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A COMPARATIVE STUDY OF PROCALCITONIN VERSUS C-REACTIVE PROTEIN : IN EARLY DIAGNOSIS OF SEPSIS AND PATIENT OUTCOME

Dr. Neelam Singh — Professor, Department of Anaesthesiology and Critical Care, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, India

Dr. Dharmendra Kumar Yadav* — Assistant Professor, Department of Anaesthesiology and Critical Care, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, India *Corresponding Author

Dr. Satyendra Singh — Junior Resident,Department of Anaesthesiology and Critical Care, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, India

ABSTRACT **Background and Aims:** Inspite of good efforts in critical care, severe sepsis mortality ranges from 28% to 50%. So we need such investigational tools which help to diagnose early sepsis. Sepsis, a syndrome of physiologic, pathologic and biochemical abnormalities induced by infection, is a major public health concern. Severe sepsis and septic shock are frequently complicated by multiple-organ dysfunction syndrome (MODS), so the severity of organ dysfunction is an important determinant of prognosis in sepsis.

KEYWORDS : Sepsis, Multiple-organ Dysfunction Syndrome, Procalcitonin, CRP.

INTRODUCTION

Inspite of good efforts in critical care, severe sepsis mortality ranges from 28% to 50%. So we need such investigational tools, who help to diagnose early sepsis.

Septic shock defined as a subset of sepsis in which profound circulatory, cellular, metabolic abnormality are associated with greater risk of mortality than with sepsis alone. Septic shock criteria 2016: despite of adequate fluid resuscitation vasopressor needed to maintain MAP > 65 mmhg and lactate lavel>2 mmol / lit.

Procalcitonin (PCT): PCT is a prohormone of calcitonin which composed of 116 amino acids. Which is very useful in diagnosis of sepsis particularly culture negative patients. Its label is associated with sepsis severity. A PCT concentration above 0.1ng/ml indicate clinically relevant bacterial infection, requiring antibiotic treatment.[1,3,4] At PCT concentration>0.5ng/ml, a patient should considered at risk of developing septic shock.[1,2] Hypercalcitonemia in systemic infection occurs within 2 to 4 hours, often reaches peak value in 8-24 hours, and persist for long as the inflammatory process persist. The half life of is about 24 hours hence concentration falls quickly with recovery of patient.

C-Reactive Protein (CRP): CRP is an annular (ring shaped), pentameric protein found in blood plasma. Whose label rises in response to infection. It is acute phase protein of hepatic origin[3]. Normal concentration in healthy human serum is between 5-10 mg/L, increasing with aging.[3] Higher levels are found in late pregnant women, mild inflammation and viral infections(10–40 mg/L), active inflammation, bacterial infection (40–200 mg/L), severe bacterial infections and burns (>200 mg/L).[3]

METHODS:

The proposed prospective study was carried out in M.L.N. Medical College, Allahabad and associated hospitals, after approval from Ethical Committee and obtaining written and informed consent from the patients. The present study aimed to examine the clinical utility of procalcitonin (PCT) and c–reactive protein (CRP) as an indicator of sepsis and septic shock. The purpose of this study was to evaluate the PCT (procalcitonin) as marker of sepsis over traditional biochemical marker CRP (C-reactive protein) admitted to ICU patient. Serial values of Procalcitoin (PCT) and C-reactive protein (CRP) were used to predict outcome of patients having sepsis.

Patients were divided into two groups:

Group A: Patients who were investigated for total leucocyte count (TLC).

Group B: Patients who were investigated for C- reactive protein (CRP).

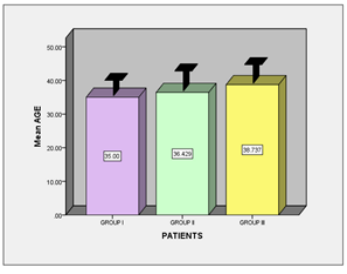
Group C: Patients who were investigated for Procalcitotin (PCT).

Adult male and female patients aged between 18 years to 60 years were admitted to ICU having altered mentation, systolic blood pressure ≤100 mmHg, respiratory rate ≥22/min and temperature >38 ºC or < 36 ºC were included in the study whereas patient's refusal, patients on anticoagulant therapy, patients having acute coronary syndrome, patients who were pregnant, Immuno-compromised patients, patients with active gastrointestinal bleeding were excluded from the study.

Demographic Data

Patients	Mean	Std. Deviation	ANOVA(p) value
GROUP A	35.0000	10.01052	0.610
GROUP B	36.4286	13.27619	
GROUP C	38.7368	11.73713	
Total	36.6833	11.67859	

Table -1: Age wise distribution of patients



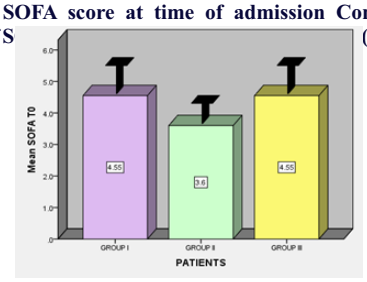
Bar diagram of age wise distribution of patients

INFERENCE

Mean age of the group patients were compared and showed no significant difference with p value > 0.05.

Patients	Mean	Std. Deviation	ANOVA (p)
GROUP I	4.550	1.9595	.165
GROUP II	3.600	1.4290	
GROUP III	4.550	1.9595	
Total	4.233	1.8261	

Table- 2: SOFA score at time of admission Comparison and analysis of S (T_0)



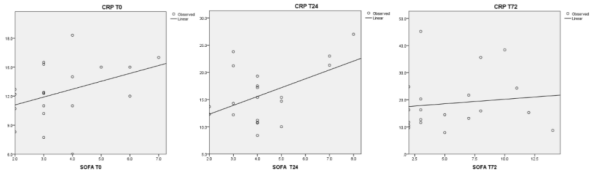
Bar Diagram showing Comparison and analysis of SOFA scores at time of admission to ICU (T_0)

INFERENCE: Statistically (P value >.05), hence there is no significant co-relation were present among SOFA score at time of admission (T0).

GROUP B STATISTICAL ANALYSIS

	CRP T0	CRP T24	CRP T72
Pearson Correlation	0.386	0.122	0.497*
p- value	0.093	0.607	0.026
No of patients	20	20	20

Table-3 Correlation between SOFA and CRP at the time of admission (T0), at the end of first day (T24) and at the end of second day (T72)

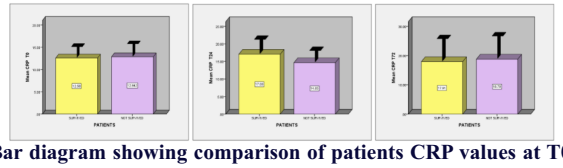


Bar diagram showing correlation between SOFA and CRP at the time of admission (T0), at the end of first day (T24) and at the end of second day (T72)

There was no significant correlation between SOFA and CRP Score at the time of admission to ICU (T0) in patients by Karl Pearson correlation (p>.05 and r=.386). There was no significant correlation between CRP and SOFA Score after time of admission to ICU (T24) in patients by Karl Pearson correlation (p>.05 and r=.122). There was significant co-relation between SOFA score and CRP at the time of admission to ICU (T72) in patients by Karl Pearson correlation (<.05) and r=.497).

	PATIENTS	Number of patients	Mean	Std. Deviation	p-value
CRP at T0	SURVIVED	10	12.5800	3.45504	.876
	NOT SURVIVED	10	12.8420	3.95304	
CRP at 24	SURVIVED	10	17.0300	5.71957	.318
	NOT SURVIVED	10	14.6500	4.57463	
CRP at T72	SURVIVED	10	17.9100	10.70280	.858
	NOT SURVIVED	10	18.7800	10.75544	

Table-4 Comparison of patients CRP values at T0, T24 and T72 between survivor and non-survivor



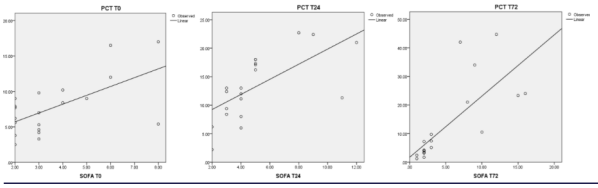
Bar diagram showing comparison of patients CRP values at T0, T24 and T72 between survivor and non-survivor

There was no statistical significance (p-value>0.5) difference of CRP values between survivor and non-survivor at the time of admission (T0), after 24 hrs of admission (T24) and after 72 hrs of admission (T72).

GROUP C STATISTICAL ANALYSIS

		PCT T0	PCT T24	PCT T72
SOFAT24	Pearson Correlation	0.61416	.74684	0.65035
	P value	0.003	.0001	.0.001
	No of patients	20	20	20

Table- 5 Correlation between SOFA and PCT at time of admission (T0), after 24 hrs of admission (T24) and at time the third day (T72).

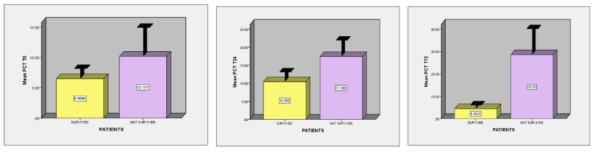


Bar diagram showing correlation between SOFA and PCT at time of admission (T0), after 24 hrs of admission (T24) and at time the third day (T72).

There was significant co-relation between PCT and SOFA Score (p value <0.05) at the time of admission to ICU (T_0) and at the time of admission to ICU (T24) whereas a highly significant correlation (p value <0.001) was observed between PCT and SOFA Score at the time of admission to ICU (T72) in patients by Karl Pearson correlation.

	Patients	Number of patients	Mean	Std. Deviation	P- value
PCT T0	SURVIVED	13	6.4846	2.61561	.045*
	NOT SURVIVED	7	10.1571	5.08424	
PCT T24	SURVIVED	13	10.3854	4.22405	.003*
	NOT SURVIVED	7	17.3857	4.72914	
PCT T72	SURVIVED	13	4.3923	2.42709	.000*
	NOT SURVIVED	7	28.5000	12.26431	

Table- 6 Comparison of PCT values among survivor and non-survivor at time of admission (T0), after 24 hrs of admission (T24) and after 72 hrs of admission (T72).



Bar diagram showing comparison of PCT values among survivor and non-survivor at time of admission (T0), after 24 hrs of admission (T24) and after 72 hrs of admission (T72).

There was statistical significance (p- value <0.05) difference of PCT values between survivor and non-survivor at time of admission (T0).and after 24 hrs of admission (T24) whereas highly significant significance (p- value < 001) was observed between survivor and non-survivor after 72hrs of admission (T72).

DISCUSSION:

Various published studies indicate that there is a significant relationship of PCT not only to infection and systemic inflammation, but also to organ dysfunction as well as various types of tissue trauma[1].

Our study was conducted on 60 Patients diagnosed as having, sepsis or septic shock. Their age ranged from 18 to 60 years. There were no statistical significant difference of age and sex among the groups and there were no statistical difference among SOFA score of patients of all the groups. Out of 60 patients included in study all patients having sepsis. Respiratory tract infection was the most common source of infection and acute lung injury was the most common organ dysfunction in the study groups.

In our study we observed that,

1) - There was no significant correlation between SOFA score and CRP at T0, T24 hr and there was a significant correlation between SOFA score and CRP at T72 hr. (Table 3).
2) - There was no significant relation between CRP values of survivor and non –survivor at T0, T24 and T72 hrs (Table 4).
3) - There was a significant correlation between SOFA score and PCT AT T0, T24 and T72 hr (Table 5).
4) - There was a significant relation between PCT values of survivor and non -survivor at T0, T24 and T74 hr (Table 6).

Miro et al 2011.[5] our findings were similar to the study conducted by Miro et al. they enrolled 64 post-operative patients complicated by septic peritonitis. PCT values and SOFA score were recorded on ICU admission, at 24hr. and 48hr. after admission. Linear correlation done between PCT & SOFA score showed (r=0.299 with a p=0.037), (r=0.355 with a p=0.024 and (r=0.445 with a p=0.007) respectively. Also linear correlation was found between SOFA score and PCT for all patients where r was 0.374 with a p-value of <0.001.

In our study we also found linear correlation between SOFA score and PCT. PCT values and SOFA score were recorded on ICU admission, at

24hr. and 72hr. after admission. Linear correlation done between PCT & SOFA score showed (r=0.61416 with a p=0.003), (r=0.65035with a p=0.001and (r=0.74684with a p=0.0001) respectively.

SAMEH EL MARAGHI, AHMED YEHIA et al 2014.[6] This prospective study conducted in 25 patients. They found statistically significant difference in PCT levels between survivors (18pts.) and non-survivors (7pts.) on 1st day (3.317± 3.978 vs. 9.740±4.847ng/ml; p=0.002), 5th day (0.7858±0.907 vs. 10.608±4.592; p=0.001) and on discharge or the day of death (0.2951±0.195 vs. 15.920±2.769; p<0.0001) while there were no differences in CRP between survivors and non-survivors. *They were concluded that PCT* was prognostically superior to CRP for its strong correlation with mortality & significant correlation to both SOFA and APACHE II scores. PCT plays a diagnostic as well as prognostic role in systemic sepsis, while CRP had a diagnostic role only but does not serve as a prognostic marker in sepsis.

Our study was in accordance to this study. In our study we found that there were a statistical significant difference in PCT levels between survivor (13 patients) and non- survivor (7 patients) on 1st day (6.4846±2.61561 vs. 10.157±5.08424ng/ml; p=0. 045), 2th day (10.3854 ±4.22405vs.17.3857±4.72914; p=0.003) and on 3rd day (0.4.3923 ±2.42709 vs. 28.50±12.2643; p<0.000) while there were no differences in CRP between survivors and non-survivors in group B patients.

Silvestre et al.(2009)[7] Conducted a study in 158 septic patients. They found that there was no difference between survivors and non-survivors (outcome and mortality) in CRP levels and they did not recommend the use of CRP level for sepsis diagnosis and as a marker of prognosis and risk stratification. Our study agreed with this, CRP levels of survivor and non- survivor were not significantly different. In our study CRP levels of survivor and non-survivor on admission (12.58±3.45 vs.12.842±3.95; p=.876), 2nd day(17.03±5.519 vs.14.65±4.57 ;p= value0.318) and on 4th day(17.9±10.7 vs18.78 ± 10.75 ;p value 0.858) not significantly related. Hence CRP values could not be used for diagnosis of sepsis.

On the contrary; in a study done by **Lobo et al**., **[101]** 2003 in which 313 ICU patients were enrolled and classified into three groups according to their CRP level. They found that elevated concentrations of serum CRP on admission correlated with an increased risk of organ failure and death. Moreover, persistently high CRP concentrations are associated with a poor outcome

Cicarelli et al.(2009).[8] our study was also similar to this study for CRP (group B) after admission and at 48 hr. they found no significant correlation between CRP level and SOFA score whether in patients with or without organ affection; who found that there was no correlation between CRP and SOFA score in either SIRS or Septic shock patients (r=0.004 &p-value 0.99). we also found that SOFA score does not correlate with CRP at T0 and T72hr but contrary to this study we got significant relation relationship of SOFA and CRP at T24hr with r 0.650 and p value 0.001.

In relation to the outcome, the current study showed a positive correlation between PCT and mortality. A statistically significant difference was found between mean PCT levels of survivors and non-survivors on 1st day, 2nd and 4rd day indicating that PCT plays an important prognostic role in systemic sepsis where it has a good predictive value for the outcome of septic patients. This observation was comparable to study conducted by **Tschaikowsky et al.,(2011)**[9] **in 2011** In Germany University Hospital involving patients with severe sepsis and septic shock. Plasma PCT were serially measured from day 1 (onset of sepsis) to the 14th day in parallel with clinical data until day 28. They found that PCT was significantly decreased in survivors, while mostly increased in non- survivors within the time of observation with a p-value of <0.05.

Michael Meisner,[10] Klaus Tschaikowsky et al (1999).[11] Our study was also supported by them. They were studied 40 patients with SIRS or sepsis.

They were finally evaluated on a total of 316 observation days. Median of PCT concentrations significantly increased with increasing SOFA score levels of the patients In contrast, CRP concentrations were found highly elevated also at low SOFA scores and showed no significant difference between these groups. Only a few measurements detected very high PCT levels, whereas the majority of the PCT concentrations are in the intermediate range. Thus, correlation coefficients between PCT levels and SOFA scores were low (r = 0.20). Likewise, there was only a weak correlation between SOFA scores and CRP levels (r = 0.19).

In our study we were also found weak correlation between SOFA score and CRP at T0 and T72 with r values .386 and .122 and their p value also >.05. In contrast, Median of PCT concentrations significantly increased with increasing SOFA score levels of the patients with correlation with correlation values r were 0.61416, 0.65035 and 0.746.
Suberviola et al. (2009).[12] They conducted a study in which they enrolled 88 septic shock patients. They were found that the serial determination of PCT could offer a better prediction of patient's outcome than a single quantification of the marker.

Our study also agrees with this study, in our study we were found positive co-relation between SOFA score and PCT labels at T0, T24 and T72 hr.

Conclusion

On the basis of observations and statistical comparison following conclusions were made:

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern. The reported incidence of sepsis is increasing, likely reflecting aging populations with more comorbidities, greater recognition. Although the true incidence is unknown, conservative estimates indicate that sepsis is a leading cause of mortality and critical illness worldwide. Furthermore, there is increasing awareness that patients who survive sepsis often have long-term physical, psychological, and cognitive disabilities with significant health care and social implications.

There was a significant difference in the serum Procalcitonin level between the survivors and the non-survivors and there was a gradual increasing and decreasing trend in the serum Procalcitonin levels on subsequent measurements in non-survivors and survivors respectively. Therefore early procalcitonin measurements and early goal directed therapy should be started in sepsis patients with procalcitonin greater than 0.2ng/ml according to US Food and drug administration.

There was a highly significant positive correlation between SOFA score and serum Procalcitonin at T0,T24 and at T72hrs. among survivor and non-survivor patients.

- There was a no significant positive correlation between SOFA score and serum CRP at T0, T72hrs. among survivor and non-survivor patients and significant correlation at T24 of survivor and non-survivor.
- There was significant difference of serum procalcitonin labels at T0, T 24 and T72. But no significant level of serum CRP at T0 and T72 and at T24 CRP has significant difference.
- PCT is superior to CRP as PCT had a strong correlation with SOFA score indicating that PCT plays a diagnostic as well as prognostic role in systemic sepsis.
- No demographic predisposition has been reported in the causation of sepsis.
- Morbidity and Mortality can be significantly reduced by following preventive measures and treatment protocols as per the Survival Sepsis Campaign (2012) and thereby the bed turnover can be increased reducing in-turn the ICU burden.
- Though short term increases in cost occur when ICU across the globe follow strict protocols and strategies to limit infection, there is in fact a long term cost reduction in terms of healthcare when viewed as a whole.

REFERENCES

1. Cone JB. Inflammation. Am J Surg. 2001; 182 – 62.
2. Thomas, Lothar, Labor und Diagnose. TH-Books, Frankfurt, 2008, p. 1010
3. Pepys MB, Hirschfield GM (Jun 2003). The Journal of Clinical Investigation. 111 (12):1805–12.
4. Mark Hatherilla, Shane M Tibbya et al: 1999: 81;417-421
5. Miro M., Del Valle, García S., et al.: Correlation between SOFA score and procalcitonin blood levels in peritonitis patients. European Journal of Anaesthesiology June, Volume 28, Issue, p. 173, 2011.
6. Sameh EL Maraghi, M.D.; Ahmed Yehia, M.D.*; Osama Mahmoud, M.D.** and Aliaa Abd EL Hamid, M.Sc.**; Procalcitonin Versus C-Reactive Protein at Different SOFA Scores in I.C.U. Sepsis: Diagnostic Value and Therapeutic Implicat Med. J. Cairo Univ., Vol. 82, No. 1, March: 29-36, 2014;www.medicaljournalofcairouniversity.net
7. Silvestre J., P. Po´Voa L., Coelho, et al.: Is c-reactive protein a good prognostic marker in

septic patients. Intensive Care Med., 35: 909-91, 2009.
8. Cicarelli D.D., Joaquim Edson Vieira, Ben-Señor I., et al.: C-reactive protein is not a useful indicator for infection in surgical intensive care units Sao-Paulo. Med. J., 127 (6): 350-4, 200
9. Tschaikowsky K., Monika H., Giovanni G., et al.: Predictive value of procalcitonin, interleukin-6,and C-reactive protein for survival in postoperative patients with severe sepsis Journal of Critical Care, 26: 54-64, 2011.
10. Suárez M., Francisco S., et al.: Prognostic value of inflammatory markers (notably cytokines and procalcitonin), nutritional assessment, and organ function in patients with sepsis Eur. Cytokine Netw, 21: 19-26, 20 10.
11. Michael Meisner,Klaus Tschaikowsky,Thomas Palmaers andJoachim Schmidt Critical Care 19993:45https://doi.org/10.1186/cc306 © Current Science Ltd 1999 Received: 28 February 1998Accepted: 12 February 1999 Published: 16 March 1999
12. Suberviola A., Castellanos O., Gonzlez C., et al.: The Procalcitonin and Survival Study (PASS) BMC Infect. Dis., 8: 91-101, 2011.