciences Research
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Scales used in the study
Sofa scores

Sequential [Sepsis-Related] Organ Failure Assessment (SOFA) Score

System	0	1	2	3	4
Respiration PaO2/FiO2, mmHg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation Platelets, $x10^3$/uL	≥150	<150	<100	<50	<20
Liver Bilirubin, mg/dL (umol/L)	<1.2 (20)	1.2 - 1.9 (20 - 32)	2.0 - 5.9 (33 - 101)	6.0 - 11.9 (102 - 204)	>12.0 (204)
Cardiovascular	MAP ≥70mmHg	MAP <70mmHg	Dopamine <5 or Dobutamine (any dose)	Dopamine 5.1 - 15 or Epinephrine ≤0.1 or Norepinephrine ≤0.1	Dopamine >15 or Epinephrine >0.1 or Norepinephrine >0.1
CNS GCS Score	15	13 - 14	10 -12	6 - 9	<6
Renal Creatinine, mg/dL (umol/L) Urine Output, mL/d	<1.2 (110)	1.2 - 1.9 (110 - 170)	2.0 - 3.4 (171 - 299)	3.5 - 4.9 (300 - 440) <500	>5.0 (440) <200
*Catecholamine Doses = ug/kg/min for at least 1hr					

Glasgow coma scale

Component tested	Score
Eye response	
Eyes open spontaneously	4
Eye opening to verbal command	3
Eye opening to pain	2
No eye opening	1
Motor response	
Obeys command	6
Localises pain	5
Withdraws from pain	4
Flexion response to pain	3
Extension response to pain	2
No motor response	1
Verbal response	
Oriented	5
Confused	4
Inappropriate words	3
Incomprehensible sounds	2
No verbal response	1

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III. STATISTICAL ANALYSIS

Collected data were entered into MS Excel (Microsoft Corp.), cleaned and analyzed using SPSS version 20. ((IBM-SPSS-version 20). Data were presented using the principles of descriptive and analytical statistics. Continuous data were presented as mean ± standard deviation, and comparison between data between groups were done by unpaired student's t test. A p value of less than 0.05 was considered statistically significant. Correlation between continuous variables demonstrated by the scatter plot and analyzed using the Pearson's correlation coefficient.

Ethical considerations: The protocol of thesis was submitted and subsequently approved by the Institutional Ethics Committee of Tirath Ram Shah Hospital, Delhi. All patients were ensured of confidentiality and anonymity of data. An informed consent was taken for each patient/ caregivers (in case the patient was not able to give consent) before data collection.

IV. RESULTS

Table 1: Distribution of study participants by age groups (n=87)

Age groups	Frequency	Percent
30-39	14	16.1
40-49	24	27.6
50-59	31	35.6
60-69	18	20.7
Total	87	100.0

The commonest age group in the study population were between 50-59 years of age (35.6%) while the least common age group were 60-69 years (20.7%).

Table 2: Descriptive of age of the study population (n=87)

Variable	Mean	Standard deviation	Minimum	Maximum
Age	50.4	9.0	34	65

The mean age of the study population was 50.4 years with a standard deviation of 9 years. The minimum and maximum age of patients included in the study were 34 and 65 year

Table 3: Distribution of study participants based on sex (n=87)

Sex	Frequency	Percent
Female	43	49.4
Male	44	50.6
Total	87	100.0

Almost half (49.4%) of the study population were female and 50.6% male

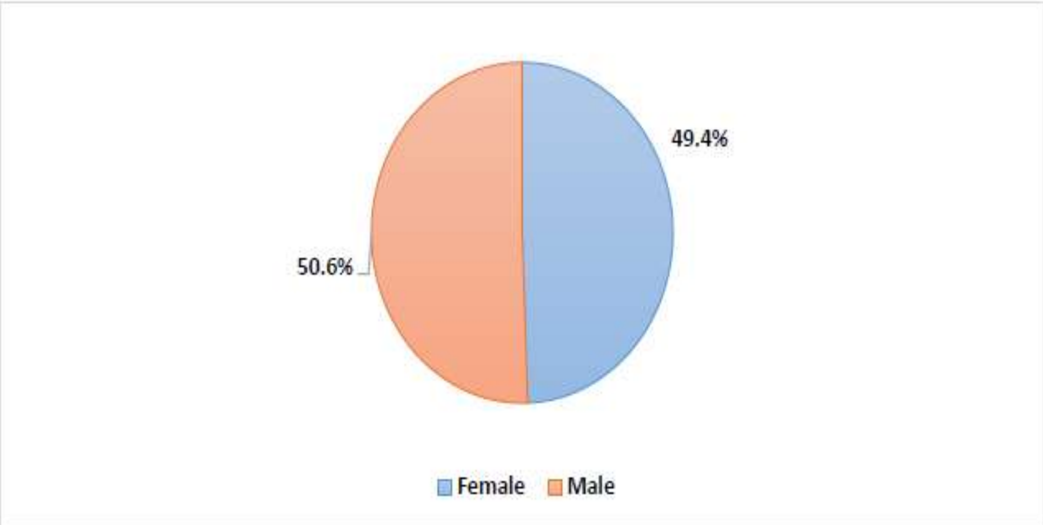

Figure 1 : Pie chart showing distribution of study participants based on sex (n=87)

Table 4: Distribution of patients based on diagnosed co-morbidity before admission (n=87)

Comorbidity	Frequency	Percent
Diabetes	32	36.8
Hypertension	8	9.2
IHD	5	5.7
Asthma	2	2.3
COPD	7	8.0
Liver disease	24	27.6
CKD	13	14.9

International Journal Dental and Medical Sciences Research
Volume 7, Issue 2, Mar - Apr 2025 pp 288-302 www.ijdmsrjournal.com ISSN: 2582-6018

*Numbers may add up to more than 87 (>100%) because of the presence of more than one co-morbidity in some patients. The most common comorbidity in the study was diabetes(36.8%) followed by liver disease(27.6%) and hypertension(9.2%). The least commonly seen comorbidity was asthma(2.3%).

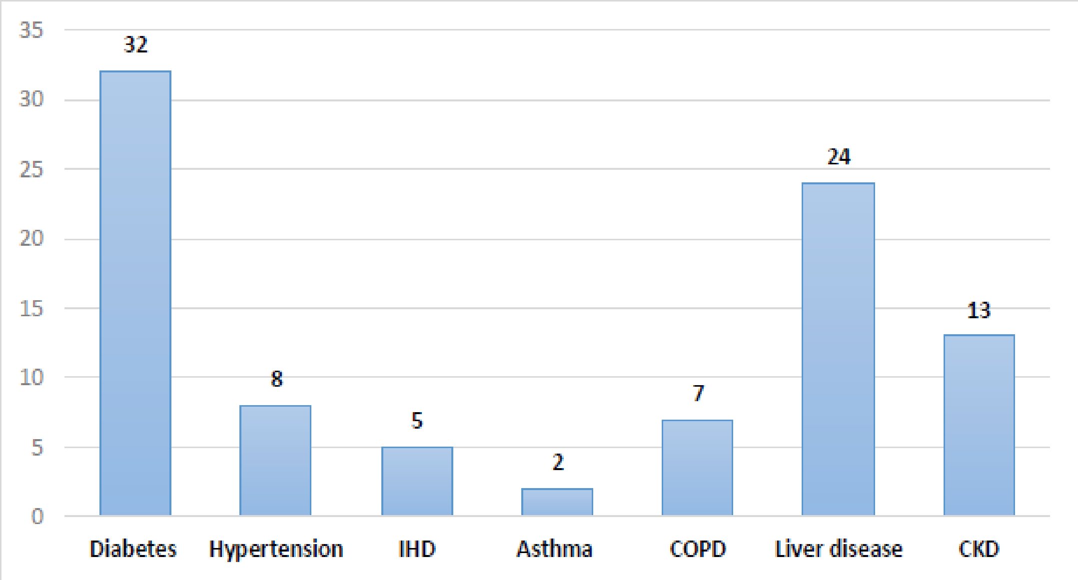

Figure 2: Simple bar diagram showing the distribution of patients based on diagnosed co-morbidity before admission (n=87)

Table 5: Distribution of patients based on serum lactate levels (n=87)

Serum lactate (mmol/L)	Frequency	Percent
<4	56	64.4
≥4	31	35.6
Total	87	100.0

Conclusion: 64.4% population had serum lactate < 4 mmol/L and the rest had a value more than equal to 4 mmol/L

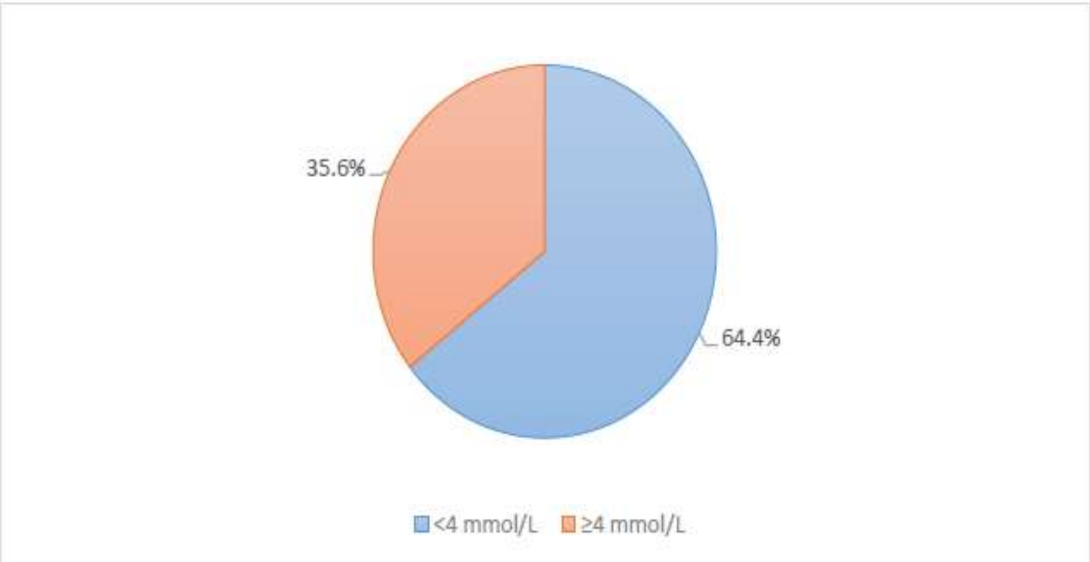

Figure 3: Pie chart showing distribution of patients based on serum lactate levels (n=87)

Table 6: Distribution of study participants based on the presence of growth on blood culture (n=87)

Growth on blood culture	Frequency	Percent
No growth	23	26.4
Growth	64	73.6
Total	87	100

After 72 hours of incubation there was growth in blood culture in 73.6% of cases and 26.4% had no growth

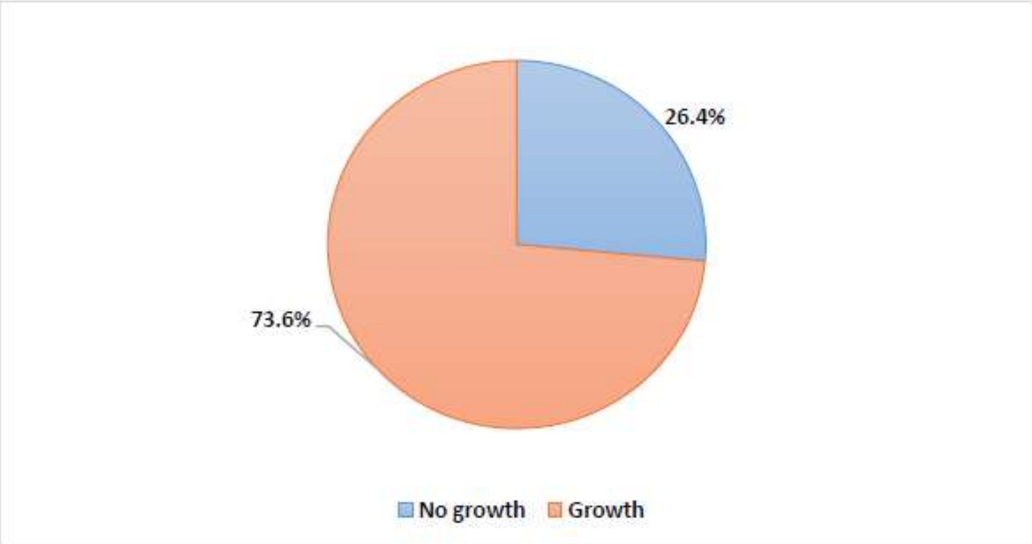

Figure 4: Pe chart showing the distribution of study participants based on the presence of growth on blood culture (n=87)

Table 7: Distribution of organisms isolated on blood culture (n=64)

Organisms isolated on blood culture	Frequency	Percent
Gram positive organisms	37	57.8
Enterococcus faecalis	2	3.1
Staphylococcus aureus	6	9.4
Staphylococcus epidermidis	4	6.3
Staphylococcus haemolyticus	7	10.9
Staphylococcus hominis	16	25.0
Streptococcus spp	2	3.1
Gram negative organisms	27	42.1
Escherichia coli	9	14.1
Klebsiella pneumoniae	4	6.3
Proteus vulgaris	1	1.6
Pseudomonas spp	3	4.7
Acinetobacter spp	4	6.3
Burkholderia cepacian	3	4.7
Enterobacter spp	3	4.7
Total	64	100.0

Conclusion: 57.8% of the cultures revealed a gram-positive organism with staphylococcus hominis as the predominant organism(25%) and 42.1% of cultures revealed Gram-negative organisms with Escherichia coli being the most commonly cultured Gram-negative organism (14.1%)

International Journal Dental and Medical Sciences Research
Volume 7, Issue 2, Mar - Apr 2025 pp 288-302 www.ijdmsrjournal.com ISSN: 2582-6018

Table 8: Mean (SD) of continuous variable included in the study (n=87)

Variables	Age
Age	50.4 (9.0)
Haemoglobin	10.0 (1.2)
WBC	95.2 (10.9)
Hospital stay (in days)	7.5 (2.4)
Pro-calcitonin	22.6(29.6)
PaO2/FiO2	390.9 (102.6)
Platelets (X10^3)	1.3(0.7)
Liver Bilirubin mg/dl (µm/L)	3.6 (3.6)
SBP (mmHg)	111.0 (40.2)
DBP (mmHg)	71.4 (26.1)
MAP (mmHg)	84.5 (29.0)
GCS Score	11.9 (3.5)
Creatinine mg/dl (µm/L)	2.8 (2.9)
SOFA Total score	7.0 (4.5)

The mean (standard deviation) of variables used in the study.

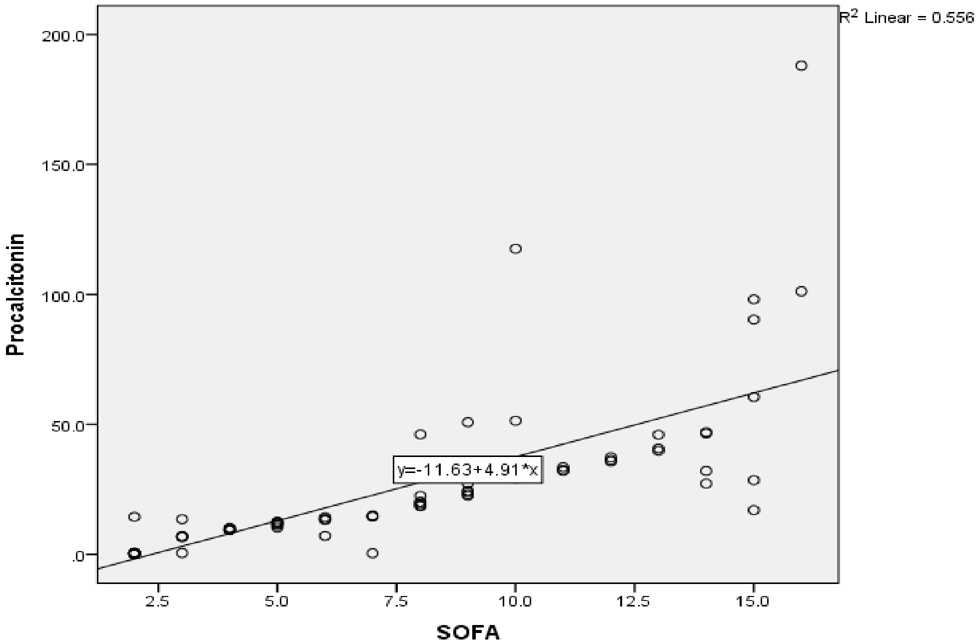

Figure 5: Scatterplot showing correlation between Pro-calcitonin and SOFA (n=87)

Table 9: Correlation between Pro-calcitonin and SOFA

Correlation	Correlation coefficient	p value
Pro-calcitonin-SOFA	0.746	0.000*

*Statistically significant

Conclusion: Pro-calcitonin levels in patients revealed a strong positive correlation with their SOFA score

International Journal Dental and Medical Sciences Research
Volume 7, Issue 2, Mar - Apr 2025 pp 288-302 www.ijdmsrjournal.com ISSN: 2582-6018

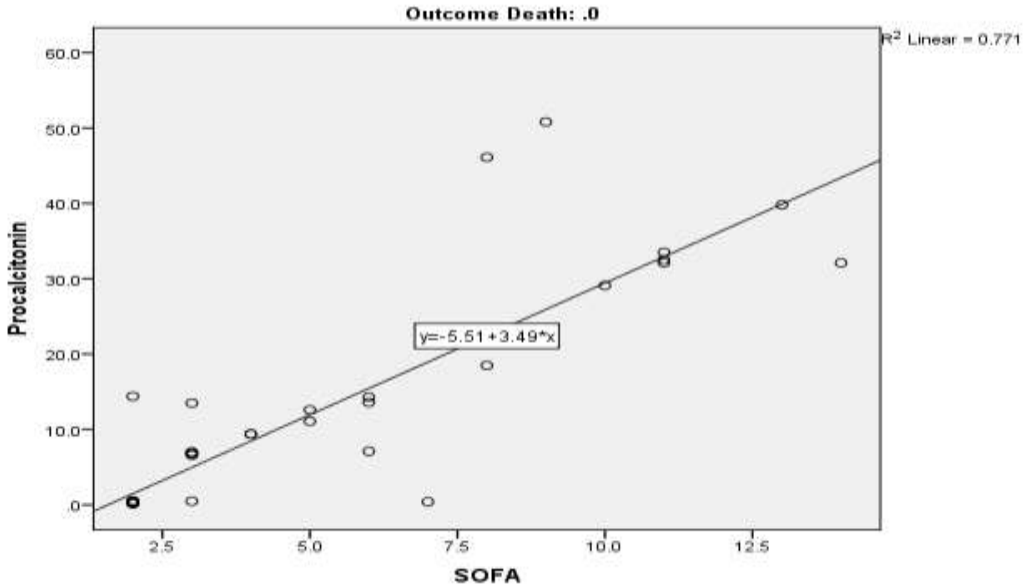

Figure 6: Scatterplot showing correlation between Pro-calcitonin and SOFA in survivors (n=48)

Table 10: Correlation between Pro-calcitonin and SOFA in survivors

Correlation	Correlation coefficient	p value
Pro-calcitonin-SOFA	0.878	0.000*

*Statistically significant

Conclusion: Pro-calcitonin levels in survivor patients revealed a strong positive correlation with their SOFA score

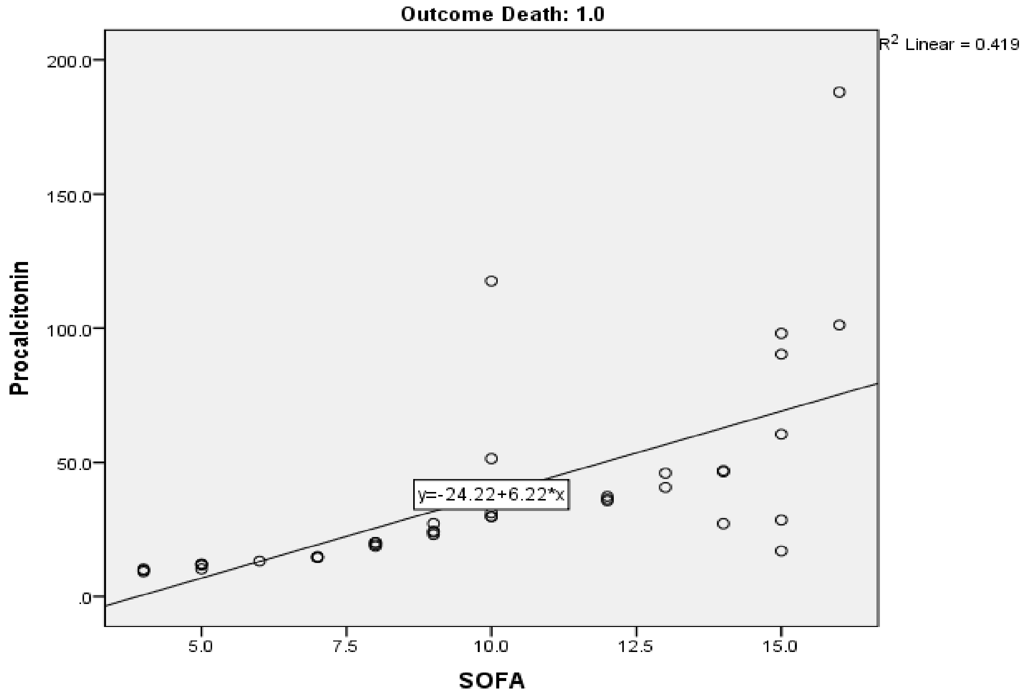

Figure 7: Scatterplot showing correlation between Pro-calcitonin and SOFA in non- survivors (n=39)

International Journal Dental and Medical Sciences Research
Volume 7, Issue 2, Mar - Apr 2025 pp 288-302 www.ijdmsrjournal.com ISSN: 2582-6018

Table 11: Correlation between Pro-calcitonin and SOFA in survivors

Correlation	Correlation coefficient	p value
Pro-calcitonin-SOFA	0.647	0.000*

*Statistically significant

Conclusion: Pro-calcitonin levels among patients who did not survive revealed a positive correlation with their SOFA score

Table 12: Distribution of study participants based on outcome n(=87)

Outcome	Frequency	Percent
Discharged	48	55.2
Death during admission	39	44.8
Total	87	100.0

Conclusion – 55.2% of the study population survived and were discharged and 44.8% patients died during admission

Table 13: Distribution of patients based on outcome at 3 months following discharge (n=48)

Outcome	Frequency	Percent
Alive	24	50.0
Death within 30 days of discharge	24	50.0
Total	48	100.0

Conclusion – At 3-month follow-up among the patients who were discharged from the hospital 50% of the patients were alive and 50% were not

Table 14: Comparison between pro-calcitonin levels between survivors and non-survivor sepsis patients (n=87)

Variables	Discharge	Death	Independent sample t test	p value
Pro-calcitonin	10.4 (13.8)	37.7 (36.4)	-4.782	0.000*
SOFA score	4.6 (3.5)	9.9 (3.8)	-6.902	0.000*

*Statistically significant

The mean (SD) pro-calcitonin value was higher in patients with death [37.7 (36.4)] than in patients that were discharged [10.4 (13.8)], the differences being statistically significant. The mean SOFA score of patients that died was significantly higher [9.9(3.8)] than those that were discharged [4.6 (3.5)].

V. DISCUSSION

Sepsis is a life-threatening organ failure caused by an infection-related dysregulated host response, affecting millions of people worldwide annually. It is the primary cause of serious disease and mortality, and survivors often develop post-sepsis syndrome, a chronic disability. The World Health Organization designated sepsis a global health priority in 2017, urging member nations to reduce its financial and social costs. Sepsis epidemiological research primarily comes from high-income countries, with estimates showing 48.9 million cases in 2017, leading to 11.0 million fatalities. Low- and middle-income countries (LMICs) had the highest rate of sepsis-related deaths, accounting for 85% of all cases. Addressing the sepsis burden requires understanding the prevalence, death rates, and microbiologic characteristics of sepsis at regional and national levels.[9] Biomarkers can predict sepsis effects, guide antibiotic therapy, assess patient response, and determine sepsis severity. PCT is a more reliable biomarker for bacterial infections-related SIRS, sepsis, and septic shock.

In the present study, 87 candidates with a diagnosis of sepsis were enrolled after fulfilling the inclusion and exclusion criteria after obtaining written informed consent. Along with all routine hematological and biochemical parameters as per the institutional management protocol, the pro-calcitonin(PCT) level in all study participants was determined. All candidates were scored based on SOFA scoring and their outcome was noted in the form of death or hospital discharge. Three months

International Journal Dental and Medical Sciences Research
Volume 7, Issue 2, Mar - Apr 2025 pp 288-302 www.ijdmsrjournal.com ISSN: 2582-6018

later follow-up of all the enrolled patients was done and the number of survivors at three months was noted.

Of the 87 patients included in the study, 50.6%(44) were males and 49.4%(43) were females. Shinde et al in 2023 conducted a prospective cohort study on 80 patients >18 years of age with suspected sepsis presenting to the emergency room within 24–36 hours of illness. In their study 58.7% population was male and 41.2% were female. Sakr et al. reported that the prevalence of sepsis in males was higher than in females due to the increased levels of estradiol in females that improve immune function. These findings corroborate well with our study findings.

The most common comorbidity in the present study was diabetes(36.8%) followed by liver disease(27.6%) and hypertension(9.2%). The least commonly seen comorbidity was asthma(2.3%). Mattaparathi et al, in a study done in 2018 on 56 consecutive patients admitted to the ICU found the most common co-morbidities associated were diabetes mellitus (DM) in 45%, hypertension (HTN) in 40%, respiratory diseases in 10% and others in 5% cases. In their study, Shinde et al[5] found that common co-morbidities associated were DM (75%), hypertension (32.5%), chronic kidney disease (17.5%), obstructive airway disease (16%), and coronary artery disease (15%).

Serum lactate levels play a crucial role in prognosticating outcomes and mortality in sepsis patients. Research shows a correlation between elevated lactate levels and increased fatality rates. Serum lactate levels are similar to standard ICU scores like SOFA and APACHE IV, and anion gap values are significant predictors of death. Blood lactate/albumin ratio is linked to increased mortality and hospital stay in sepsis patients, suggesting it may be a predictive marker.[36] Patients with SOFA sepsis are more likely to have poly microbial infections, with the lungs, abdomen, skin/soft tissues, and urinary tract being the most frequently reported sites of infection.

Pradhan et al, conducted a prospective descriptive cross-sectional study at a tertiary care center among patients with sepsis presenting to the ICU. Among 53 sepsis patients, the mean serum lactate level in sepsis patients was 2.84+2.02.5 Out of 30 male patients, 15 of them had low lactate levels (lactate level < 2.5 mmol/L), 9 had intermediate lactate levels (2.5 to 3.99 mmol/L) and 6 had high lactate levels (> 4 mmol/L). Among 23 female patients, 13 had low lactate levels, 6 had intermediate lactate levels and 4 had high lactate levels. A similar study by Batajoo et al, in 2014 on a total of 94 patients showed abnormal Lactate levels in 80% among which 29% had intermediate lactate levels and half of them had high lactate levels which were unlike our findings which showed that 28.3% had intermediate and 18.9% had high lactate level. In our study 64.4%(56) population had serum lactate < 4 mmol/L and the rest 35.6%(31) had a value more than equal to 4 mmol/L which correlates well with findings of similar studies conducted elsewhere in the literature.

The gut microbiome plays a crucial role in sepsis, with disruptions leading to dysbiosis, and increasing mortality rates. This dysbiosis increases intestinal permeability, a dysregulated immune response, and the growth of pathogenic bacteria. Patients with sepsis identified by the Sepsis-3 criteria (SOFA score) are more likely to be blood culture-positive. The majority of pathogens responsible for sepsis are gram-positive bacteria, with a higher frequency in the SOFA sepsis group. Patients with SOFA sepsis are more likely to have poly microbial infections, with Staphylococcus aureus, poly microbial bloodstream infections, and an unidentified group linked to higher 28-day mortality.

Vendeimiato et al in a retrospective study on 1,017 patients who met the inclusion criteria for sepsis, obtained 2.27 samples/patient an found 21% samples positive for microbiological growth. These 489 positive samples, (21% positive) were isolated from 337 patients (33.13%). The prevalent microorganisms were coagulase-negative Staphylococcus (CNS) (15.87%), Escherichia coli (13.0%), Staphylococcus aureus (11.7%), Klebsiella pneumoniae (9.8%), Enterobacter sp (9.5%), Acinetobacter baumannii (9.2%), Pseudomonas aeruginosa (5.7%) and Candida sp (5.1%).

As per the SOAP study, in sixty percent of the sepsis patients, the cultures were positive. Of the patients, 40% had isolated Gram-positive bacteria, 38% had isolated Gram-negative bacteria, and Fungi from 17% and mixed infections from 18%, respectively. The most prevalent Gram-negative organisms were Escherichia coli (13%) and Pseudomonas species (14%), with methicillin-resistant Staphylococcus aureus recovered from 14% of cultures.

The EPIC II study analyzed data from 13,796 adult patients in 1265 intensive care units across 75 countries. Of the 14,414 patients, 51% were infected, and 71% were taking antibiotics. The majority had respiratory illnesses, with 64% having positive microbiological cultures. The study found that patients with longer stays in the ICU had higher infection rates, particularly from resistant bacteria. Our Study had a culture positivity rate of 73.6%.In our study, Gram-positive organisms dominated slightly over the Gram-negative ones. Among the gram-positive organisms, the most prevalent organism was Staphylococcus hominins (25%), and among the Gram-negative organisms, the most abundant was Escherichia coli (14.1%).

Table : Showing comparison of microbiological positivity rate and profile of our study with the SOAP study and EPIC II study

Study	Culture positivity	Gram positive organisms
SOAP study	60%	40%
EPIC II	69%	46.80%
Current study	72%	57.80%

Pro-calcitonin is a useful marker for sepsis diagnosis and for estimating the severity and mortality of the illness. Although pro-calcitonin is more specific for bacterial infections, viral infections, and non-infectious inflammatory diseases also cause a rise in it. The half-life of PCT is around 24 hours, and it is detectable 3.4 hours after infection, peaking at 6-7 hours.

According to Vamseedar et al, the SOFA score and serum pro-calcitonin can be used to gauge the severity of sepsis, which can help with early intervention and avert negative consequences. Similar to our findings, every sepsis patient in his study had a high PCT and SOFA score. Pro-calcitonin was shown to be raised over the cutoff of 0.57 ng/mL in 100% of the patients, which supports the suggestion by Ashitha et al, that it is a good indicator of bacterial infection. In our investigation, the average PCT value was 5.05 ng/mL. Pro-calcitonin levels were able to distinguish between survivors and non-survivors and were an independent predictor of mortality.

In the study by Shinde et al[5], the average SOFA score of survivors was 6.1 ± 1.93 , while the average score for non-survivors was 8.3 ± 2.13. In survivors, the average PCT level was 3.7 ± 1.5, while in non-survivors, it was 6.4 ± 3.13. In our study, the SOFA score and PCT levels among survivors 10.4(13.8) and 4.6 (3.5) and non-survivors 37.7(36.4) and 9.9(3.8) respectively.

A retrospective analysis Miro M et al,[28] of all patients treated for peritonitis who were later hospitalized in the institution's intensive care unit revealed similar results. Pro-calcitonin levels and the SOFA score were noted at the time of ICU admission as well as at the 24 and 48-hour points. All PCT values and the SOFA score showed a global linear correlation. Castelli et al,[26] in 2006 conducted a prospective observational study on patients admitted to a medico-surgical ICU. The study analyzed 255 clinical occurrences, including 111 sepsis/SS, 49 trauma, 45 SIRS, and 50 No-SIRS. The optimal concentration of sepsis was determined using ROC values of 0.88 for PCT, 0.74 for CRP, 0.8 for the Sepsis score, 0.74 for SOFA, and 0.62 for neutrophils. The optimal cut-off values for sepsis diagnosis were 0.47 ng/mL. In septic shock, PCT and SOFA were greater than in sepsis and severe sepsis. Patients with trauma who experience septic sequelae showed a significant early rise in PCT. PCT and CRP may help diagnose sepsis, as they correspond with infection severity and prognosis. Pro-calcitonin levels in patients showed a strong positive correlation with their SOFA score. In our study, the Pro-calcitonin levels in survivor patients revealed a strong positive correlation with their SOFA score(0.874), and pro-calcitonin levels among patients who did not survive too revealed a positive correlation with their SOFA score(0.647). Jain et al performed a prospective observational study in 2014 to study the prognostic value of pro-calcitonin in the prediction of 28-day mortality in patients of sepsis. Fifty-four consecutive patients of sepsis, severe sepsis, and septic shock were recruited. They found that levels of serum pro-calcitonin were significantly higher in non-survivors [13.1 (6.3-42)] compared to that of survivors [5.38 (3.48-12.8)].

Arora S et al in 2015 conducted a meta-analysis demonstrating a substantial difference in PCT levels on the first day of sepsis diagnosis between survivors and non-survivors. PCT levels play a crucial role in the early stages of critical illness, as they are not significantly different between those who survive and those who do not. In vitro studies have shown that higher PCT levels in neutropenic patients are linked to better antibiotic therapy response. As the infection subsides, PCT levels decrease, with prolonged high levels linked to higher death rates. Interestingly, PCT levels are lower in survivors compared to non-survivors even on the first day of admission, possibly due to the progression of the patient beyond the early stages of sepsis and the correlation between PCT and the body's inflammatory damage.

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Suranadi et al,[33] performed a prospective cohort study in from 2018 to 2020. From January 2018 to December 2020, 228 patients were acquired, with a mean age of 53.61 years and a male preponderance of 58.8%. The 28-day mortality rate was 57.5%, with 68.5% in patients with PCT ≥ 7 ng/mL. The mean SOFA score was higher in patients with PCT ≥7 ng/mL, with a significant difference. Non-survivors had higher pro-calcitonin values than discharged patients, with a statistically significant difference.

In the present study, 55.2% of the study population survived and were discharged and 44.8% of patients died during admission. At 3-month follow-up among the patients who were discharged from the hospital 50% of the patients were alive and 50% were not. This was in agreement with the study by Wadees et al in 2021 where they studied 100 ICU patients with sepsis. The study found that over half of patients died (55%), with death being more prevalent in patients with negative blood culture results (70.5%) and severe sepsis (83.3%), with a significant association between these factors..In the study by Shinde et al,[5] 50 patients (63%) survived (survivors group) and 30 patients (37%) did not survive (non-survivors' group). R.A. de Azevedo et al in 2015 in a prospective observational study on 130 sepsis patients admitted to ICU found the proportion of survivors to be higher 74.61% than those who did not(25.38%)

Table showing a comparison of different studies with mean PCT levels and SOFA scores among survivors and non-survivors

MEAN and SD	PRO-CALCITONIN		SOFA	
	DISCHARGE	DEATH	DISCHARGE	DEATH
Our study	10.4 (13.8)	37.7(36.4)	4.2(3.8)	9.9(3.8)
Shinde et al[5]	3.7 ± 1.5	6.4 ± 3.13	6.1 ± 1.93	8.3 ± 2.13
Singh et al			6.5	9.2
de Azevedo JRA et al,[23] (* Procalcitonin clearance at 48 hours)	35.5 (−40.0 to 70.0)*	35.5 (−40.0 to 70.0) −170.0 (−887.5 to 7.5)*	4.77 (3.31)	6.55 (3.49)
Matsumura et al[29]	0.25 (0.12–0.79)	1.23 (0.67–3.21)	7.0 (4.0–10.0)	12 (10–15.5)
Suranadi et al[27]	7.1 ± 3.25	5.49 ± 2.38	5.83 ± 2.7	8.11 ± 3.3

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