Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 1.7, Oct. 2024, Supplement Issue

Manuscript ID: ZUMJ-2207-2604 (R1) **Doi: 10.21608/zumj.2022.147784.2604**

ORIGINAL ARTICLE

Presepsin, Serum Lactate and Procalcitonin in Diagnosis and Prognosis of Septic patients in Intensive Care Unit

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Submit Date 19-07-2022
Revise Date 21-08-2022
Accept Date 23-08-2022

ABSTRACT

Background: Sepsis is a worldwide health problem; it is considered as a form of organ dysfunction.

The aim of this study was to identify the role of presepsin in diagnosis of sepsis in ICU patients and its relation to the delta lactate level.

Methods: 46 adult participants were included in the study that was conducted at the clinical pathology department and the Intensive Care Unit (ICU) of zagazig university hospitals. The septic group included patients more than 18 years old with positive sepsis criteria that included; temperature > 38°c or < 36°c, leucocytes >12,000/mm3 or < 4000/mm3, heart rate>90bpm or respiratory rate>20 breaths/min. The non-septic group included healthy control individuals above 18 years old. Demographic data were collected from patients. All patients in this study were subjected to presepsin, CRP and WBCs count measurement. Delta lactate was measured using two lactate measurements. **Results**: We included 31 patients in the septic group; 64.5% (20 participants) of them were males and 15 participants in the non-septic group; 53.3% (8 participants) of them were males. Comparing the two groups regarding sepsis biomarkers; there was a highly significant difference regarding WBCs and CRP with a p-value of <0.001 in comparison to a p-value of 0.037 for the presepsin which was also significant. However, the delta lactate was non-significant with a p-value of 0.560. **Conclusions**: Presepsin can be used as a biomarker in the diagnosis of sepsis in patients of ICU but still the use of multiple biomarkers is better for accurate diagnosis of sepsis

Keywords: Sepsis; Presepsin; Delta Lactate; Procalcitonin

INTRODUCTION

Sepsis is a worldwide health problem; it is considered as a form of organ dysfunction caused by the dysregulated host response to infection. It is among the most common causes of deaths in hospitals despite the progress in medical diagnosis and treatment [1].

The incidence of sepsis has increased over the past 40 years; may be due to the increasing age of population, presence of co-morbidities, associated immunosuppressive treatment and the wrong use

of antibiotics which leads to emergence of resistant bacteria [2].

Early diagnosis of sepsis is important especially in the Intensive Care Unit (ICU) to delay the organ deterioration and to improve the survival rates. Blood culture is considered the gold standard method in diagnosis of sepsis; however, it has some limitations as it is time-consuming because it takes few days to obtain the results. Furthermore, increasing rate of negative culture results which may be due to the prior use of antibiotics [3].

Several scoring systems have been developed for the early diagnosis of sepsis in clinical practice like the systemic inflammatory response syndrome (SIRS) and the sequential organ failure assessment score (SOFA score)[4].

Serum biomarkers are also used in the diagnosis and the prognosis of sepsis and they were included in the 2001 SIRS criteria in the definition of sepsis like C-reactive protein (CRP) and Procalcitonin (PCT), therefore researchers are greatly interested in studying the role of biomarkers [5].

One of the new promising biomarkers is presepsin; it is the soluble fragment of cluster of differentiation 14 (CD14) which is a receptor that interacts with toll-like receptor 4 (TLR4) in the innate immune defense to recognize pathogen associated molecular patterns (PAMPs), therefore presepsin level increases in case of infection [6].

Elevated serum lactate level is associated with the critical tissue hypoperfusion, and it is related to the increased morbidity and mortality from sepsis [7]. Therefore, the aim of the study was to address the role of presepsin in diagnosis of sepsis in ICU patients and its relation to the delta lactate level.

METHODS

46 adult participants were included in the study that was conducted at the clinical pathology department and the Intensive Care Unit (ICU) of zagazig university hospitals. The septic group included patients more than 18 years old with positive sepsis criteria that included temperature > 38°c or < 36°c, leucocytes >12,000/mm3 or < 4000/mm3, heart rate>90bpm or respiratory rate>20 breaths/min. The non-septic group included healthy control above 18 years old. We excluded patients less than 18 years old, pregnant women and patients with end stage liver or kidney disease.

A written consent was obtained from each participant or his relatives.An ethical approval was obtained from Ethical Committee of Research center) Institutional Review Board, Faculty of Medicine, Zagazig University).

Demographic data were collected from patients including their hospital records. All patients in this study were subjected to presepsin measurement by using Enzyme linked immunosorbent assay (ELISA) kits. CRP and WBCs count were obtained from the patients' records during their stay in the ICU. Delta lactate was calculated using two lactate measurements: Delta lactate (ΔLac) = (initial lactate measurement- second lactate measurement). We compared the two groups in relation to presepsin in order to estimate a cutoff value for the diagnosis of sepsis.

STATISTICAL ANALYSIS

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows (IBM Corp., Armonk, NY, USA), MedCalc windows (MedCalc Software bvba 13, Ostend, Belgium) and Microsoft Office Excel 2010 for windows (Microsoft Cor., Redmond, WA, USA). Continuous Quantitative variables were expressed as the mean ± SD & median (range), and categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies (percentage). Continuous data checked for normality by using Shapiro Walk test. The Mann-Whitney U test was used to compare two groups of non-normally distributed data. The Kruskal Wallis H test was used to compare more than two groups of non-normally distributed data. Categorical data were compared using Chi-square test or Fisher's exact test when appropriate. Receiver operating characteristic (ROC) curve

analysis was used to identify optimal cut-off values of biomarkers with maximum sensitivity and specificity for diagnosis of sepsis. Area Under Curve (AUROC) was also calculated, criteria to qualify for AUC were as follows: 0.90 - 1 = excellent, 0.80-0.90 = good, 0.70-0.80 = fair; 0.60-0.70 = poor; and 0.50-0.6 = fail. The optimal cutoff point was established at the point of maximum accuracy. All tests were two sided. p-value < 0.05 was considered statistically significant (S), p-value < 0.001 was considered highly statistically significant (HS), and p-value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

We included 31 patients in the septic group; 64.5% (20 participants) of them were males and 15 participants in the non-septic group; 53.3% (8 participants) of them were males **Figure(1).** However. There was no statistically significance in relation to genderof the participants in each group. The mean age for the septic group was 50.71 ± 21.40. However, it was about 36.33 ± 8.88 in the non-septic group with statistically significant difference between the two groups **Table (1)**.

Comparing the septic and the healthy group regarding the sepsis biomarkers; in the septic group the WBCs and CRP showed a highly significant difference with a p-value of <0.001 while the presepsin showed a p-value of 0.037 which was also significant **table(2).**However, the delta lactate was non-significant with a p-value of 0.560

As regards the diagnosis of sepsis; CRP and WBCs count were the most specific and CRP was the most sensitive. The accuracy of CRP (100%) was the highest followed by WBCs count (95.65%) while presepsin showed accuracy of (74.1%). The WBCs had a Sensitivity of 93.55% (78.6– 99.2), Specificity of 100% (78.2 – 100), Positive Predictive Value of 100%, Negative Predictive Value of 88.2% (66.2– 96.6), Area Under curve of 0.935 (0.822– 0.987) and a p-value of <0.001 (high significant) **Figure(2).** The CRP had a Sensitivity of 100% (88.8 – 100), Specificity of 100% (78.2 – 100), Positive Predictive Value of 100%, Negative Predictive Value of 100%, Area Under curve of 1.000 (0.923– 1.000) and a p-value of <0.001 (high significant) **Figure(3).** The presepsin had a Sensitivity of 68.06% (39.1– 75.5), Specificity of 86.67% (59.5– 98.3), Positive Predictive Value of 90% (70.5– 97.1), Negative Predictive Value of 50% (38.7– 61.3), Area Under curve of 0.691 (0.538– 0.819) and a p-value of 0.014 (significant).Presepsin cutoff value in our study is >65.879pg/ml **Figure (4)**.

Table (1): Comparison between septic group and non-septic group regarding demographic data

Basic characteristics	Septic group (N=31)		Non-septic group (N=15)		Test	p-value (Sig.)
	No.	%	No.	%		
Sex						
Male	20	64.5%	8	53.3%	0.531[a]	0.466 (NS)
Female	11	35.5%	7	46.7%		
Age (years)						
Mean ± SD	50.71 ± 21.40		36.33 ± 8.88		-2.427[b]	0.015 (S)
Median (Range)	55 (20 – 86)		39 (20 – 50)			

a: Chi-square test; b: Mann Whitney U test; p-value< 0.05 is significant; Sig.: Significance.

Table (2): Comparison between septic group and non-septic group regarding sepsis markers

Sepsis markers	Normal range	Non-Septic group (N=15)	septic group (N=31)	Test[b]	p-value (Sig.)
WBC ($X10^3$/ul)	4-11($X10^3$/ul)				
Mean ± SD		7.56 ± 1.88	16.79 ± 6.63	-4.747	<0.001 (HS)
Median (Range)		7.50 (4.80 – 10.80)	15 (2.40 – 30)		
CRP (mg/L)	1-5 (mg/L)				
Mean ± SD		3.53 ± 1.24	212.83 ± 114.09	-5.453	<0.001 (HS)
Median (Range)		4 (1 – 5)	200 (56 – 549)		
Presepsin (pg/ml)	40.4 – 73.1 pg/ml)				
Mean ± SD		57.010 ± 11.105	65.066 ± 17.330	-2.086	0.037 (S)
Median (Range)		61.261 (40.412 – 73.118)	69.979 (24.994 – 95.779)		
Delta serum lactate (mmol/l)	-0.50–0.10 mmol/l				
Mean ± SD		-0.16 ± 0.15	0.02 ± 0.52	-0.582	0.560 (NS)
Median (Range)		-0.10 (-0.50 – 0.10)	-0.20 (-0.60 – 2.30)		

b: Mann Whitney U test; p-value< 0.05 is significant; Sig.: Significance.

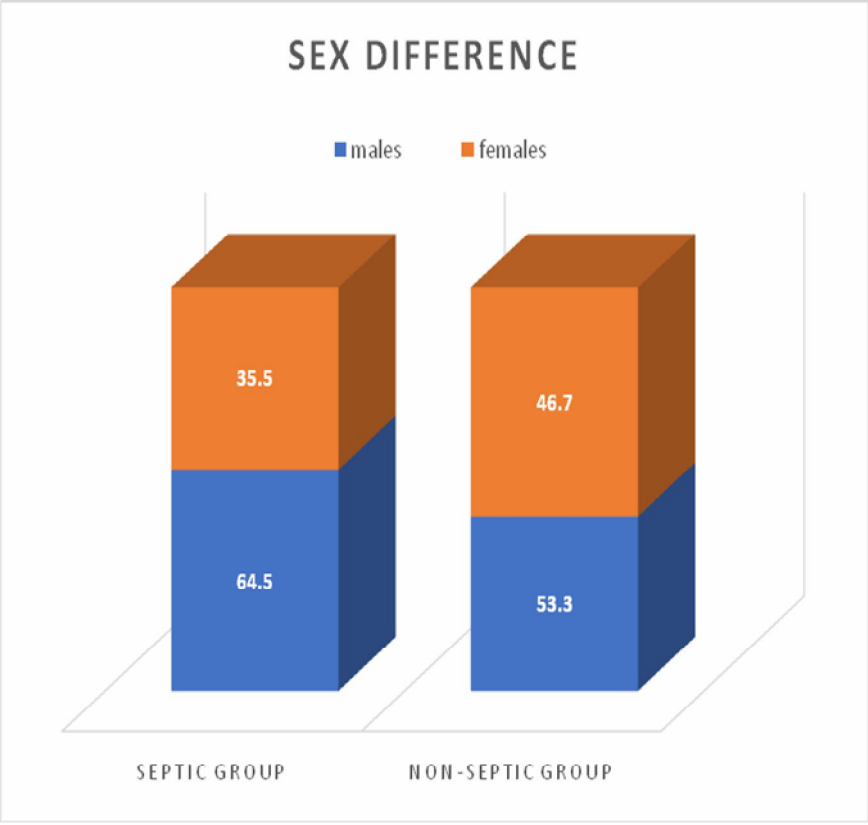

Figure (1): Comparison between septic and non-septic groups regarding sex difference.

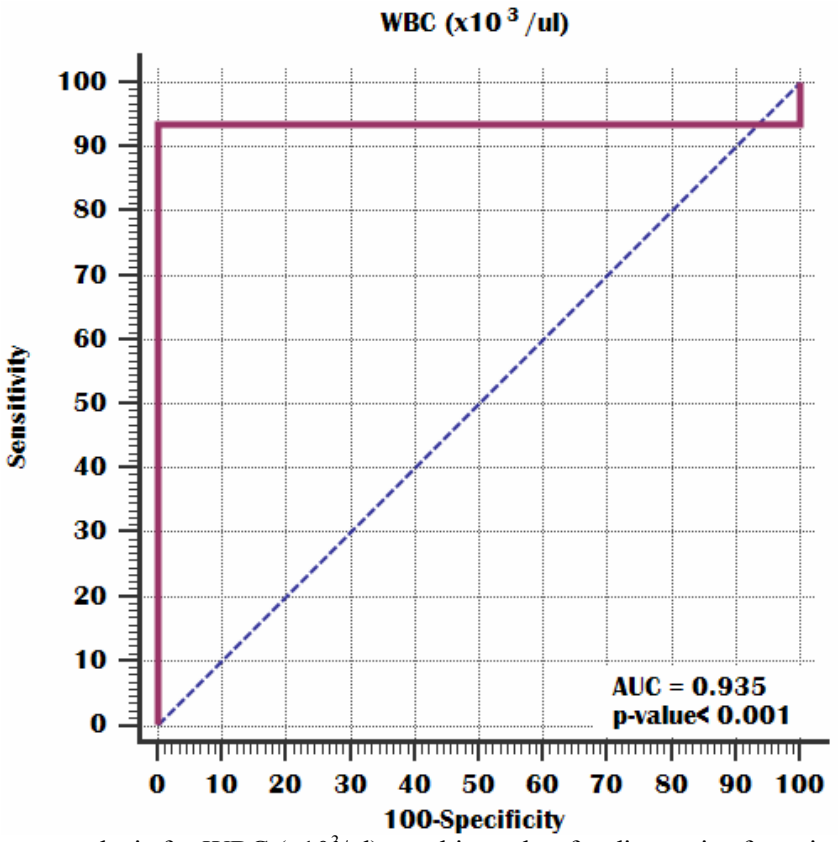

Figure (2): ROC curve analysis for WBC (x10^3/ul) as a biomarker for diagnosis of sepsis.

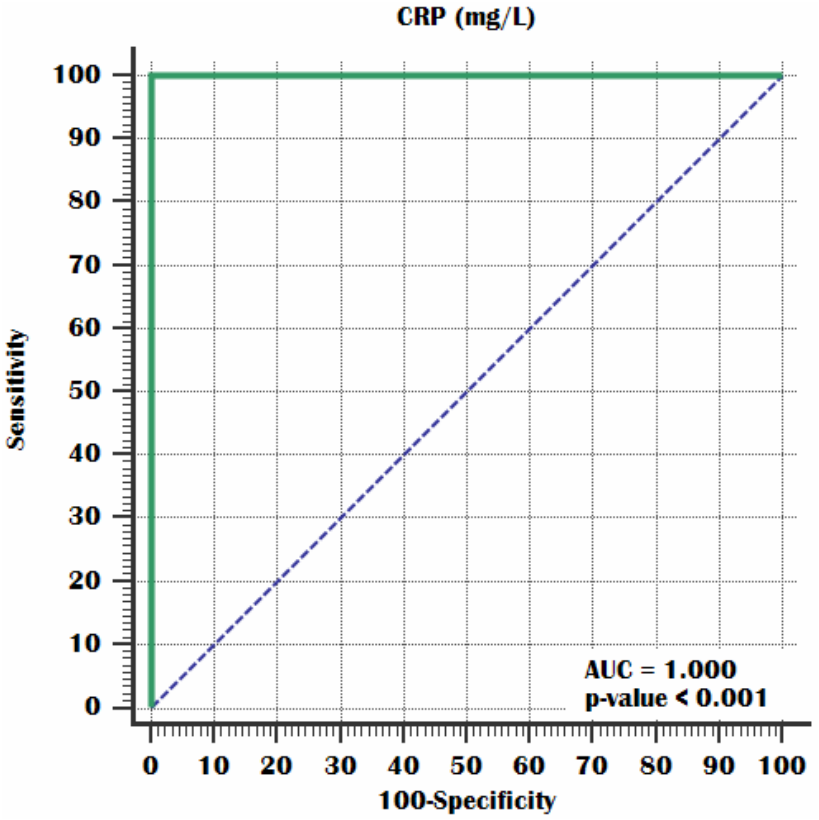

Figure (3): ROC curve analysis for CRP (mg/L) as a biomarker for diagnosis of sepsis.

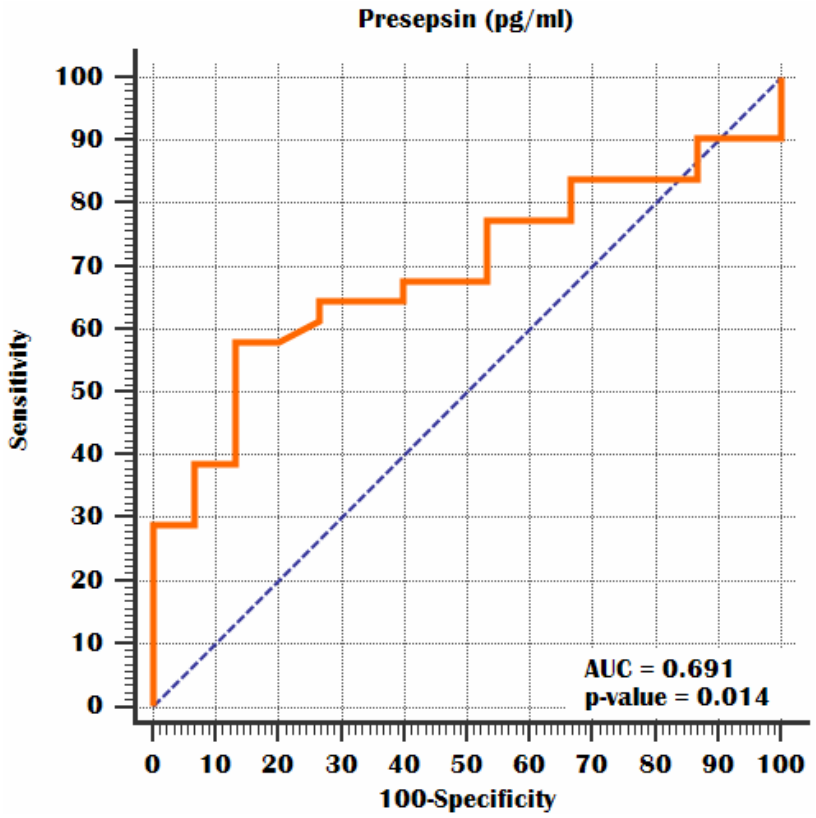

Figure (4): ROC curve analysis for Presepsin (pg/ml) as a biomarker for diagnosis of sepsis.

DISCUSSION

The increased incidence of sepsis and septic patients has directed the efforts of most of the recent research for early diagnosis and risk stratification of septic patients. The 28-day mortality from sepsis varies from 39% up to 74%[8]. The aim of this study was to evaluate the role of presepsin in the diagnosis of sepsis in comparison to delta lactate level in ICU patients.

Recently, different biomarkers are used in the diagnosis of sepsis whether alone or in combination with each other to increase the accuracy of identification of septic patients in sake of better resuscitation. However, there is still controverse about the clinical value of these biomarkers[9].

Regarding demographic data, in our study, there was a statistically significant difference between septic and non-septic groups regarding age, with mean age of 50.71 in the septic group. On the other hand, there was no statistically significant difference regarding sex. However, most of septic group patients were males (64.5%). This was in contrast to the study of Giavarina , D et al, [10]which showed no significant difference regarding both age and sex , the discrepancy in the results may be due to the difference in selection of patients as the non-septic group in our study was normal healthy volunteers.

Presepsin levels are expected to be elevated in sepsis. In our study, presepsin was elevated with a cut off value of >65.879pg/ml in the septic group. However, it had less sensitivity and specificity (AUC=0.691) than the CRP (AUC=1.000), in comparison to Godnic. M et al,[11] who found that the presepsin had less specificity but higher sensitivity (AUC=0.705) than the CRP ,furthermore, the study of Memar et al, [12] about role of presepsin in diagnosis of bacterial infections, showed that presepsin had less sensitivity and more specificity (AUC=0.775) than CRP (AUC=0.588), the difference in the results between our study and other studies may be due to different study type and different materials used.

Presepsin level may be affected by multiple factors that were studied by many investigators like Tsuchida, T et al.[13] who included 1840 outpatients who where suspected to had a bacterial infection and at least performed one measurement of presepsin and concluded that although presepsin increases significantly in bacterial infection, it is also affected by renal dysfunction so presepsin levels should be

interpretated with caution in patients with kidney diseases. Also, Papp, M et al.[14] examined the pitfalls in presepsin especially in cirrhotic patients and concluded that the diagnostic accuracy of presepsin decreases in advanced liver or kidney disease. In our study we excluded patients with advanced liver or kidney disease, also we measured the presepsin within first 6 hours of ICU admission to exclude any affection by previous medication.

Our study results showed that WBCs count was highly significant($p<0.001$) than the presepsin ($p=0.014$) in diagnosis of sepsis, in contrast to the study of Behnes et al ,[١٥] on the diagnostic performance of both presepsin and WBCs count in sepsis which showed that presepsin ($p=0.0001$) was more significant than WBCs count ($p=0.009$) , the discrepancy in results may be due to the single measurement of presepsin in our study while serial measurements would provide more statistical power.

Several studies have illustrated the oxygen consumption in tissue hypoxia and its relation to the increased lactate level in sepsis, furthermore, lactate levels are associated with the patient outcome [١٦].

Single lactate measurement as a predictive for mortality from sepsis was investigated in several studies ,furthermore second lactate measurement was done to quantify the change from the first lactate measurement in the form of delta lactate [١٧].

In our study, delta lactate was calculated for the septic group but it was non-significant ($p=0.560$) as a tool for diagnosis of sepsis as delta lactate was considered to guide the prognosis rather than the diagnosis in several studies like Brio-Ibañez et al , [١٨] who studied the role of delta lactate in the prediction of mortality and stated that lactate clearance is more predictive for mortality than a baseline lactate measurement. However, in the study of Adnan et al,[١٧] on the clinical predictors of early death from sepsis, delta lactate was non-significant in the prognosis of sepsis but serially measured serum lactate levels were significant ,the controverse in results may be due to the selection and duration bias.

This study had several limitations like being single center study, small sample size, single measurement of presepsin not serially and delta lactate was not measured during the resuscitation that might guide the treatment and predict the prognosis which could be an idea for further research.

Conclusion:

Presepsin can be used as a biomarker in the diagnosis of sepsis in patients of ICU but still the use of combined biomarkers is better for accurate diagnosis.

Conflict of interest : none

Financial disclosures : none

REFERENCE:

1. **Moor M, Rieck B, Horn M, Jutzeler CR, Borgwardt K.** Early Prediction of Sepsis in the ICU Using Machine Learning: A Systematic Review. *Front Med*. 2021;8(May). doi:10.3389/fmed.2021.607952
2. **Gotts JE, Matthay MA.** Sepsis: pathophysiology and clinical management. *BMJ*. 2016;353:i1585. doi:10.1136/bmj.i1585
3. Liu Y, Hou J, Li Q, Chen K, Wang S-N, Wang J. Biomarkers for diagnosis of sepsis in patients with systemic inflammatory response syndrome: a systematic review and meta-analysis. *Springerplus*. 2016;5(1):2091. doi:10.1186 /s40064-016-3591-5
4. **Teggert A, Datta H, Ali Z**. Biomarkers for Point-of-Care Diagnosis of Sepsis. *Micromachines*. 2020;11(3):286. doi:10.3390 /mi11030286
5. **Lippi G.** Sepsis biomarkers: Past, present and future. *Clin Chem Lab Med*. 2019;57(9):1281-1283. doi:10.1515/cclm-2018-1347
6. **Zou Q, Wen W, Zhang X.** Presepsin as a novel sepsis biomarker. *World J Emerg Med*. 2014;5(1):16. doi:10.5847/wjem.j.issn.1920-8642.2014.01.002
7. **Freund Y, Delerme S, Goulet H, Bernard M, Riou B, Hausfater P.** Serum lactate and procalcitonin measurements in emergency room for the diagnosis and risk-stratification of patients

with suspected infection. *Biomarkers*. 2012;17(7):590-596. doi:10.3109 /135475 0X.2012.704645

8. **Drăgoescu AN, Pădureanu V, Stănculescu AD, Chiuțu, L, Florescu, D, Gheonea, I, et al.** Presepsin as a Potential Prognostic Marker for Sepsis According to Actual Practice Guidelines. *J Pers Med*. 2020;11(1):2. doi:10.3390/jp m11010002
9. **Nakamura Y, Hoshino K, Kiyomi F, Kawano, Y, Mizunuma, M, Tanaka, J et al**. Comparison of accuracy of presepsin and procalcitonin concentrations in diagnosing sepsis in patients with and without acute kidney injury. *Clin Chim Acta*. 2019;490(August2018):200-206. doi:10.101 6/j.cca.2018.09.013
10. **Giavarina D, Carta M.** Determination of reference interval for presepsin, an early marker for sepsis. *Biochem Medica*. 2015;25(1):64-68. doi:10.11613/BM.2015.007
11. **Godnic M, Stubjar D, Skvarc M, Jukic T.** Diagnostic and prognostic value of sCD14-ST—presepsin for patients admitted to hospital intensive care unit (ICU). *Wien Klin Wochenschr*. 2015;127(13-14):521-527. doi:10.1007/s00508-015-0719-5
12. **Memar MY,** Baghi HB. Presepsin: A promising biomarker for the detection of bacterial infections. *BiomedPharmacother*.2019;111(December 2018):649-656. doi:10.1016/j.biopha.2018.12.124
13. **Tsuchida T, Ie K, Okuse C, Hirose, M, Nishisako, H, Torikai, K, et al.** Determining the factors affecting serum presepsin level and its diagnostic utility: A cross-sectional study. *J Infect Chemother*. 2021;27(4):585-591. doi:10.1016 /j.jiac.2020.11.013
14. **Papp M, Tornai T, Vitalis Z, Tornai, I, Tornai, D, Dinya, T, et al.** Presepsin teardown - pitfalls of biomarkers in the diagnosis and prognosis of bacterial infection in cirrhosis. *World J Gastroenterol* .2016;22(41):9172. doi:10.3748 /wjg.v22.i41.9172
15. **Behnes M, Bertsch T, Lepiorz D, Lang, S, Trinkmann, F, Brueckmann, M, et al.** Diagnostic and prognostic utility of soluble CD 14 subtype (presepsin) for severe sepsis and septic shock during the first week of intensive care treatment. *Crit Care*. 2014;18(5):507. doi:10.1186/s13054-014-0507-z
16. **Filho RR, Rocha LL, Corrêa TD, Souza Pessoa CM, Colombo G, Cesar Assuncao MS**. Blood lactate levels cutoff and mortality prediction in sepsis - Time for a reappraisal? A retrospective cohort study. *Shock*. 2016;46(5):480-485. doi:10.1097/ SHK. 0000000000000667
17. **Javed A, Guirgis FW, Sterling SA, Puskarich, M, Bowman, J, Robinson, T, et al.** Clinical predictors of early death from sepsis. J Crit Care. 2017;42:30-34. doi:10. 1016/j.jcrc.2017.06.024
18. **Brio-Ibañez P del, López-Izquierdo R, Martín-Rodríguez F, Mohedano-Moriano, A, Polonio-López, B, Maestre-Miquel, C, et al.** Clinical Utility of Delta Lactate for Predicting Early In-Hospital Mortality in Adult Patients: A Prospective, Multicentric, Cohort Study. *Diagnostics*. 2020;10(11):960. doi:10.3390/diagnostics10110960

Citation:
Hamada, R., E. Amr, G., saad aldeen, S., Afifi, A. Presepsin versus Delta Lactate in Diagnosis of Sepsis in Intensive Care Unit. *Zagazig University Medical Journal*, 2022; (4210-4217): -. doi: 10.21608/zumj.2022.147784.2604