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Presepsin, procalcitonin and C-reactive protein as diagnostic biomarkers of sepsis in intensive care unit patients

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ABSTRACT

Background: Sepsis is a global, life-threatening health priority. Blood culture is the gold standard of diagnosis of sepsis, however, it requires several days, which delays the diagnosis of the sepsis. Biomarkers could play a pivotal role in diagnosis, grading and predicting the outcome of sepsis. **Objectives:** To assess the potential role of C-reactive protein **(**CRP), procalcitonin (PCT) and presepsin for diagnosis, grading and predicting the prognosis of sepsis. **Methods:** The study included 28 patients diagnosed with sepsis, and 28 intensive care unit (ICU) patients presented by different presentations but with no sepsis. For patients with sepsis, APACHE II score was calculated, blood culture was done using BacT/Alert system, and Vitek 2 to identify bacterial isolates. For all subjects included in the study, quantitative measurement of CRP, PCT and presepsin were done using PA54 Specific Protein Analyzer, VIDAS® immune-analyzer, and PATHFAST fully automated immunoassay analyzer, respectively. **Results:** APACHE II score positively correlated with PCT (*p=0.026*) and presepsin (*p=0.034*), but not CRP (*p=0.291*). Differences between cases and control group for the three biomarkers' levels were statistically significant (*P value <0.001*). For sepsis severity, there were significant increase in PCT and presepsin on admission (P value <0.001) among septic shock compared to sepsis cases. Procalcitonin was slightly superior than presepsin. Procalcitonin and presepsin showed statistically significant increase (*P <0.001* & *p=0.02* respectively) among died compared to survived subgroups. **Conclusion:** PCT and presepsin are reliable biomarkers for early diagnosis, grading and predicting of the prognosis of sepsis.

Introduction

Sepsis is a life-threatening condition recognized by World Health Organization (WHO) as a global health priority and a great challenge among the critical care population [1]. Sepsis has a significant and increasing impact on health sector and is one of the leading causes of mortality. It has been estimated that it affects more than 30 million people worldwide every year, potentially leading to 6 million deaths [2]. The mortality rate ranges from 25-30% for severe sepsis and from 40-70% for septic shock [3].

Early diagnosis of sepsis and administration of effective antibiotics are associated with decreased mortality rates, while the failure to intervene causes significant morbidity and mortality. Also, limiting

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irrational use of antibiotics is exceedingly important to decrease drug resistance [4].

Blood culture is the gold standard for diagnosis of sepsis; however, it usually requires several days for results to be known and may be plagued by some false negative cases, especially in patients undergoing antibiotic therapy [5]. The use of biomarkers for diagnosis of sepsis are thus encouraged not only for the diagnosis of sepsis but also to provide prognostic insights for the disease severity and mortality [4].

Among several sepsis biomarkers, the acute phase reactant, C reactive protein (CRP) is thought to be a useful and relatively common biomarker to evaluate sepsis severity and prognosis, and to monitor treatment response [6]. More recently suggested other substances involved in the antibacterial immunity as procalcitonin (PCT) [7], (a 116-amino acid polypeptide elevated in response to bacterial infection), and presepsin (a soluble CD14 subtype) may be promising biomarkers for both diagnosis and prognosis of sepsis [8].

The present work aimed to assess the potential role of CRP, PCT and presepsin as early diagnostic and prognostic markers of sepsis among critically ill patients in intensive care unit (ICU) in relation to blood culture results and Acute Physiology And Chronic Health Evaluation II (APACHE II) scoring system.

Patients and Methods

The current study was conducted on 56 patients admitted to Intensive Care Unit (ICU) department, Theodor Bilharz Research Institute (TBRI) hospital, Egypt from August 2018 to March 2019. The study protocol was approved by the TBRI Research Ethics Committee (REC) (FWA#000010609). Patients (or relatives of comatosed patients) provided informed consent for study participation.

They were divided into two groups:

1) **Case group:** It included 28 critically ill patients diagnosed with sepsis; have 2 of 4 criteria for Systemic inflammatory response syndrome (SIRS), and presumptive source of infection. SIRS criteria are: (i) temperature >38°C or <36°C, (ii) heart rate >90 beats/minute, (iii) respiratory rate >20 breaths/minute or PaCO2 <32 mmHg when on mechanical ventilation, (iv) WBCs count >12,000/mm3 or <4000/mm3 [9].
2) **Control group:** It included 28 ICU patients presented by different presentation but, with no sepsis.

Exclusion criteria

Patients with age less than 18 years and patients on antibiotic therapy at time of blood collection, patients with immunodeficiency, end-stage liver disease, acute pancreatitis, medullary C-cell carcinoma of the thyroid, major trauma, and severe burns or recent surgery during the previous 72 h.

After enrollment, the case group was subdivided according to the severity of sepsis into sepsis and septic shock subgroups. Diagnosis of septic shock is considered when patient with sepsis suffers from profound circulatory, cellular, and metabolic abnormalities and it is associated with a greater risk of mortality [10]. According to the outcome, the case group was further subdivided into died and survived subgroups.

Clinical calculation of APACHE II score

Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated in the present study by the ICU physicians for the case group to provide a general measure of disease severity and to predict mortality within 24 h of admission of patient to ICU. It was interpreted according to **Knaus et al**. [11].

Blood culture

Blood samples for blood culture were inoculated in BacT/Alert blood culture bottles and incubated in the automated BacT/Alert system (BioMérieux, France) [12]. Bacterial isolates were introduced to Vitek 2 compact system for identification using identification cards for Gram-negative and Gram-positive organisms following Manufacturer's instructions (BioMérieux, France).

Quantitative measurement of CRP

C-reactive protein (CRP) was measured using the PA54 Specific Protein Analyzer (Genrui Biotech Inc., China). The analyzer uses a nephelometric technique to detect CRP in the serum. Measurement range is 3-300 mg/L and reference value: ≤10 mg/L [13].

Quantitative measurement of PCT

We used non-hemolyzed fresh human for the VIDAS® immune analyzer (BioMérieux, France) to measure PCT. The automated instrument uses the enzyme-linked fluorescent immunoassay (ELFA) technique. Results were interpreted following the Manufacturer's instructions, <0.05 ng/ml is found in healthy individuals, <0.5 ng/ml: low risk of sepsis.

Local bacterial infection is possible between ≥0.5 and < 2 ng/ml. Sepsis is possible if ≥2 ng/ml [14].

Quantitative measurement of presepsin

It was measured by a fully automated immunoassay analyzer PATHFASTTM (Mitsubishi Chemical Medicine Corporation, Japan) which combines the progressive chemiluminescence technology with the Magtration® technology. Assay range: 20-20000 pg/ml. Reference values:>200 pg/ml [15].

Statistical analysis

The collected data were statistically analyzed using Statistical Package for Social Science (SPSS) program version 18.0 software for analysis.

Results

1) Demographic and baseline clinical data of the studied groups:

The mean age (years) ± SD of the case group was 63 ± 10.35 ranging from 44 to 80 while the mean age (years) ± SD of the control group was 62 ± 10.63 ranging from 45 to 78. The cases were 11 males (39.3%) and 17 females (60.7%) while the control group was 12 males (42.9%) and 16 females (57.1%). There were no significant statistical differences between the two groups regarding age and sex.

2) Primary site of infection, most common organisms, and relation to biomarkers:

Among the 28 septic patients of the case group; the respiratory tract infections were the most common primary site of infection (14/28) representing 50% of the all cases followed by blood stream-related infections (8/28) representing 28.6%, then urinary tract infections (5/28) representing 17.8% and finally skin and soft tissue infections (1/28) representing 3.6% of all cases

The most isolated bacteria were gram negative bacteria, *E.coli* 12(42.9%) followed by *Klebsiella* species 8(28.6%). Gram positive cocci, Enterococci 2(7.1%), Followed by *Methicillin resistance staphylococcus aureus (MRSA)* 2 (7.1%), *Methicillin resistant coagulase negative staphylococci (MRCONs)* 1(3.6%). Combined infections *E.coli* + *Enterococci* 1(3.6%), *MRSA* + *Enterococci* 1(3.6%).

There were no significant relations between the values of the sepsis biomarkers and blood culture result whether it was Gram-negative, Gram-positive or combined infection. P values were (*0.59, 0.97, 0.66*) respectively

3) Classification of the case group according to the severity and final outcome:

The case group was subdivided according to the severity of sepsis into two subgroups patients with sepsis (18/28, 64.3 %) and those with septic shock (10/28, 35.7%). The case group was followed during the ICU stay and subdivided according to the outcome into two subgroups: died (18/28, 64.3%) and survived (10/28, 35.7%) subgroups.

4) The ability of different markers to diagnose sepsis at the time of admission, correlation with APACHE II score and their diagnostic power:

The median values for the three biomarkers on admission showed highly statistically significant difference between cases and control group in the three biomarkers' levels all *p values* were *<0.001* **(Table 1)**.

There were positive significant correlations between values of PCT and presepsin on admission, and the APACHE II score. Higher APACHE II score was accompanied with higher PCT and presepsin levels and vice versa, p values were *0.026* and *0.034* respectively. While there was no correlation between CRP and APACHE II score (*p=0.291*) **(Table 2)**.

The Receiver Operating Characteristic (ROC) curve was calculated for the studied biomarkers to reveal their role in diagnosis of sepsis on patient's admission. The Area Under the Curve (AUC) was highly significant regarding the three biomarkers with superiority of PCT followed by presepsin (0.99 & 0.96 respectively). The accuracy of the PCT (92.9%) at cut off 0.83 ng/ml was the highest followed by that of the presepsin (85.7%) at cut off 596.5 pg/ml and that of the CRP (83.9%) at cut off 88.89 mg/L in diagnosis of sepsis **(Figure 1)**.

5) The ability of different markers to differentiate between sepsis and septic shock (grading of sepsis) at the time of admission, and their diagnostic power.

There was a significant increase in mortality rate (*P value =0.03*) among septic shock compared to sepsis subgroups. APACHE II score and blood culture results showed that there were no statistical differences among the two subgroups. However, there was highly significant increase in the values of PCT and presepsin on admission (*P value <0.001*) among septic shock compared to sepsis cases with no significant difference in CRP values among the two subgroups **(Table 3)**.

The ROC curve was calculated for the studied biomarkers to reveal their role in diagnosis of septic shock on patient's admission. The AUC was highly significant regarding PCT and presepsin (0.91 & 0.90 respectively) with slight superiority of PCT as it had better sensitivity (90%) and specificity (94.4%). The accuracy of the PCT (92.9%) at cut off 9.61 ng/ml

was the highest followed by that of the presepsin (82.1%) at cut off 3975.5 pg/ml. While the accuracy of CRP (64.3%) at cut off 138.07 mg/dl was the least one in diagnosis of septic shock **(Figure 2)**.

6) The ability of different markers to differentiate between died and survived groups (prognosis of sepsis), correlation with APACHE II score and their diagnostic power.

The present study showed that there was highly significant increase in the APACHE II score among died compared to survived subgroup. Although there was no statistical difference in the blood culture results among the two subgroups, Gram-negative bacilli were the most common isolated pathogens in the dyed subgroup. Regarding the sepsis biomarkers, PCT and presepsin values on admission showed significant increase (*P <0.001* & *P=0.02* respectively) among died compared to survived subgroups. While CRP values on admission showed no significant difference among the two subgroups **(Table 4)**.

The ROC curve was calculated for the studied biomarkers and APACHE II score as predictors of mortality on admission. The AUC was highly significant regarding PCT and APACHE II score (0.89 & 0.84 respectively) followed by that of presepsin (0.77) but was non-significant regarding the CRP (0.6). Results showed that the accuracy of the PCT (85.7%) at cut off 4.96 ng/ml was the highest in prediction of mortality followed by that of the APACHE II score (82.1%) at cut off 19.5, then that of the presepsin (71.4%) at cut off 2171 pg/ml. While the accuracy of CRP (67.9%) at cut off 143.17 mg/dl was the least one in prediction of mortality **(Figure 3)**.

Table 1. Distribution of the sepsis biomarkers among the studied groups on admission.

Sepsis biomarkers	Case group	Control group	MW	*P value*
CRP (mg/L)	(n=28)	(n=28)		
Mean ± SD	148.09 ± 70.73	36.18 ± 50.34	**5.21**	***<0.001****
Median (Range)	149.08 (24.84 – 290.69)	8.5 (1 – 190)		
PCT (ng/ml)	(n=28)	(n=28)		
Mean ± SD	11.52 ± 16.17	0.34 ± 0.25	**6.23**	***<0.001****
Median (Range)	5.61 (0.53 – 79.7)	0.26 (0.10 – 1.01)		
Presepsin (pg/ml)	(n=28)	(n=28)		
Mean ± SD	4249.39 ± 3570.34	366.57 ± 207.12	**5.9**	***<0.001****
Median (Range)	3511.5 (1118 – 13979)	311 (100 – 790)		

CRP:C-reactive protein, PCT: Procalcitonin, SD: Standard deviation, MW: Mann Whiteny test, *: Highly significant (*P<0.01*).

Table 2: Correlation between the values of sepsis biomarkers and APACHE II score.

Sepsis biomarkers		APACHE II score
CRP	r	0.207
	P value	*0.291* NS
PCT	r	**0.420**
	P value	***0.026****
Presepsin	r	**0.403**
	P value	***0.034****

CRP:C-reactive protein, PCT: Procalcitonin, r: Spearman's correlation coefficient, NS: Non-significant (*P >0.05*), *: Significant (*P<0.05*), **: Highly significant (P<0.001).

Table 3: Differences in characteristics among sepsis and septic shock subgroups.

Variables		Sepsis (n=18)	Septic shock (n=10)	Test	*P value*
APACHE II score	Mean ± SD Median (Range)	20.56 ± 8.14 20.5 (9 – 38)	28 ± 8.81 31.5 (11 – 37)	1.93●	*0.06* NS
Blood culture results	Gram-negative bacilli Gram-positive cocci Combined No growth	13 (72.2%) 2 (11.1%) 2 (11.1%) 1 (5.6%)	7 (70%) 3 (30%) 0 (0%) 0 (0%)	2.96#	*0.4* NS
Mortality rate	Died Survived	9 (50%) 9 (50%)	9 (90%) 1 (10%)	**4.48#**	***0.03****
CRP (mg/L) on admission	Mean ± SD Median (Range)	134.9 ± 72.67 132.12 (24.84 –263.89)	171.82 ± 63.72 165.26 (84.75 – 290.69)	1.10●	*0.27* NS
PCT (ng/ml) on admission	Mean ± SD Median (Range)	4.42 ± 3.37 4.12 (0.53 – 15.12)	24.30 ± 21.93 18.25 (0.69 – 79.71)	**3.5●**	***<0.001******
Presepsin (pg/ml) on admission	Mean ± SD Median (Range)	2505.28±2039.96 2009 (353 – 8572)	6931.80±4427.26 4729.5 (2202 – 13979)	**3.51●**	***<0.001******

CRP:C-reactive protein, PCT: Procalcitonin, SD: Standard deviation, # : $\chi 2$ chi square test, ●: MW Mann Whitney test, NS: Non significant (*P >0.05*), *: Significant (*P <0.05*), **: Highly significant (*P <0.01*).

Table 4: Differences in characteristics among died and survived subgroups.

Variables		Died (n=18)	Survived (n=10)	Test	*P value*
APACHE II score	Mean ± SD Median (Range)	27 ± 8.19 26.5 (11 – 38)	16.4 ± 5.95 16.5 (9 – 27)	**2.98●**	***0.003******
Blood culture results	Gram-negative bacilli Gram-positive cocci Combined No growth	12 (66.7%) 3 (6.7%) 2 (11.1%) 1 (5.6%)	8 (80%) 2 (20%) 0 (0%) 0 (0%)	1.87#	*0.60* NS
CRP (mg/L) On admission	Mean ± SD Median (Range)	155.93 ± 76.78 165.3 (24.84 – 290.69)	133.98 ± 59.41 132.12 (31.36 – 243.9)	0.86●	*0.39* NS
PCT (ng/ml) On admission	Mean ± SD Median (Range)	16.31 ± 18.57 12.5 (0.90 – 79.71)	2.88 ± 2.07 2.8 (0.53 – 7.2)	**3.40●**	***0.001******
Presepsin (pg/ml) on admission	Mean ± SD Median (Range)	5163.72 ± 4125.99 4121.5 (518 – 13979)	2146.6 ± 1627.94 3345 (353 – 4693)	**2.30●**	***0.02****

CRP:C-reactive protein, PCT: Procalcitonin, SD: Standard deviation, # : $\chi 2$ chi square test, ●: MW Mann Whitney test, NS: Non significant (*P >0.05*), *: Significant (*P <0.05*), **: Highly significant (*P <0.01*).

Figure 1. ROC curve for ability of CRP, PCT and presepsin in diagnosis of sepsis on admission.

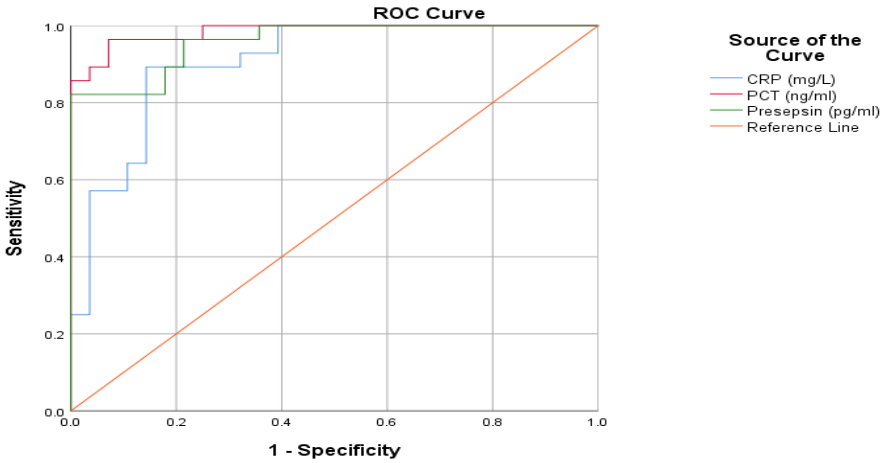


Figure 2. ROC curve for ability of CRP, PCT, presepsin in diagnosis of septic shock on admission.

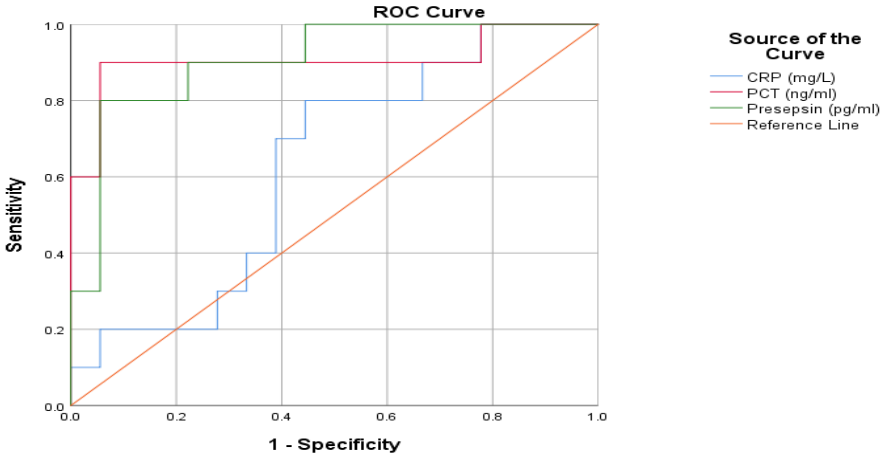
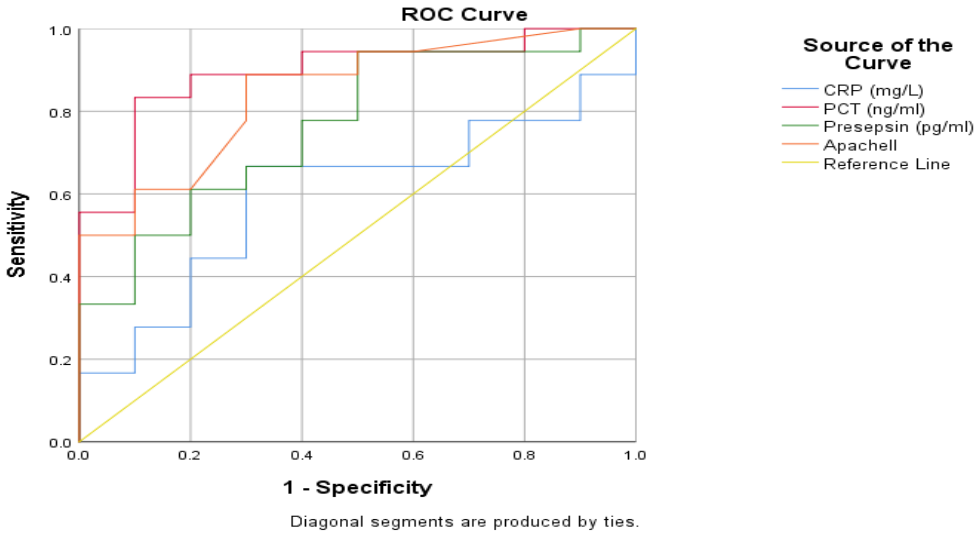


Figure 3. ROC curve for ability of CRP, PCT, presepsin and APACHE II score in prediction of mortality.



Discussion

According to our results, respiratory infections were the most common source of sepsis representing 50% of the studied 28 patients of the case group. Such finding was comparable with an Egyptian study that was conducted on 80 critically ill septic patients admitted to the Critical care department at Cairo university hospital and the ICU at TBRI and showed that the respiratory infections was the etiology of sepsis in 40% of their patients [16].

We demonstrated that Gram-negative bacilli infection (71.5%) was the predominant over the Gram-positive cocci infection (17.8%) among the 28 patients of the cases group. Both *E. coli* and *Klebsiella* species were the most common isolated pathogens. This was in agreement with a previous study [17] where most of the septic patients had Gram-negative bacterial infection (67.6%). On the other hand, others [18,19] revealed that Gram-positive bacteria may have a higher percentage than that of Gram-negative bacteria in the blood cultures. Such a difference in the predominant bacterial type may result from geographic variation and antibiotic prescription habits.

The levels of different sepsis biomarkers were not dependent on the type of infection and the causative organism [5,20]. This finding was compatible with the present study which revealed that there was no significant relation between the levels of the studied biomarkers and the causative organism whether it was Gram-negative or Gram-positive organism.

Regarding the sepsis severity, patients in this study were classified into sepsis (64.3%) and septic shock (35.7%). These figures were in agreement with an Egyptian study which was conducted on 28 patients where 57.1% of the patients were with sepsis and 42.9% with septic shock [20].

Sepsis is considered a major cause of mortality in ICUs. In the present study, the case group was further subdivided into died (64.3%) and survived (35.7%) subgroups. The mortality rate in our study was similar to that reported by **Hassan et al.** [17] at Assiut University where the mortality rate was 64.7%. However, it was higher than that reported by another Egyptian study (39%) [20].

It is known that the mortality rates increased with the severity of sepsis due to the acute circulatory failure and the multiple organs dysfunction associated with the septic shock that are profound enough to substantially increase the death rate [10]. Similarly, the present study revealed that the mortality rate was higher in septic shock than septic patients. Such result was similar to previous Egyptian studies [17, 20].

The CRP is one of non-specific acute phase reactants used in clinical practice to aid in the diagnosis and management of infection. However, these acute phase reactants rise indiscriminately in response to any inflammation even without bacterial infection [21,22]. On the other hand. PCT, is more sensitive and specific in the assessment of sepsis and the risk of mortality [23]. Presepsin, is released in circulation faster than CRP and PCT and produced in response to the host cell activation and phagocytosis of bacteria after the recognition of bacterial LPS or other surface bacterial ligands including Gram-positive peptidoglycans. So, its production is restricted to infection rather than the degree of inflammation [24].

Regarding their role in diagnosis of sepsis, current results revealed that the values of CRP, PCT and presepsin were significantly higher in the case group than in the control group. Such finding was in agreement with others [21,24] who suggested the reliability of such biomarkers in diagnosis of sepsis. **Kondo et al.** and **Dellinger et al.** reported that the plasma CRP and PCT values more than 2 SD above the normal levels, if associated with documented or suspected infection, are considered as part of the definition of sepsis [2,25]

APACHE II score has an important role in predicting the outcome of sepsis in critical care practice [26]. Our results showed that there was a positive significant correlation between the values of PCT, presepsin and the APACHE II score on ICU admission in the studied septic patients, suggesting a role for PCT and presepsin as reliable markers for the disease severity and for ongoing organ dysfunction. These results agreed with other research works [27,28]. On the contrary, the CRP values in our study could not reveal any correlation with the APACHE II score, a finding which was also supported by other studies [29,30].

Kondo et al. suggested that both PCT and presepsin were helpful biomarkers for the early diagnosis of sepsis in critically ill adult patients and also recommended the use of PCT or presepsin tests in combination with other clinical modalities for sepsis diagnosis in ICUs to improve diagnostic accuracy and patient outcomes [2].

The ROC curve analysis was performed to evaluate the role of the sepsis biomarkers in diagnosis of sepsis on ICU admission. The current study showed that the AUC was significantly high regarding the three biomarkers with superiority of PCT in diagnosis of sepsis. The PCT at cut off 0.83 ng/ml had higher AUC and better sensitivity and specificity than presepsin (cut off=596.5 pg/ml) and CRP (cut off=88.89 mg/L). Such findings were remarkably similar to the results of **Takahashi et al.** that revealed that PCT at cut off 0.85 ng/ml had better sensitivity and specificity than presepsin and CRP (cut offs=685pg/ml & 10.4 mg/L respectively) [31] and similar to another study which was performed by **Lai et al.** who showed that the PCT was a helpful biomarker for early diagnosis of sepsis in critically ill patients when compared with the CRP [32] On the contrary, **Juroš et al.** showed that the presepsin had higher AUC than PCT in diagnosis of sepsis [33].

Considering the ability of biomarkers to predict the severity of sepsis on admission, PCT and presepsin level were significantly higher in septic shock than in sepsis patients identifying patients at higher risk of organ dysfunction and adverse outcomes. On the other hand, no significant difference in CRP levels existed between the two subgroups. Such results agreed with the another study which demonstrated that the PCT and presepsin levels were good parameters for reflecting the severity of sepsis [21] On the contrary, **Ulla et al.** reported no differences in the presepsin levels between the sepsis and septic shock groups, and **Zhu et al.** showed no significant association between the level of PCT and the grade of sepsis [34,35].

To discriminate between sepsis and septic shock on ICU admission, ROC curve analysis showed that AUC of PCT at cut off 9.61 ng/ml was slightly higher than that of presepsin at cut off 3975.5 pg/ml, while it showed non-significant AUC regarding CRP at cut off 138.7 mg/L. It also revealed that PCT had the best sensitivity and specificity. Similarly, **Contenti et al.** showed that PCT had slightly higher AUC than presepsin. However, **Amer et al.** revealed that the AUC of presepsin was higher than that of PCT and displayed higher sensitivity in diagnosis of septic shock [20,36]. Such findings strengthened the hypothesis of using both PCT and presepsin in prediction and diagnosis of more severe infections and reflecting the grade of sepsis.

The comparison between the died and survived subgroups showed that CRP values did not differ significantly among the two subgroups on admission and follow up. Similar finding was reported by **El-Shafie et al.** where 31 patients admitted with sepsis to El-Sahel Teaching Hospital, Egypt, and their CRP levels did not show any significant difference between survivors and non-survivors on days 0, 2 or 4 [30]. On the contrary, another study conducted on 20 septic patients, reported that the non-survivors had a significantly higher median CRP concentration than the survivors [37].

The present study revealed that both PCT and presepsin levels on the day of admission were associated with sepsis-related mortality, as both biomarkers were significantly higher in died than in survived patients. Such results agreed with previous studies which reported that the increase of the PCT and presepsin values on the day of hospitalization could predict ICU mortality [17, 38].

For the performance of sepsis prognosis and mortality prediction, a ROC curve was calculated for the three sepsis biomarkers and the APACHE II score on ICU admission. The results showed that the AUC of PCT at cut off 4.96 ng/ml was the highest, followed by the APACHE II score at cut off 19.5 point and the presepsin at cut off 2171pg/ml. So, both biomarkers and the APACHE II score could be good predictors for the mortality that necessitates the construction of more intensive measures to reduce the high mortality rates. These findings agreed with the results of **Kondo et al.** [2]. On the contrary, **Dahaba et al.** and **Schuetz et al.** did not find PCT as a good predictor of mortality [39,40] Also, **Mahmoud et al.** revealed that presepsin had the highest AUC for the mortality prediction in the septic patients when compared to CRP and PCT [38].

On the other hand, although CRP is widely used in the critical care setting and its value as a prognostic and predictor marker is proven in many diseases including sepsis, the levels of CRP in the current study could not predict the mortality in the studied septic patients. Such findings agreed with others who reported that the initial CRP values did not predict mortality in septic ICU patients [35,41].

Conclusion

Our findings suggest that PCT and presepsin may be reliable biomarkers to detect sepsis, grade its severity and predict its prognosis. However, we recommend further studies with larger sample size to assess the application of sepsis biomarkers in the diagnosis, and to provide deeper insight on the

application of PCT and presepsin in determining the therapeutic approaches for sepsis.

Conflict of interest

Authors declare no conflict of interest

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