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Serum long pentraxin 3 as a predictive marker of mortality and disease severity in critical Ill septic patients with multiple organ dysfunction

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Abstract

This study involves assessing the diagnostic and prognostic value of serum long pentraxin-3 in septic patients with multiple organ dysfunction. Sixty-three ICU patients included forty-six septic patients with organ dysfunction in different sepsis categories. Procalcitonin, C-reactive protein, and pentraxin-3 serum levels were assessed on admission and on day seven. There were significant changes in mean SOFA score in septic shock patients (14.62) versus septic patients (5.75). The serum pentraxin-3 (PTX-3) level on days 1 and 7 was strongly positively correlated to SOFA (r=0.805) (r=0.894), respectively, and MODS scores (r=0.809) (r=0.875), respectively, which means changes in PTX-3 level were accompanied by significant changes in SOFA and MODS scores. PTX-3 at day 1 showed a strong correlation with procalcitonin and CRP (r=0.712), (r=0.533), respectively, (P<0.001). ROC curve for PTX-3 yielded an AUC of 0.962, higher than AUC for PCT (0.917) and CRP (0.941) in the diagnosis of sepsis. In septic patients, both initial and follow-up PTX-3 levels (ng/ml) were consistently significantly higher in non-survivors than survivors (Day 1: 97.84, 66.9, respectively, P=0.001), and (Day 7: 132.5, 41.7, respectively, P<0.001). The ROC curve for PTX-3 yielded an AUC of 0.787, higher than AUC for PCT (0.707) and CRP (0.724) in the prediction of 30-day mortality. The most cut-off level of PTX-3 at day 1 to predict 30-day mortality was 57.5 ng/ml. Significant associations were found between in-hospital mortality and PTX-3 levels. Serum pentraxin-3 has significant diagnostic and predictive value for hospital mortality and disease severity in septic patients with multiple organ dysfunction.

Keywords: Long pentraxin 3, Procalcitonin, C-reactive protein, Sepsis, Intensive care unit, Multiple organ dysfunction.

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1. Introduction

Despite advances in medical treatment, sepsis still poses significant challenges in clinical practice due to its high morbidity and mortality rate. The incidence of sepsis and sepsis-related mortality are increasing [1]. To quickly identify patients who are septic and might benefit from empirical therapy and other supportive treatments, clinicians require reliable diagnostic and prognostic markers. Many markers are used to identify and evaluate the prognosis of severe sepsis and septic shock. The prototype of short pentraxin, C-reactive protein (CRP), has been utilized extensively, while it is not a good prognostic marker and has low specificity as a diagnostic tool [2]. Procalcitonin (PCT) has been suggested as a more precise diagnostic and prognostic marker than CRP, although its usefulness has also been questioned. It is important to take into account the many limitations of PCT as an infection and sepsis marker. Serious sepsis or septic shock caused by Candida may not always result in a significant rise in serum PCT levels. Thus, the value of procalcitonin for diagnosis of sepsis with fungal infection is poor [3]. The search for better biomarkers of sepsis continues. One of these biomarkers is Pentraxin-3 (PTX-3) which is a long pentraxin that is structurally related to the short pentraxins e.g., CRP. Various cells, including leukocytes and endothelial cells, secrete the acute-phase protein known as long pentraxin-3 (PTX-3). It is a member of the pentraxin superfamily, just like C-reactive protein (CRP) [4]. Although both PTX-3 and CRP are acute phase proteins that are part of the pentraxin family, PTX-3 is different from CRP in that it is released directly from the inflammation site by distinct cell types, reflecting more tissue damage than the host response [5]. Widespread inflammation, like sepsis, causes a large increase in plasma PTX-3 levels. In such scenarios, macrophages, dendritic cells, and/or activated endothelium cells may be the main sources of PTX-3. Six hours after the onset of sepsis, PTX-3's maximum plasma level will reach [6]. Pentraxin-3 is a microbial recognition-triggered protein that has the ability to attach to particular pathogens, including viruses, bacteria, and fungi. This encourages the infection to be cleared through phagocytosis.

Thus, PTX-3 plays a non-redundant role in innate immunity regulation as it helps to opsonize and remove necrotic or apoptotic cells [4]. The aim of this study was to evaluate the prognostic and diagnostic value of serum pentraxin-3 levels in relation to the clinical outcome of critically ill septic patients and to compare it with the prognostic and diagnostic value of the classical biomarkers (PCT and CRP), which have been most widely used to diagnose sepsis.

2. Materials and Methods

2.1. Study design

Our study was a prospective cohort study that was conducted on sixty-three ICU adult patients, included forty-six patients admitted with sepsis in different sepsis categories (34 septic shock patients) and (12 septic patients) according to the criteria of The Third International Consensus Definitions for Sepsis and Septic Shock (sepsis-3). Seventeen ICU patients with no identified source of sepsis were included as controls for comparison. The forty-six consecutive critically ill septic patients with organ dysfunction were included in the study, fulfilling the criteria of the new sepsis definition, which was established in February 2016: that any patients with suspected infection with 2 out of 3 variables in qSOFA (Quick SOFA) score are considered to have sepsis. qSOFA (Quick SOFA) score criteria [7]:

- Hypotension: SBP less than or equal to 100.
- Altered mental status (any GCS less than 15).
- Tachypnea: RR greater than or equal to 22.

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [7]. Organ dysfunction can be identified as an acute change of two points or more in the Sequential Organ Failure Assessment (SOFA) score consequent to the infection [8]. A patient with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥ 65 mm hg and having a serum lactate level >2 mmol/l (18 mg/dl) despite adequate volume resuscitation.

2.2. Study Exclusion Criteria

- Age less than 18.
- Acute myocardial infarction and cardiogenic shock.
- Severe crushed trauma.
- Known cases of rheumatoid arthritis, progressive systemic sclerosis.
- Known cases of Wegener's granulomatosis and microscopic polyangiitis.
- Systemic steroid treatment greater than 10 mg of oral prednisolone daily

2.3. Assay

This assay uses the quantitative sandwich enzyme immunoassay technique (ELISA) for the accurate quantitative detection of human pentraxin-3, CRP, and procalcitonin in serum. This assay has excellent sensitivity and high specificity for the detection of human pentraxin or human procalcitonin and CRP. After the withdrawal of 10 cc of the patient's blood, the collected blood sample was centrifuged for 20 minutes at 3,000 rpm within one hour. Assay immediately aliquots and store samples at $\leq$ 20℃. Human serum samples were analyzed with ELISA kits for measurement of serum long pentraxin-3, CRP, and procalcitonin levels.

2.4. Statistical Methods

Data were entered using the statistical package for the social sciences version 25 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whitney tests. For comparing categorical data, the Chi-square (X2) test was performed. An exact test was used instead when the expected frequency was less than 5. Correlations between quantitative variables were done using the Spearman correlation coefficient. Spearman correlation coefficient (rho) (r) to know the strength and direction of the correlation. If rho is positive, then the direction of the correlation is positive, and if it's negative, then the direction of the correlation will be negative. The strength of the correlation will be determined by the amount of rho, irrespective of its sign.

- If rho value < 0.3, there is a weak correlation.
- If rho value is 0.3-0.49, there is a moderate correlation.
- If rho value > 0.5, there is a strong correlation.

The ROC curve was constructed with area under curve (AUC) analysis performed to detect the best cut off values of different parameters for the detection of mortality and sepsis. P-values less than 0.05 were considered statistically significant. P-value less than 0.001 was considered statistically significant.

3. Results and Discussion

This study was carried out on sixty-three patients, our patients had a mean age of 59.46 ± 20.2 years, with 15 males (32.6%). Our patients divided into two groups: the control group comprised seventeen consecutive ICU patients with no identified source of sepsis, and the study group comprised forty-six critically ill patients admitted to the ICU with sepsis. According to severity, our study group was subdivided into two subgroups that included the sepsis group (12 patients) and the septic shock group (34 patients). There was no significant difference between sepsis subgroups and controls regarding age, sex, or demographic data. In our model, we enrolled ICU scoring systems, e.g., APACHE II, SOFA, and MODS, to assess the severity of organ dysfunction. We documented a higher degree of illness severity, organ supportive measures, and organ failure in both sepsis groups than the control group, as indicated by significantly higher APACHE II and SOFA scores in the septic patients (P-value < 0.001). Also, patients with septic shock have higher scores than the septic group (P-value < 0.001) (Figure 1). Sepsis is a condition that is often easy to recognize clinically but much harder to define.

There is evidence to supports early detection and diagnosis of sepsis, and failure of that results in significant morbidity and mortality [9]. An ideal marker of infection would be highly sensitive, highly specific, easy to measure, and correlated with the prognosis and severity of infection. Many markers are used to identify and evaluate the prognosis of severe sepsis and septic shock, e.g., C-reactive protein (CRP) and procalcitonin (PCT) [10]. One of these inflammatory markers is pentraxin. Pentraxin-3 (PTX-3) is a long pentraxin that shares structural similarities with short pentraxins as a CRP. It is well known that it contributes significantly to innate immunity and inflammatory regulation [2,11]. The aim of this study was to evaluate the diagnostic and prognostic significance of serum pentraxin-3 level in relation to the clinical outcome of critically ill septic patients and to compare it with the diagnostic and prognostic value of the classical biomarkers (PCT and CRP). This study was carried out on sixty-three patients, divided into two groups: the control group comprised seventeen consecutive ICU patients with no identified source of sepsis, and the study group comprised forty-six critically ill patients admitted to the ICU with sepsis. According to severity, our study group was subdivided into two subgroups that included the sepsis group (12 patients) and the septic shock group (34 patients). Cases were also divided into survivors and non-survivors according to the mortality outcome. We found a higher degree of illness severity, mortality, organ supportive measures, and organ failure in septic groups than the control group, as indicated by significantly higher APACHE II and SOFA scores in the septic group (P-value < 0.001). Also, patients with septic shock have higher scores than those in the septic group (P-value < 0.001), especially on admission. A similar result of Liu et al., (2013), a study of 859 patients divided into four groups: sepsis, severe sepsis, septic shock and SIRS, showed that the groups with septic shock and severe sepsis had significantly higher APACHE II score than the groups with sepsis and SIRS (P-value < 0.001) [12]. Our study also found a significant change in mean SOFA score on days 1 and 7 between the survivors (7.6, 2.89, respectively) and the non-survivors (14.58, 14.11, respectively) with a P-value < 0.001, similar to the recent study of 75 septic shock ICU patients by Perez-San Martín et al., (2020) that showed a significant change in mean SOFA score at ICU admission between survivors (= 9) and non-survivors (= 14) with a P-value < 0.001 [13]. Procalcitonin has been studied extensively to diagnose sepsis and provides prognostic insights for sepsis [14-15]. In our study, the mean procalcitonin level was significantly higher in the septic shock group (10.88±11.48 ng/ml) than the septic group (4.59 ± 0.93 ng/ml), with a P-value of 0.022. Our work correlated well with the study done by Yunus et al., (2018), where they studied 364 patients who were admitted with sepsis and septic shock and found mean procalcitonin level (13.9±31.6 ng/ml), which was significantly higher in septic shock patients (median = 8.1 ng/ml) than septic patients (median = 1.4 ng/ml) [16]. Our work found that there was no statistical difference in procalcitonin on admission (day 1) between the survivors (7.23 ng/ml) and the non-survivors (10.21 ng/ml) with a P-value of 0.188. In a meta-analysis of the previous 7 studies with 459 patients with severe sepsis and septic shock, Arora et al., (2015) found the same: in severe sepsis and septic shock group, there was no difference in procalcitonin values between survivors (6.73 ng/ml) and non-survivors (10.16 ng/ml) on day 1 (P-value = 0.069) [17]. In a recent study in 2020, Perez-San Martín et al., (2020) showed that serum PCT concentrations at ICU admission showed no statistically significant differences between these groups (P-value = 0.49) [13]. However, we observe in our work that there was a pattern of decremental changes in procalcitonin levels on days 1 and 7 in the survivors and another non-decremental pattern in procalcitonin levels on days 1 and 7 in the non-survivors. In our study, there was a statistical difference in mean procalcitonin level on day 7 between the survivors (3.94 ng/ml) and the non-survivors (15.78 ng/ml) with a P-value < 0.001. Our work goes hand in hand with the study done by Arora et al., (2015), where they studied data from previous 8 studies with 449 septic patients and found that there was a statistically higher mean procalcitonin level on day 3 between survivors (2.15 ng/ml) and non-survivors (9.78 ng/ml) with a P-value of 0.002 [17]. Our work correlated well with the study done by Magrini et al., (2013), where they studied 261 patients admitted to the emergency unit with signs and symptoms of infection and found that on day 5, the mean PCT values of septic non-survivors (10.7±16.2 ng/ml) were much higher than those of septic survivors (5.1±11.6 ng/ml) with a P-value < 0.02 [18]. In our study, the mean CRP level on day 1 was non-significantly higher in the septic shock group (182.76 mg/l) compared to the septic group (121.64 mg/l), with a P-value of 0.072. Our work was different from the study done by Li et al., (2018), a study of 60 septic ICU patients (stratified into sepsis, severe sepsis, and septic shock groups) that found that the average CRP level in the septic shock group (88 mg/l) was significantly higher than that in the septic group (40 mg/l) with a P-value < 0.005 [19-20]. The higher CRP level in our study was due to different disease severity, as our selected study group was septic patients with multiple organ dysfunction and different septic categories according to the new sepsis definition established in 2016. In our study, there was no statistical difference in CRP level (P-value = 0.182) on admission (day 1) between the survivors (137.66 mg/l) and the non-survivors (180.93 mg/l). Our results were in accordance with a previous study by Mauri et al., (2010), a study of 90 patients admitted to ICU and enrolled when severe sepsis and septic shock were diagnosed. They found the CRP level on admission remained equally high in both the survivors (214 mg/l) and the non-survivors (167 mg/l), with a non-significant P-value of 0.08 [21]. In our data, there was a statistical difference in CRP level (P-value < 0.001) on day 7 between the survivors (60.06 mg/l) and the non-survivors (205.72 mg/l). Our results are similar to results of Kim et al., (2017), a prospective study of 83 severe septic patients who managed by early goal directed therapy, who concluded that CRP levels showed significantly higher levels in non-survivors (median 102.5 mg/l) compared to survivors (median 35.3 mg/l) only at day 7 from admission with sepsis (P-value = 0.004) [22]. A newly discovered acute phase protein, pentraxin 3 is a long pentraxin that is structurally related to the short pentraxins as C reactive protein [23-24]. In our data, a strong statistically significant positive correlation was found between PTX-3 and another inflammatory marker, e.g., procalcitonin (r = 0.712, P-value < 0.001) and C reactive protein (r = 0.533, P-value < 0.001).

Perez-San Martin et al., (2020), also found that PTX-3 levels showed a statistically positive correlation with procalcitonin level (r = 0.329, P-value = 0.005) [13]. In our study, the mean Pentraxin-3 level was significantly greater in the septic shock group (103±66.1 ng/ml) than the septic group (44.4±15.1 ng/ml) on admission, with a P-value < 0.001. We found that the mean PTX-3 level in the septic shock group was similar to previously reported studies, e.g., Kim et al., (2017) (122.0 ng/mL), a prospective study of 83 severe septic patients who managed by early goal directed therapy [22]. The mean pentraxin level of our study goes hand in hand with the results of a previous study by Bastrup-Birk et al. (2013), a study of 261 ICU patients admitted with SIRS [25]. They concluded that a higher level of PTX-3 was associated with the development of sepsis, severe sepsis, and septic shock (mean level of 76±10 ng/mL in patients with SIRS, 118±11 ng/mL in patients with severe sepsis, and 139±13 ng/mL in patients with septic shock). This similarity is related to sepsis severity, with a P-value < 0.001. The ROC curve was calculated to assess pentraxin-3 level on admission as a diagnostic marker for sepsis. The optimal cut off value was 46.5 ng/ml with a sensitivity of 91.3% and a specificity of 100% (AUC 0.96, P-value < 0.001). In our study, PCT and CRP levels on admission had the same P-value < 0.001 as a diagnostic marker for sepsis but less sensitivity (69.6% and 78.3%, respectively). Those results suggest that pentraxin may be advantageous in early diagnosis of sepsis. Our study goes hand in hand with the results of a previous study by Song et al., (2019), a study of 124 ICU patients enrolled into no sepsis (n = 45), sepsis (n = 51), and septic shock (n = 28) groups, using Sepsis-3 definitions, they concluded that the optimal cut off value to discriminate septic shock was 58.28 ng/ml for PTX-3 (93.2% sensitivity, 60.7% specificity), and the AUC to discriminate septic shock was 0.7 with a P-value < 0.001 [26]. Our data showed that serum pentraxin level on day 1 was strongly positively correlated to APACHE II (r = 0.726), SOFA (r = 0.805), and MODS (r = 0.809) scores with a P-value < 0.001, and there was a strong positive correlation between procalcitonin level and SOFA, MODS scores (P-value < 0.001). Similar results by Perez-San Martín et al., (2020), showed that plasma PTX-3 levels at ICU admission showed a statistically significant positive correlation with SOFA score (r = 0.378, P-value = 0.001) and APACHE II score (r = 0.402, P-value < 0.001) [13]. Perez-San Martin et al., (2020) study is similar to our study, which enrolled septic shock patients admitted to the ICU but didn`t exclude immunosuppression disease and had no pentraxin-3 level follow-up at day 7 like our study [13]. In our data, there was a statistically significant positive correlation between PTX-3 levels on day 7 and the SOFA (r = 0.894) and MODS (r = 0.875) scores calculated on day 7 with a P-value < 0.001, i.e., changes in the PTX-3 level were accompanied by significant changes in the SOFA and MODS scores. A high PTX-3 level has been shown to be related to mortality in severe sepsis and septic shock [4,27]. In our study, the mean PTX-3 level on days 1 and 7 was statistically higher in the non-survivors (97.84, 132.5 ng/ml, respectively) than in the survivors (66.9, 41.7 ng/ml, respectively), with a P-value ≤ 0.001. Song et al., (2019), also found that PTX-3 levels within 6 hours of clinical diagnosis of sepsis were significantly higher in the non-survivors (126 ng/ml) than the survivors (29 ng/mL) with a P-value of 0.007, and follow-up PTX-3 levels within 24 hours of discharge were higher in the non-survivors (118 ng/ml) than in the survivors (4 ng/ml) with a P-value of < 0.001 [26,28]. For more optimum results, we studied the relationship between raising PTX-3 levels and mortality. The optimal PTX-3 cut off value to predict ICU mortality was 57.5 ng/ml with a sensitivity of 63.9% and a specificity of 92.6% for ICU mortality (AUC was 0.79, P-value < 0.001) in comparison with procalcitonin and CRP, which showed less specificity (55.6% and 66.7%, respectively) as prognostic markers of ICU mortality in sepsis (P-value = 0.005, 0.003, respectively). Song et al., (2019), also concluded that the optimal cut off value to predict 30-day mortality was 36 ng/ml for PTX-3 (72.2% sensitivity, 59% specificity), and the AUC to discriminate against septic shock was 0.645 with a P-value of 0.017 [26]. The AUC for mortality prediction of PTX-3 in our study (AUC = 0.79) was similar to those in previously reported studies (0.82 by Huttunen et al., (2011), and 0.69 by Uusitalo-Seppälä et al., (2013) [4,29]. Perez-San Martin 2020 et al., also found that at ICU admission, the AUC value of PTX-3 level (AUC 0.698) was significantly better than CRP (AUC = 0.48) and PCT (AUC = 0.43) in predicting in-hospital mortality, and PTX-3 was more accurate in predicting the mortality risk in septic patients than traditional biomarkers (CRP, PCT). Those results with our results conclude that pentraxin levels were superior in the prognosis of mortality in septic patients [13]. According to the mortality outcome, cases were divided into survivors and non-survivors (Table 1). Our data showed significant changes in the mean SOFA score on days 1 and 7 between the survivors (7.6, 2.89, respectively) and the non-survivors (14.58, 14.11, respectively) with a P-value < 0.001, as well as between the septic shock group and the septic group (Table 2). In our study, blood samples collected on day one and day seven from sepsis onset. The mean serum procalcitonin level in our study was significantly higher in the septic shock group (10.88 ng/ml) than the septic group (4.59 ng/ml), with a P-value of 0.022. While the mean serum CRP level was not significantly higher on day 1 between the septic shock group (182.76 mg/l) compared to the septic group (121.64 mg/l) with a P-value of 0.072 (Table 3). We observe in our work that there was no statistical difference in PCT (P-value = 0.188) or CRP level (P-value = 0.182) on admission (day 1) between the survivors (7.23 ng/ml) (137.66 mg/l) and the non-survivors (10.21 ng/ml) (180.93 mg/l), respectively. However, there was a pattern of decremental changes in PCT and CRP levels on days 1 and 7 in the survivors and another non-decremental pattern in PCT and CRP levels on days 1 and 7 in the non-survivors. In our study, there was a statistical difference in mean PCT and CRP levels on day 7 between the survivors (3.94 ng/ml) (60.06 mg/l), respectively, and the non-survivors (15.78 ng/ml) (205.72 mg/l), respectively, with a P-value < 0.001. We observed that serum long pentraxin-3 had a strong statistically positive correlation with another inflammatory marker, e.g., PCT (r = 0.712, P-value < 0.001) and CRP (r = 0.533, P-value < 0.001) (Table 4 & Figure 2). In our study, the PTX-3 level was significantly higher in the septic shock group (103±66.1 ng/ml) than the septic group (44.4±15.1 ng/ml) on admission, with a P-value < 0.001.

Our data showed that serum pentraxin level on day 1 was strongly positively correlated to APACHE II (r = 0.726), SOFA (r = 0.805), and MODS (r = 0.809) scores with a P-value < 0.001 (Table 5). Also, a statistically significant positive correlation was reported between the PTX-3 level on day 7 and the SOFA (r = 0.894) and MODS (r = 0.875) scores calculated on day 7 with a P-value < 0.001, i.e., changes in the PTX-3 level were accompanied by significant changes in the SOFA and MODS scores (Figure 3). The ROC curve was calculated to assess pentraxin-3 level on admission as a diagnostic marker for sepsis. The optimal cut off value was 46.5 ng/ml with a sensitivity of 91.3% and a specificity of 100% (AUC 0.96, P-value < 0.001). In our study, PCT and CRP levels on admission had the same P-value value < 0.001 as a diagnostic marker for sepsis but less sensitivity (69.6% and 78.3%, respectively) than PTX-3. Those results suggest that pentraxin may be advantageous in early diagnosis of sepsis (Table 6 & Figure 4). A high PTX-3 level has been shown to be related to mortality in severe sepsis and septic shock. In our study, the mean PTX-3 level on days 1 and 7 was statistically higher in the non-survivors (97.84 and 132.5 ng/ml, respectively) than in the survivors (66.9 and 41.7 ng/ml, respectively), with a P-value < 0.001 (Table 3). For more optimum results, we studied the relationship between raising PTX-3 levels and mortality. The optimal PTX-3 cut off value to predict ICU mortality was 57.5 ng/ml with a sensitivity of 63.9% and a specificity of 92.6% for ICU mortality (AUC was 0.79, P-value < 0.001) in comparison with PCT and CRP, which showed less specificity (55.6% and 66.7%, respectively) as prognostic markers of ICU mortality in sepsis (P-value = 0.005, 0.003, respectively) (Table 7 & Figure 5).

Table 1: Mortality distribution in studied groups.

		septic shock patients		septic patients		P value
		Count	%	Count	%	
Hospital Mortality	**Non-survivor**	29	85.3%	2	16.7%	< 0.001
	Survivor	5	14.7%	10	83.3%	

Table 2: Distribution of sepsis categories and hospital outcome as regard ICU score (ICU score as regards hospital outcome and Sepsis categories).

	Hospital Mortality			Sepsis category		
	Non-survivor	survivor	P Value	Septic shock	Septic patients	P value
	Mean	Mean		Mean	Mean	
Apache II	32.97	15.80	< 0.001	32.29	13.42	< 0.001
SOFA Day 1	14.58	7.60	< 0.001	14.62	5.75	< 0.001
SOFA Day 7	14.11	2.89	< 0.001	12.55	4.14	0.003
MODS Day 1	11.97	5.47	< 0.001	11.85	4.17	< 0.001
MODS Day 7	11.89	2.56	< 0.001	10.50	3.86	0.009

Table 3: Distribution of serum Pentraxin 3, Procalcitonin and CRP level as regards sepsis categories and Mortality.

		Hospital Mortality		Sepsis category	
		Non-survivor	survivor	Septic shock	Septic patient
PTX1	Mean	97.84	66.9	103	44.6
	P value	0.001		< 0.001	
PTX7	Mean	132.5	41.7	123	42.9
	P value	< 0.001		0.001	
PCT 1	Mean	10.21	7.23	10.88	4.59
	P value	0.188		0.022	
PCT 7	Mean	15.78	3.94	14.52	4.19
	P value	< 0.001		0.002	
CRP1	Mean	180.93	137.66	182.76	121.64
	P value	0.182		0.072	
CRP7	Mean	205.72	60.06	186.98	72
	P value	< 0.001		0.013	

Table 4: Correlation between serum pentraxin 3 level with Procalcitonin and CRP level (day 1 & 7).

		PTX1	PTX7
PCT1 (n 46)	Correlation Coefficient	0.712	-0.109-
	P value	< 0.001	0.587
PCT7 (n 27)	Correlation Coefficient	0.528	0.952
	P value	0.005	< 0.001
CRP1 (n 46)	Correlation Coefficient	0.533	0.060
	P value	< 0.001	0.767
CRP7 (n 27)	Correlation Coefficient	0.277	0.834
	P value	0.161	< 0.001

Table 5: Correlation between inflammatory markers on day 1 & 7 (PTX, PCT and CRP) and ICU score (APACHE II, SOFA, MODs and charlson index).

		Apache II	SOFA Day 1	MODS Day 1	SOFA Day 7	MODSDay 7	Charlson Index
PTX1 (n 46)	**Correlation Coefficient**	0.726	0.805	0.809	0.427	0.402	0.204
	P value	< 0.001	< 0.001	< 0.001	0.026	0.038	0.174
PTX7 (n 27)	**Correlation Coefficient**	0.830	0.772	0.801	0.894	0.875	-0.024-
	P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.906
PCT1 (n 46)	**Correlation Coefficient**	0.404	0.530	0.533	-0.069-	-0.088-	0.087
	P value	0.005	< 0.001	< 0.001	0.732	0.662	0.564
PCT7 (n 27)	**Correlation Coefficient**	0.818	0.777	0.838	0.879	0.863	-0.045-
	P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.824
CRP1 (n 46)	**Correlation Coefficient**	0.380	0.370	0.384	-0.106-	-0.105-	0.102
	P value	0.009	0.011	0.008	0.598	0.601	0.502
CRP7 (n 27)	**Correlation Coefficient**	0.712	0.548	0.613	0.720	0.722	0.109
	P value	< 0.001	0.003	0.001	< 0.001	< 0.001	0.589

Table 6: ROC Curve analysis of Pentraxin, Procalcitonin and CRP on admission as a diagnostic marker for sepsis.

	Area Under Curve	P value	Cut off	Sensitivity %	Specificity %	Accuracy %
PTX1	0.962	< 0.001	46.5	91.3	100	93.7
PCT1	0.917	< 0.001	1.725	69.9	100	77.8
CRP1	0.941	< 0.001	80.5	78.3	94.1	82.5

Table 7: ROC Curve analysis of Pentraxin, Procalcitonin and CRP on day 1 as a prognostic marker for ICU mortality.

	Area Underthe Curve	P value	Cut off	Sensitivity %	Specificity %	Accuracy %
PTX1	0.787	< 0.001	57.5	63.9	92.6	76.2
PCT1	0.707	0.005	3.65	83.3	55.6	71.43
CRP1	0.724	0.003	97	66.7	66.7	66.7

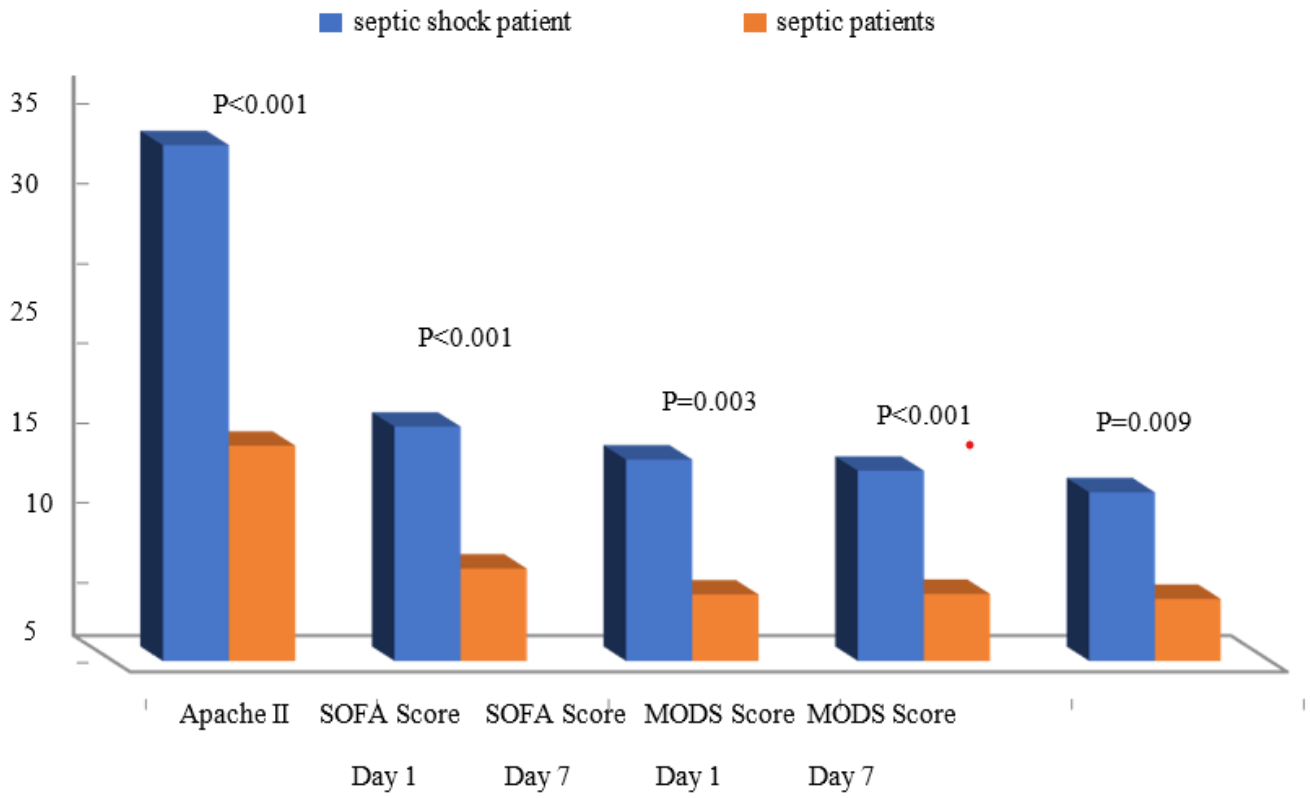

Figure 1: APACHE II, SOFA and MODS score in septic categories.

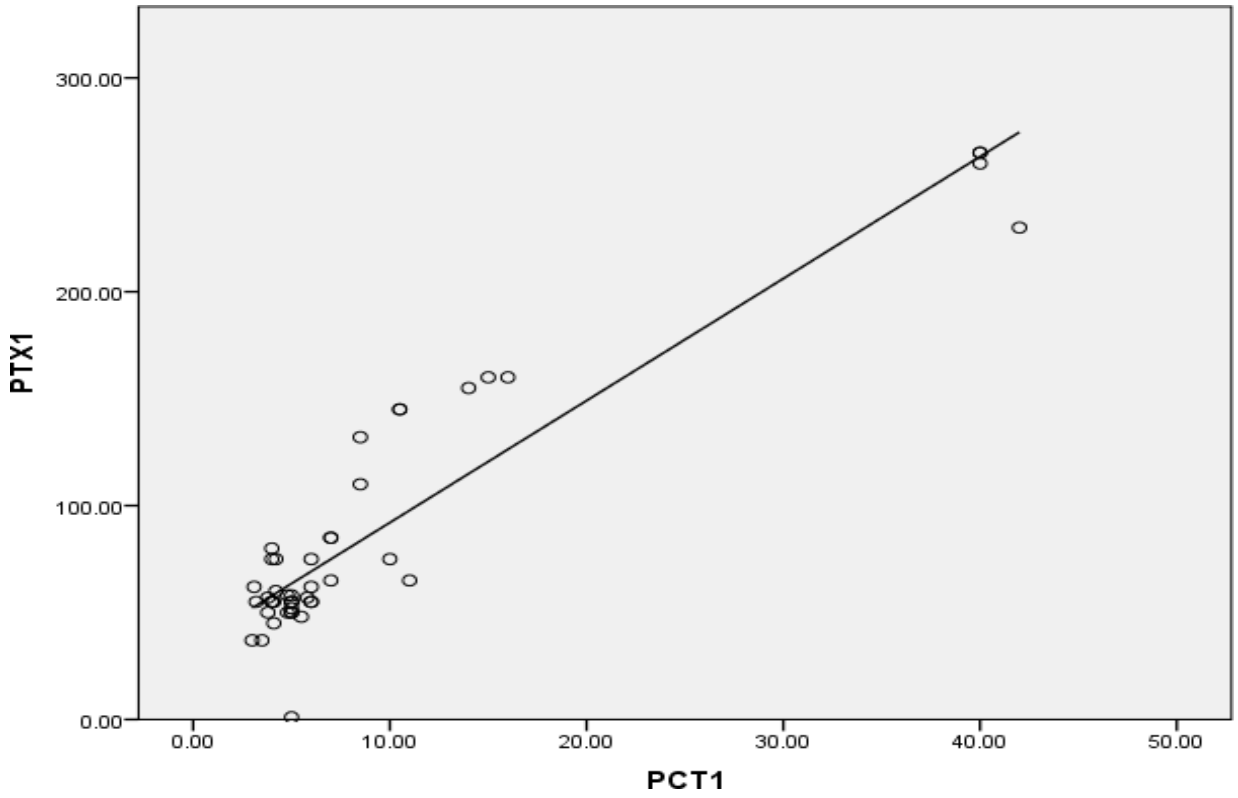

Figure 2: Correlation between Pentraxin day 1 and PCT level day 1.

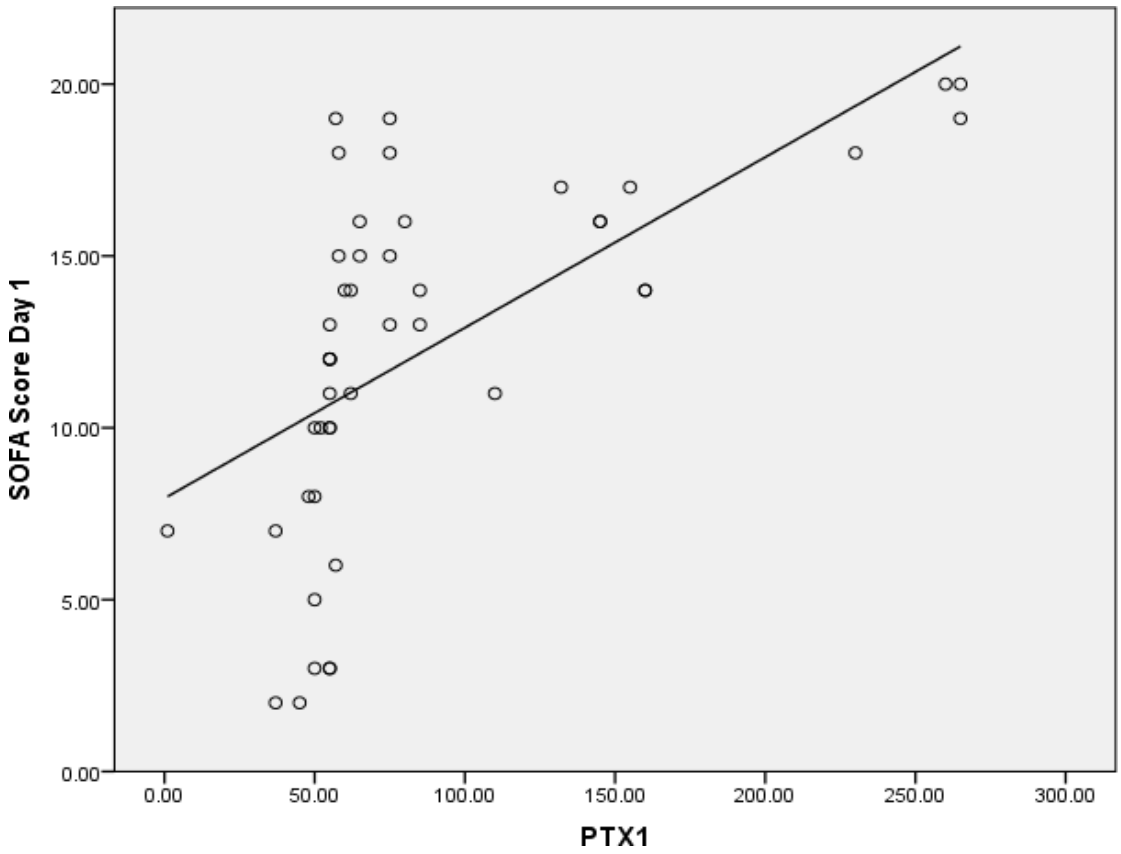

Figure 3: Correlation between Pentraxin day 1 and SOFA score (day 1).

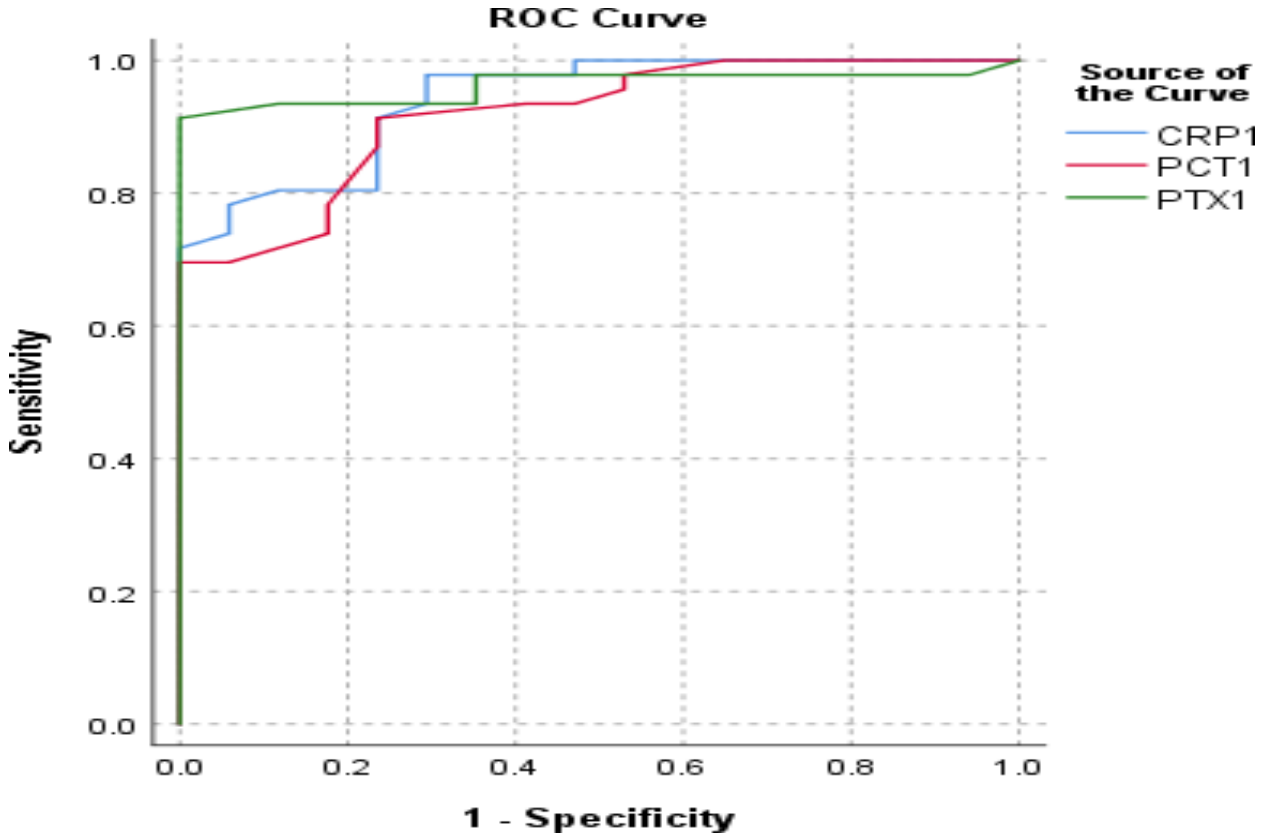

Figure 4: ROC curve for Pentraxin, PCT and CRP on day 1 as a diagnostic marker for sepsis.

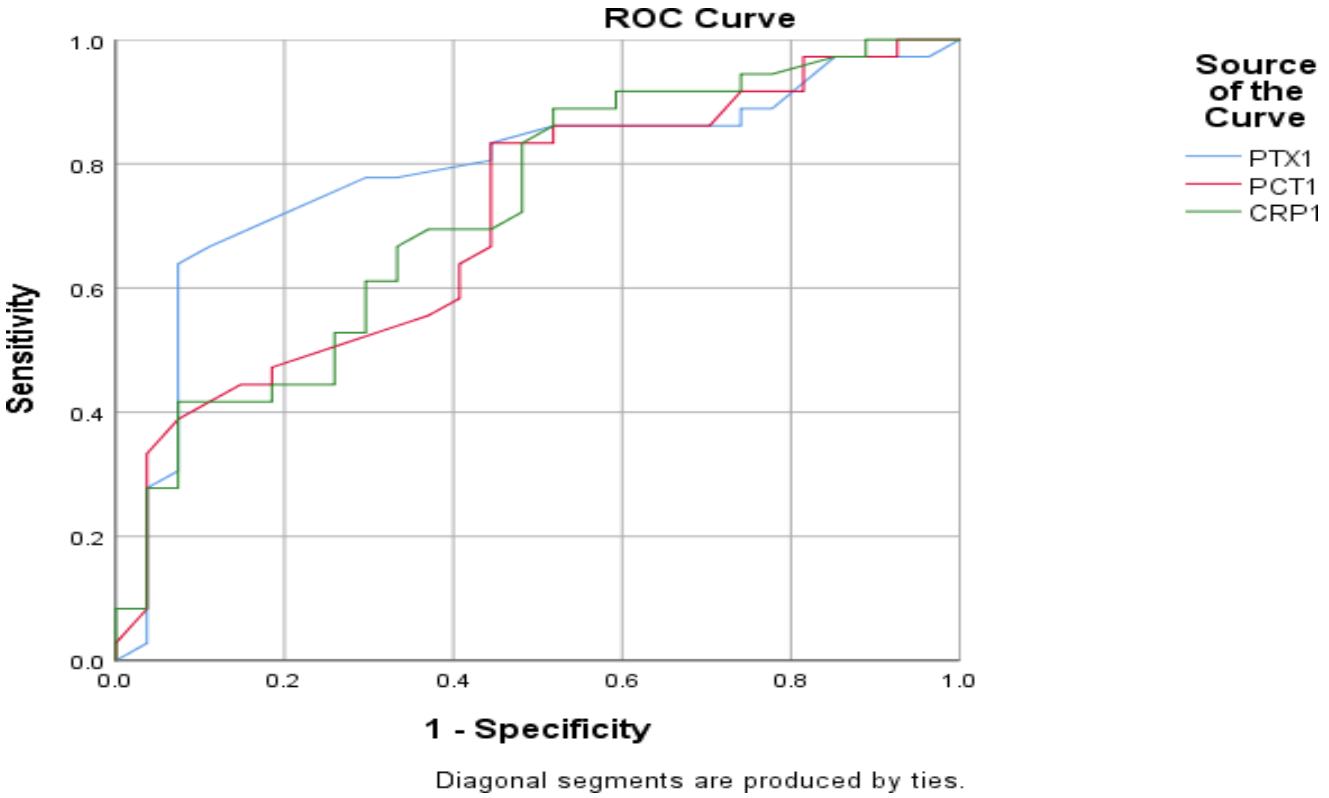

Figure 5: ROC curve for Pentraxin, PCT and CRP on day 1 as a prognostic marker for sepsis to predict ICU Mortality.

4. Conclusions

This study shed light on the novel marker pentraxin-3 for early detection of sepsis and as a prognostic tool for the severity of the disease. We conclude that a serum Pentraxin-3 assay in conjunction with other laboratory markers can help to identify those patients who could potentially benefit from early sepsis management. Pentraxin-3 could serve as a good prognostic marker in critically ill septic patients. Compared to the survivors, the non-survivors had statistically significantly higher serum pentraxin-3 levels from the first day of admission. While there was no statistically significant difference in serum CRP and PCT on admission day between the survivors and the non-survivors. This highlights the importance of rising PTX-3 levels as a prognostic marker and its relation to mortality. Serum pentraxin-3 has a strong significant positive correlation with ICU scoring systems (SOFA, MODS, and APACHE II). Pentraxin-3 level has a significant positive correlation with sepsis severity, which is associated with the development of multiple organ failure and fatal outcomes secondary to acute insult.

Acknowledgment

None

Conflicts of interest

None

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