

A Comparative Study Of Serum Pro-Calcitonin (S-Pct) & C-Reactive Protein (Crp) in Patients with Sepsis.

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Keywords

S-PCT, CRP, Sepsis, SOFA Score, Biomarker.

Abstract

Background: Studies have shown that, early diagnosis & treatment of sepsis can lower the mortality rates & improved their related outcomes. Furthermore, studies revealed that, S-PCT can used as biomarker for early diagnosis & guiding therapeutic decision for treatment of sepsis. Thus, in our study our aim was to evaluate & compare the utility of S-PCT & CRP as diagnostic markers, calculate SOFA score and finally, relate these biomarkers with SOFA score.

Material And Methods: Our study was a single center hospital-based, prospective, observational and non- interventional type of study with total of 58 patients with sepsis.

Results: Out of 58 patients in total, 31 (53.4 %) were males & 27 (46.6%) were females. The mean S-PCT and mean CRP measured as markers of sepsis showed 17.97 (± 21.78) ng/mL & 46.81 (± 34.21) mg/L respectively. The mean SOFA score of the patients was 8.51 (± 3.34). Mean S-PCT levels were higher in patients with a higher SOFA score which was statistically significant.

Conclusion: In our present study we have concluded that, both S-PCT & CRP levels were consistent markers for systemic infection.

1. Introduction:

“According to various past studies, sepsis is a systemic inflammatory response of the host to several infections. Hence, it remains one of the major causes of morbidity & mortality in critically ill patients.”^[1] “Studies have also shown that, its early diagnosis & management can lower the mortality rates and improved their related outcomes”.^[2]

“Recent studies have also focused on the use of an ideal biomarker for the diagnosis & prognosis of sepsis”.^[3,4] “Researchers have proved & concluded that, S-PCT has been suggested as a novel biomarker & therefore, it can be used in early diagnosis & guiding therapeutic decision making for it”.^[5] “According to studies, S-PCT concentrations are below the detectable level in healthy persons (0.5 ng/ml), however it can increase to 1000 ng/ml in severe bacterial infection or sepsis”.^[5] “Studies revealed that, S-PCT & CRP is another biomarker used to diagnose both acute & chronic inflammatory responses. patients diagnosed with sepsis or septic shock, it may be used to establish the severity of these conditions and prognosis”.^[6,7] “Henceforth, studies have concluded, sequential Organ Failure Assessment (SOFA) score to assess the morbidity of a critical

illness at a population level”.^[8]

In addition, since ages, bacterial culture are considered as the gold standard but their delayed process finally delays the diagnosis. Thus in our study our aim was to evaluate & compare the utility of S-PCT & CRP as diagnostic markers for sepsis, calculate SOFA score & relate these biomarkers with SOFA score.

2. Material and Methods

Aim of the study:

To compare & evaluate S-PCT & CRP levels in patients with sepsis and correlate them with SOFA score.

Study Design: We have conducted single center hospital-based, prospective, observational & non-interventional type of research.

Study population: In our research we have enrolled total of 58 patients.

Inclusion criteria:

1. Patients with 18 years or more were included in our study.

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2. All those who got admitted with suspected sepsis in our hospital were enrolled in our study.
3. Both male & female were included.

Exclusion criteria:

1. All those patients who underwent any major thoracoabdominal surgery within 3 weeks or underwent any trauma or burns.
2. Patients who have refused to sign consent form.

Study Setting: In our research we have included patients who all were admitted to the Intensive Care unit of KIMS, Karad starting from February 2021 ending to October 2022 with a total of 58 patients after getting ethical approval from University followed which written informed consent was taken. Sepsis or septic shock were included, according to ‘The American College of Chest Physicians and the Society of Critical Care Medicine’ convened in 1991.

Table 1: Criteria for SIRS, sepsis and septic shock ^[9]

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 CO ₂ lower than 32 mmHg
	White blood cell count >12 000 cells/μL or lower than 4000 cells/μL
Sepsis	SIRS criteria with presumed or proven infection
Septic shock	Sepsis with hypotension despite adequate fluid Resuscitation

Patient history was recorded by general & physical examination which includes CBC, renal function tests, liver function tests and cultures- blood/sputum/urine etc. The complete blood count was performed, in a 3-part mechanized analyzer via Nihon Kohden. (MEK 6420P). Serum creatinine via Modified Jaffe’s process. Liver function tests were done by calorimetry. The Finecare S-PCT Rapid Quantitative fluorescence immunoassay was used to determine S-PCT levels in the range of 0.5-100 ng/mL. The Rhelax-CRP slide test was used to calculate the CRP levels. The SOFA score was calculated on the day of admission. The patients were subsequently followed till discharge or death.

Statistical Analysis and Methods

We have entered our data into Microsoft Excel spreadsheet wherein, p value was considered as statistically significant at ≤ 0.05 . Further, analysis was done using SPSS version 20 windows software program. The chi square test was used for quantitative data comparison of all clinical indicators. The unpaired t test was applied to compare the difference between the mean and standard deviation of 2 variables.

3. Results:

31 (53.4 %) were males & 27 (46.6%) were females. The male to female ratio was 1: 0.9. The mean S-PCT and mean CRP were 17.97 (± 21.78) ng/mL and 46.81 (± 34.21) mg/L respectively. The mean SOFA score of the patients was 8.51 (± 3.34). [Table 2]

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Table 2: Mean and standard deviation of study variables in the study population

Variables		Mean	(± SD)
Age (in years)		60.15	(±13.57)
	Males	62.5	(±12.2)
	Females	57.44	(±10.7)
Temperature (In °F)		99.67	(±1.51)
Heart rate (HR) (per minute)		96.48	(±14.76)
Respiratory rate (RR) (per minute)		33	(±6.07)
Mean arterial pressure (MAP) (mmHg)		66.68	(±15.63)
P/F ratio		306.26	(±79.21)
Hemoglobin (gm/dl)		10.69	(±1.70)
Total leucocyte count (TLC) (/mm ³)		21,386	(±5570)
Platelet count (/ μL)		1,54,689	(±9120.1)
Serum bilirubin (mg/dl)		2.0	(±1.53)
Serum creatinine (mg/dl)		3.04	(±1.34)
CRP (mg/L)		46.8	(±34.21)
S-PCT (ng/mL)		17.97	(±21.78)
SOFA score (0 – 24)		8.51	(±3.34)

Table 3: Association of SOFA score with S-PCT levels.

Frequency distribution of SOFA score	S-PCT (ng/mL)								Total		Mean serum PCT
	<2		2 – 5		6- 10		>10		(n=58)	%	
	(n=9)	%	(n=14)	%	(n=5)	%	(n=30)	%			
0 – 5	9	60	6	40	0	0	0	0	15	25.86	1.26 (±0.99)

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6 - 10	0	0	4	14.81	6	22.22	17	62.96	27	46.55	17.25 (±18.56)
11 - 15	2	12.5	2	12.5	2	12.5	10	62.5	16	27.58	33.37 (±24.7)
Total	9	15.51	14	24.13	5	8.62	30	51.7	58	100.0	
Chi-square = 24.95; df = 6; p = 0.003											

In our research we found that, the mean S-PCT levels were higher for high SOFA score patients. Hence, showed statistically significance at p = 0.003. [Table 3]

Table 4: Association of SOFA score with CRP levels .

Frequency distribution of SOFA score	C-reactive protein (mg/L)								Total		Mean CRP
	≤ 10		11 - 20		21 - 30		>30		(n=58)	%	
	(n=5)	%	(n=8)	%	(n=13)	%	(n=32)	%			
0 - 5	3	20	4	26.66	4	26.66	4	26.66	15	25.86	23.66 (±16.03)
6 - 10	2	7.4	3	11.11	7	25.92	15	55.55	27	46.55	43.63 (±28.96)
11 - 15	0	0	1	6.25	2	12.5	13	81.25	16	27.58	73.87 (±35.5)
Total	5	8.62	8	13.75	13	22.41	32	55.17	58	100	
Chi-square (χ^2) = 10.85; df = 6; p = 0.93											

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In our study we have found that , CRP was higher in patients with a higher SOFA score. Hence, association between the SOFA score and CRP showed statistically not significant at $p=0.93$. [Table 4]

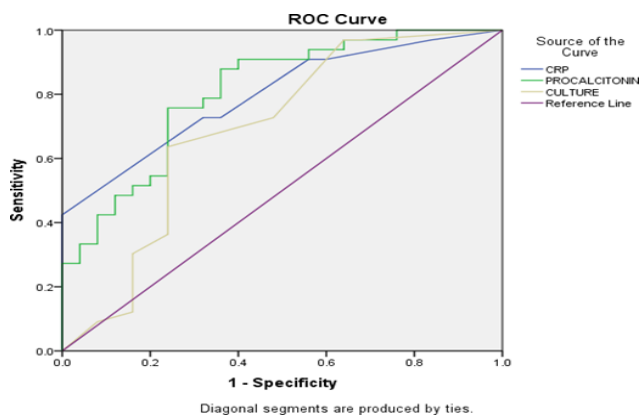
ROC curve of CRP, S-PCT and culture report to predict mortality as an outcome

The below table shows the area under the Curve for 58 patients. It was observed that on comparing biomarkers of sepsis such as S-PCT & CRP with the culture report for mortality as an outcome, S-PCT (0.807) showed better sensitivity and specificity when compared with to CRP. [Table 5]

Table 5: ROC curve of CRP, serum Procalcitonin and culture report to predict mortality as an outcome

	Area Under the Curve	p- value	95% Confidence Interval	
			Lower Bound	Upper Bound
CRP	0.796	0.0001	0.684	0.908
PROCALCITONIN	0.807	0.0001	0.695	0.920
CULTURE	0.692	0.01	0.546	0.838

Figure 1: ROC curve of CRP, serum Procalcitonin and culture report to predict mortality as an outcome



Correlation between SOFA score, S-PCT and CRP

Association between the SOFA score, S-PCT level & CRP level concluded moderately positive correlation between the 2 variables. [Table 6, Figure2 and 3]

Table 6: Correlation between SOFA score, S-PCT and CRP

SOFA score	S-PCT		CRP	
	Correlation coefficient	p-value	Correlation coefficient	p-value
	$r = 0.507$	$p = 0.0049$	$r = 0.590$	$p = 0.001$

Figure 2: Correlation between SOFA score and serum Procalcitonin level .

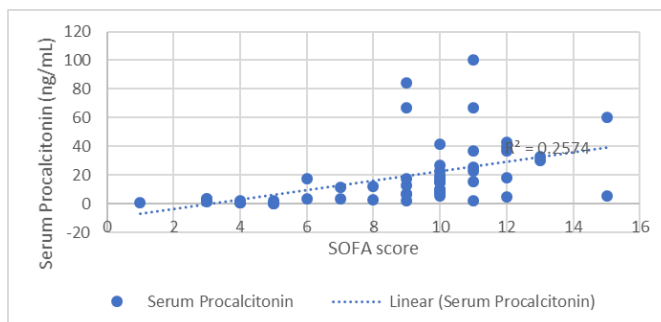
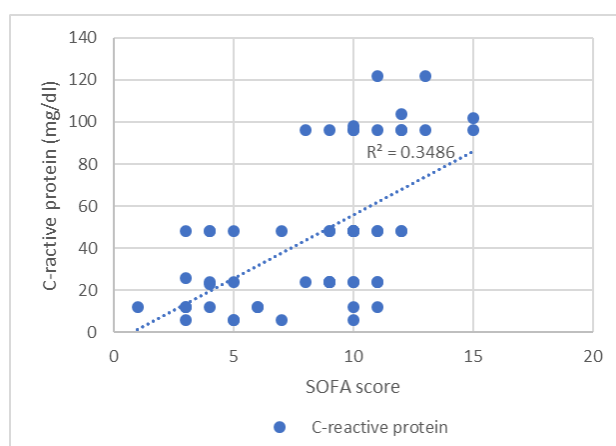


Figure 3: Correlation between SOFA score & CRP level .



4. Discussion:

“According to studies, sepsis is the leading cause of morbidity & mortality among patients admitted to the ICU. Studies have concluded that important aspects of sepsis management include its timely diagnosis & specific treatment in the early hours of triage. However, it have also proved that diagnosis and differentiation from non-infectious causes is often the reason for a potential delay”.^[10] “Furthermore, studies have found that , cultures are considered as the gold standard for the confirmation of bacteremia and subsequently test the antimicrobial sensitivity, but the delayed process of it delays its diagnosis. White blood cell count, CRP & IL-1 are the conventional markers used for diagnosis. Compared to CRP, S-PCT had better diagnostic & prognostic value and may help in distinguishing viral from bacterial infections”.^[11] “Studies showed, cytokines like TNF- α , IL-1 and IL-6 are also elevated during sepsis, but they do not possess sufficient sensitivity or specificity to be used as clinical markers”.^[12] S-PCT had emerged as the most studied & promising sepsis biomarker. Additionally, studies have

also proved that , S-PCT is better than CRP.^[13]

In our study, a majority of patients were 51 to 60 years (19,32.7%) and mean age of the study population was 60.15 (\pm 13.57) years. Similar study was conducted by “Artero et al, where the mean age was 63.5 years”.^[14] Further “ mean age reported by Watanbe et al in Japan was 73.8 (\pm 15.6) years, which is considerably higher than that observed”.^[15] Further, the mean age in the group of patients who recovered was 59.84 (\pm 13.4) years and the mean age in the group of patients who succumbed was 60.39 (\pm 13.49) years. In our study males were 31 (53.4%) and females were 27 (46.6%). “The male dominance in the study population was similar to that reported by Nargis et al which was 63%.”^[16] “The percentage of male subjects in the study population were higher than those reported by Khan A.A et al.”^[17] In our study, mean S-PCT and CRP levels of the population were 17.97 (\pm 21.78) ng/mL and 46.81 (\pm 34.21) mg/L, respectively. Further, severity of sepsis was assessed with SOFA score, with minimum score of 0 & maximum score of 15 and the mean SOFA score was 8.51 (\pm 3.34). In the current study a total 49 (84.49 %) patients with diagnosis of sepsis had raised

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(positive) S-PCT levels while 53 (91.37 %) patients had raised (positive) C-reactive protein levels. A total of 43 (74.1 %) patients had higher SOFA score, that corresponded to an increasing severity of sepsis.

In patients with SOFA score of 6 to 10, mean S-PCT was 17.25 (\pm 18.56) ng/mL and in those with a SOFA score of 11 to 15, the mean S-PCT level was 33.37 (\pm 24.7) ng/mL. It was observed that the mean S-PCT levels was higher in patients with a higher SOFA score. “Similar studies showed increasing trends of S-PCT level with sepsis (11.9 ng/mL) and septic shock (40.8 ng/mL).”^[16] It was observed that S-PCT levels increase proportionately with severity of sepsis and can be used to identify patients with higher risk of adverse outcomes. In our study, patients with a SOFA score of 7 to 10, had a mean CRP level of 43.63 (\pm 28.96) mg/L and in patients with a SOFA score of 11 to 15, the mean CRP level was 73.87 (\pm 35.5) mg/L. It was observed that the mean CRP was higher in patients with a higher SOFA score. Thus, CRP levels show a significant rise with the severity of infection. These findings were in contrast with Meisner et al who reported that CRP concentrations were highly elevated even at low SOFA scores.^[18]

In the present study, the sensitivity and specificity were 80 % and 60.38 % respectively for CRP levels. The sensitivity and specificity were 76.19 % and 75.68 % respectively for serum Procalcitonin levels. It was observed that both biomarkers of sepsis had similar sensitivity and specificity.

Several authors have compared the diagnostic and

prognostic ability of S-PCT to CRP. “Another study reviewed and analyzed 33 studies with a total of 3943 patients. They observed that the receiver operating characteristics (ROC) curve for S-PCT was better than that for CRP indicating that S-PCT is superior to CRP. Thus, should be used in clinical practice”.^[19] “In contrast to above findings, another study observed that S-PCT could not reliably differentiate sepsis from other non-infectious causes of systemic inflammatory response syndrome”.^[20]

“Furthermore, studies found that both S-PCT and CRP were useful as diagnostic and prognostic markers of sepsis, but also concluded that S-PCT were much more better & earlier marker than CRP”.^[21] “Wang et al. found in their study that the serum PCT level, could be used as a negative predictor for excluding bloodstream infections with a sensitivity of 83% and specificity of 65% than CRP level.”^[22] Another similar study found & concluded that S-PCT levels are a more accurate diagnostic parameter than CRP.^[23,24] “Rau et al also found S-PCT to be useful, and better than CRP levels, in predicting infections and multiorgan dysfunction syndrome.”^[25]

“Additionally, in one study, when serum PCT, CRP concentrations were analyzed by researchers according to the severities of organ dysfunction with the help of SOFA score. They found an increase in values of both parameters which was similar result to that of what we got in our study”.^[26] As a result, we found in our research that S-PCT and CRP with a severity SOFA score may be employed as a diagnosis and treatment component.

Table 7: Comparative studies

Author	Study design	Sample size (n)	Conclusion
Prasanna Sridharan et al. (2013) ^[27]	Systematic review and meta-analysis		Higher S-PCT levels suggested a systemic bacterial infection as .
Waheeda Nargis et al.(2014) ^[28]	Cross-sectional study	73	S-PCT and CRP levels showed limited diagnostic marker value.
Stephen Harbath et al. (2000) ^[23]	Prospective observational study	78	Of three different biomarkers in patients with diagnosis of sepsis, S-PCT proved to be the best indicator of infection.
Castelli GP et al.	Prospective	150	S-PCT & CRP are more strongly related with infection

(2004) [26]	observationalstudy		presence.
Luzzani A et al. (2003) [24]	Prospective observationalstudy	70	S-PCT level is a better marker of sepsis than CRP.
Patil HV et al. (2020) [5]	Prospective observationalstudy	64	S-PCT and CRP were higher with increase severity .
Mina Hur et al. (2009) [29]	Prospective observationalstudy	1270	The diagnostic utility of S-PCT is superior to that of CRP in patients with diagnosis of sepsis who have a positive culture report.
Wang et al. (2015) [30]	Retrospectivestudy	201	S-PCT levels were better than CRP Hence, S-PCT is a good indicator of severity & prognosis.
Anand et al. (2014) [28]	Prospective observationalstudy	71	S-PCT levels were directly proportional to organ dysfunction.
Karlsson et al. (2010) [31]	Prospective observationalstudy	242	S-PCT concentrations are elevated in patients with positive culture reports & high SOFA score.
Present study	Prospective observationalstudy	58	S-PCT and CRP were higher with high SOFA scores.

5. Conclusion:

S-PCT & CRP both are the most often used biomarkers in treatment of sepsis. Thus in our study we found that both serum PCT and CRP levels were consistent markers of systemic infection. Henceforth, S-PCT and CRP were significantly raised in patients of severe sepsis with higher SOFA scores.

References:

- [1] Kaukonen K, Bailey M, Suzuki S, et al. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000– 2012. *JAMA* 2014; 311(13): 1308–1316.
- [2] Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013; 41:580–637
- [3] James D. Faix. Biomarkers of sepsis. *Crit Rev Clin Lab Sci.* 2013; 50:23–36
- [4] Szederjesi J, Almasy E, Lazar A, Huțanu A, Georgescu A. The Role of Angiotensin-2 in the Diagnosis and Prognosis of Sepsis. *J Crit Care Med.* 2015;1:18-23
- [5] Patil HV, Patil VC. Comparative study of procalcitonin and C-reactive protein in patients with sepsis. *J Nat Sc Biol Med* 2020; 11:93-9.
- [6] Enguix-Armada A, Escobar-Conesa R, La Torre AG, De La Torre-Prados MV. Usefulness of several biomarkers in the management of septic patients: C- reactive protein, procalcitonin, presepsin and mid-regional pro-adrenomedullin. *Clin Chem Lab Med.* 2015 17.
- [7] Samraj RS, Zingarelli B, Wong HR. Role of biomarkers in sepsis care. *Shock.* 2013; 40:358-65.
- [8] Lambden, S., Laterre, P. F., Levy, M. M., & Francois, B. The SOFA score-development, utility and challenges of accurate assessment in clinical trials. *Critical care (London, England).* 2019; 23(1), 374.
- [9] American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference. *Crit Care Med.* 1992;20(6):864–74.
- [10] Gregoriano C, Heilmann E, Molitor A, Schuetz P. Role of procalcitonin use in the management of

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- sepsis. *J Thorac Dis.* 2020 Feb;12(Suppl 1):S5-S15.
- [11] Alkholi UM, Abd Al-Monem N, Abd El-Azim AA, Sultan MH. Serum procalcitonin in viral and bacterial meningitis. *J Glob Infect Dis.* 2011 Jan;3(1):14-8.
- [12] Chaudhry H, Zhou J, Zhong Y, Ali MM, McGuire F, Nagarkatti PS, Nagarkatti
- [13] M. Role of cytokines as a double-edged sword in sepsis. *In Vivo.* 2013 Nov- Dec;27(6):669-84.
- [14] Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. *J. Antimicrob. Chemother.* 2011;66(suppl 2):ii33-40
- [15] Artero A, Zaragoza R et al. Prognostic factors of mortality in patients with community acquired blood stream infection with severe sepsis and septic shock. *Journal of Critical Care;* 2010; 25; 2; 276-281
- [16] Watanbe Y, Oikawa N et al. Ability of procalcitonin to diagnose bacterial infection and bacteria types compared with blood culture findings. *International Journal of General Medicine.* 2016;9; 325-331.
- [17] Nargis W, Ibrahim M et al. Procalcitonin versus C-reactive protein: Usefulness as biomarker of sepsis in ICU patient. *Int J Crit Illn Inj Sci* 2014;4:195-9
- [18] Khan AA, Singh R, Singh PK. Diagnostic and prognostic significance of procalcitonin in septicemia. *Int J Adv Med* 2017;4:630-4.
- [19] Meisner, M., Tschaikowsky, K., Palmaers, T. et al. Comparison of procalcitonin (PCT) and C-reactive protein (CRP) plasma concentrations at different SOFA scores during the course of sepsis and MODS. 1999; *Crit Care* 3, 45.
- [20] Uzzan B, Cohen R, Nicolas P, Cucherat M, Perret GY. Procalcitonin as a diagnostic test for sepsis in critically ill adults and after surgery or trauma: a systematic review and meta-analysis. *Crit Care Med* 2006;34:1996-2003.
- [21] Tang BM, Eslick GD, Craig JC, McLean AS. Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: systematic review and meta-analysis. *Lancet Infect Dis.* 2007;7:210-7.
- [22] Magrini L, Travaglino F, Marino R, et al. Procalcitonin variations after emergency department admission are highly predictive of hospital mortality in patients with acute infectious diseases. *Eur Rev Med Pharmacol Sci* 2013; 17(suppl 1): 133-142.
- [23] Wang H, Yin F, Shen DX, et al. Predictive value of procalcitonin for excluding bloodstream infection: Results of a retrospective study and utility of a rapid, quantitative test for procalcitonin. *Journal of International Medical Research* 2013; 41: 1671-1681.
- [24] Harbarth S, Holeckova K, Froidevaux C, et al. Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. *Am J Respir Crit Care Med* 2001; 164:396-402.
- [25] Luzzani A, Polati E, Dorizzi R, et al. Comparison of procalcitonin and C-reactive protein as markers of sepsis. *Crit Care Med* 2003; 31: 1737-1741.
- [26] Rau BM, Kemppainen EA, Gumbs AA, Büchler MW, Wegscheider K, Bassi C, et al. Early assessment of pancreatic infections and overall prognosis in severe acute pancreatitis by procalcitonin (PCT): a prospective international multicentre study. *Ann Surg.* 2007;245:745-54.
- [27] Castelli, Gian Paolo et al. "Procalcitonin and C-reactive protein during systemic inflammatory response syndrome, sepsis and organ dysfunction." *Critical care (London, England)* vol. 8,4 (2004): R234-42.
- [28] Sridharan P, Chamberlain RS. The efficacy of procalcitonin as a biomarker in the management of sepsis: slaying dragons or tilting at windmills? *Surg Infect (Larchmt).* 2013 Dec;14(6):489-511.
- [29] Anand D, Das S et al. Inter relationship between procalcitonin and organ failure in sepsis. *Ind J Clin Biochem.* 2014;29:93-96.
- [30] Hur M, Moon HW, Yun YM, Kim KH, Kim HS, Lee KM. Comparison of diagnostic utility between procalcitonin and C-reactive protein for the patients with blood culture-positive sepsis, *Korean J Lab Med.* 2009 Dec;29(6):529-35.
- [31] Wang S, Chen D. [The correlation between procalcitonin, C-reactive protein and severity scores in patients with sepsis and their value in assessment of prognosis]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue.* 2015 Feb;27(2):97-101.
- [32] Karlsson S, Heikkinen M, Pettilä V et al. Predictive value of procalcitonin decreases in patients with severe sepsis: a prospective observational study. *Crit Care* 2010;14: R205.