ABENHA MEDICAL JOURNAL bmj
Print ISSN 1110-208X
Online ISSN 2357-0016

Original article

Presepsin as an Early Diagnostic Marker in Premature Infants with Neonatal Sepsis and Septic Shock

Ashraf M. Shahin [a], Omima M. Abdel Haie [a], Sahar M. Fayed [b], Rime A. Radwan [a]

[a] Department of Pediatrics, Faculty of Medicine Benha University, Egypt. [b] Department of Clinical and Chemical Pathology, Faculty of Medicine Benha University, Egypt.

Corresponding to: Rime A. Radwan, Department of Pediatrics, Faculty of Medicine Benha University, Egypt.

Email: rimeradwan90@gmail.com

Received: 29 October 2023

Accepted: 10 December 2023

Abstract

Background: Neonatal sepsis is a systemic condition involving hemodynamic changes and clinical manifestations caused by bacterial, viral, or fungal infection that occurs within the first 28 days of life. **This study aimed to** assess the accuracy of Presepsin for diagnosis and early detection of sepsis and septic shock among preterm neonates. **Methods:** This Cross-sectional study included 75 preterm neonates with symptoms suspicious of sepsis. They were classified into 3 groups: Group 1; Infection (suspected infection not meeting the criteria for sepsis). Group 2; Sepsis (neonatal systemic inflammatory response syndrome, SIRS, plus suspected or proven infection). Group 3; Septic shock (sepsis plus cardiovascular organ dysfunction). Detailed history, clinical examination, laboratory investigations: Complete blood picture (CBC), C-Reactive Protein (CRP), blood culture and determination of Human Presepsin level in the Blood (PSEP). **Results**: Presepsin level was significantly lower at D3 and D5 compared to D1 (P<0.001). whereas, in group 3 (Septic shock), Presepsin level was significantly lower at D5 compared to D1 (P=0.007). only PLT count, CRP, Presepsin at D1, Presepsin at D3 and Presepsin at D5- were significant predictors of neonatal sepsis and only APGAR at 5 min, PLT count, CRP, Presepsin at D1, Presepsin at D3 and Presepsin at D5- were significant predictors of septic shock in neonates. **Conclusion:** Presepsin is an accurate diagnostic biomarker for early diagnosis of sepsis compared to other acute phase reactant and inflammatory markers. Presepsin is a strong predictive marker for sepsis and septic shock from day1 to day 5 with high sensitivity and specificity.

Keywords: Presepsin; Premature infants; neonatal sepsis; septic shock.

Introduction

Neonatal sepsis is a systemic condition involving hemodynamic changes and clinical manifestations caused by bacterial, viral, or fungal infection that occurs within the first 28 days of life. It is classified as early onset

sepsis (72 hours after birth), and late onset sepsis (72 hours after birth) (1). Neonatal septic shock, a severe clinical evolution of sepsis and it is a common cause of death in critically ill newborns. The incidence of septic shock in the NICU is 1.3- 5.6%, while the mortality of septic shock is 36-40% (2).

The accurate diagnosis of sepsis in the neonatal population is challenging and problematic because of nonspecific clinical presentation and it can rapidly progress into septic shock, multisystem organ failure and death (3).

Blood culture remains the gold standard for the diagnosis of neonatal sepsis, but roughly 48-72 hours are needed to obtain a reliable response, thus isolation of a pathogen is not always successful (false negative) (4).

C-Reactive Protein (CRP) is a nonspecific marker for the diagnosis of neonatal sepsis. In fact, a raised CRP is not necessarily diagnostic for Neonatal Sepsis and may occur due to a physiologic rise after birth, infection, autoimmune disease and meconium aspiration. Also, the CRP levels do not increase significantly until almost 14-48 hours after the start of infection (5).

Presepsin (PSEP) is the cleaved truncated form of the soluble CD 14 (sCD14), which is a multifunctional cell surface glycoprotein expressed on the cell-surface of different immune cell lines and represents a specific high-affinity receptor for complexes of lipopolysaccharides. In addition, it is implicated in the recognition of a wide variety of bacterial products, including peptidoglycans and the major cell wall component of Gram-positive bacteria (6).

After its stimulation by pathogens, the CD14 complex is released by shedding from the cell surface, yielding sCD14, which is then cleaved by the plasma protease activity, generating sCD14 fragments. The 64-amino acid N-terminal fragments constitute the PSEP (7).

The purpose of this study was to assess the accuracy of Presepsin for diagnosis and early detection of sepsis and septic shock among preterm neonates.

Patients and methods

This Cross-sectional study included 75 preterm neonates with symptoms suspicious of sepsis admitted to the neonatal intensive care units of Benha University Hospital and Karmouz Health Insurance Hospital in Alexandria during the period from April 2022 to September 2022.

Approval of the study protocol by the Ethical Scientific Committee of Benha University was obtained. Informed verbal and written parental consent were obtained from the parents before enrollment in the study. **Approval code:MS.10.2.2022**

Inclusion criteria were preterm neonates born at a gestational age of 28 to < 37 weeks admitted to the NICU with an underlying sepsis evaluation. Suspected neonatal sepsis was defined according to CDC criteria, in the presence of at least one clinical symptom (e.g., fever, poor reflexes, lethargy, respiratory distress…) plus the need for antibiotic therapy upon physician's evaluation. Enrolled neonates were followed from the time of diagnosis of neonatal sepsis and start of antibiotic therapy, throughout the length of stay in NICU, and their outcomes were recorded at the end of their stays in the NICU.

Exclusion criteria were full-term neonates and severe neonatal congenital anomalies

Grouping: the cases classified into 3 groups according to Wynn et al.'s definitions: **Group 1**: Infection (suspected infection not meeting the criteria for sepsis).

Group 2: Sepsis (neonatal systemic inflammatory response syndrome, SIRS, plus suspected or proven infection). **Group 3**: Septic shock (sepsis plus cardiovascular organ dysfunction).

All studied cases were subjected to the following: Detailed history taking, including [Medical history, obstetric history, maternal risk factors, postnatal (prolonged resuscitation, respiratory distress, cyanosis, fever and jaundice). Present history: common symptoms of sepsis. **Clinical examination** included estimation of gestational age using the New Ballard score, birth weight, length, head circumference, vital signs; "pulse, respiratory rate, temperature, blood pressure" and neonatal reflexes. **The duration of antibiotic therapy**, inotropic drugs or hydrocortisone administration and the length of stay in the NICU. **Laboratory investigations**: Complete blood picture (CBC), C-Reactive Protein (CRP), blood culture and determination of Human Presepsin level in the Blood (PSEP).

Sampling details: Five milliliters of venous blood sample were taken from each participant under complete aseptic conditions and divided as follows: One milliliter in Ethylenediaminetetraacetic acid (EDTA) tube for complete blood count (CBC). One milliliter of serum sample for C-reactive protein (CRP) testing. Two milliliters of whole blood for blood culture sample were inoculated immediately into blood culture bottles. One milliliter for determination of Human Presepsin level in the Blood (PSEP)by enzyme-linked immunosorbent assay (ELISA). Detection of human presepsin level (PSPN) was done by Human presepsin（PSPN ELISA Kit (Catalogue No.201-12-5358; manufactured by SUNRED BIO, Boashan District, Shanghai).

Presepsin: One milliliter for determination of Human Presepsin level in the blood was obtained from each patient on admission before starting treatment (D1), another sample obtained on the third day (D3) and on the fifth day (D5). Blood was left for 30 minutes to coagulate and then centrifuged for 20 minutes at 3000 rpm. The sera was sprated and stored at -20˚C, avoiding multiple freeze-thaw cycles until time of assay.

Statistical analysis

Statistical analysis was done by SPSS v28 (IBM©, Armonk, NY, USA). Quantitative parametric data were presented as mean and standard deviation (SD) and were analysed by unpaired student t-test. Qualitative variables were presented as frequency (%) and analysed using the Chi-square test. A two-tailed P value < 0.05 was considered statistically significant. Pearson or Spearman's correlation was performed to estimate the degree of correlation between two quantitative variables. ROC curve analysis, the area under the curve (AUC) evaluates the overall test performance (where the area under the curve >50% denotes acceptable performance and area about 100% is the best performance for the test). Multiple regression was also used to estimate the relationship between a dependent variable and one or more independent variables.

Results

Demographic, anthropometric data and maternal history were insignificantly different between the three groups, **Table (1).**

Regarding the postnatal presentation, APGAR at 5 min was significantly lower in group 2 (Proven Sepsis) and group 3 (Septic shock) compared to group 1 (Infection) (P=0.036, 0.001 respectively) and was significantly lower in group 3 (Septic shock) compared to group 2 (Proven Sepsis) (P=0.042), whereas APGAR at 1 min was insignificantly different among the studied groups. Concerning the clinical presentations, cyanosis, hypotonia, oliguria, mottling and hepatosplenomegaly were significantly different among the studied groups (P<0.05).

Regarding the vital signs, Heart Rate (HR), Capillary refill Test (CRT), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were significantly different among the studied groups (P<0.05). Temperature and Respiratory Rate (RR) were insignificantly different among the studied groups. Regarding the laboratory investigations, Total Leucocyte Count (TLC), absolute neutrophil count, Platelet (PLT) count, and CRP were significantly different among the studied groups (P<0.001), whereas Hemoglobin (Hb) level was insignificantly different among the studied groups. Regarding the blood culture, in all neonates included in group 1 (Infection) showed no growth on the blood culture, whereas there were positive blood cultures in both group 2 (Proven Sepsis) and group 3 (Septic shock), with no significant difference between both groups regarding the culture results, **Table (2).**

At D1 and D3, Presepsin level was significantly higher in group 3 (Septic shock) compared to group 1 (Infection) and group 2 (Proven Sepsis) (P<0.05) and was significantly higher in group 2 (Proven Sepsis) compared to group 1 (Infection) (P<0.05). At D5, Presepsin level was significantly higher in group 3 (Septic shock) compared to group 1 (Infection) and group 2 (Proven Sepsis) (P<0.05) and was insignificantly different between group 1 (Infection) and group 2 (Proven Sepsis).

Within group 1 (Infection) and group 2 (Proven Sepsis), Presepsin level was significantly lower at D3 and D5 compared to D1 (P<0.001). whereas in group 3 (Septic shock), Presepsin level was significantly lower at D5 compared to D1 (P=0.007) and was insignificantly different between D1 and D3, **Figure (1).**

Regarding the fate of the studied groups, antibiotic therapy, inotropic drugs, and hydrocortisone were significantly different among the studied groups (P=0.010, <0.001, 0.004 respectively), whereas length of stay in NICU and the outcome were insignificantly different among the studied groups. There was a significant positive correlation between Presepsin at D1 and CRP level (r=0.264, P=0.022). There was a significant positive correlation between Presepsin at D3 and CRP level (r=0.347, P=0.002). There was a significant positive correlation between Presepsin at D5 and CRP level (r=0.495, P<0.001). There were insignificant correlations between Presepsin at D1 and gender, GA at delivery, birth weight and mode of delivery, **Table (3).**

CRP is a significant factor in the early diagnosis of infection in group 1 (Infection) with AUC= 0.845, P value <0.001, at cut off ≤5 mg/dl, 92% sensitivity, 72% specificity, 62.2% PPV and 94.7 % NPV. CRP is a significant factor in the early diagnosis of septic shock in group 3 (Septic shock) with AUC= 0.926, P value <0.001, at cut off >6 mg/dl, 96% sensitivity, 80% specificity, 70.6% PPV and 97.6 % NPV. CRP is an insignificant factor in the early diagnosis of neonatal sepsis in group 2 (Proven Sepsis), **Figure (2).**

In group 1 (Infection), Presepsin level at D1 is a significant factor in the early diagnosis of infection with AUC= 0.869, P value <0.001, at cut off ≤1120 ng/L, 80% sensitivity, 70% specificity, 57.1% PPV and 87.5% NPV. In group 2 (Proven Sepsis), Presepsin level only at D5 is a significant factor in the early diagnosis of neonatal sepsis with AUC= 0.549, P value =0.027, at cut off =685 ng/L, 64% sensitivity, 52% specificity, 40% PPV and 74.3% NPV. Presepsin level at D1 and D3 is an insignificant factor in the early diagnosis of neonatal sepsis. In group 3 (septic shock), Presepsin level at D1 is a significant factor in the early diagnosis of septic shock with AUC= 0.817, P value <0.001, at cut off >1065 ng/L, 96% sensitivity, 70% specificity, 54.5% PPV and 96.8% NPV, **Table (4).**

On multiple regression analysis, we found that only PLT count, CRP, Presepsin at D1, Presepsin at D3 and Presepsin at D5 were significant predictors of neonatal sepsis and only APGAR at 5 min, PLT count, CRP, Presepsin at D1, Presepsin at D3 and Presepsin at D5 were significant predictors of septic shock in neonates, **Table (5).**

Table 1: Demographic, anthropometric data and maternal history of the studied groups

		Group 1 (Infection) (n=25)	Group 2 (Proven Sepsis) (n=25)	Group 3 (Septic shock) (n=25)	P value
Age on admission (days)		2.84 ± 3	2.72±3.3	1.92±2.83	0.513
Gender	Male	14 (56%)	13 (52%)	16 (64%)	0.682
	Female	11 (44%)	12 (48%)	9 (36%)	
GA at delivery (w)		32.96± 2.03	33.4±2	32.52±2.24	0.336
Birth weight (Kg)		1.98 ± 0.48	2.04±0.43	1.85±0.49	0.346
Mode of delivery	CS	17 (68%)	16 (64%)	15 (60%)	0.840
	Vaginal delivery	8 (32%)	9 (36%)	10 (40%)	
Anthropometric data					
HC (cm)		30.16± 2.06	30.36±1.97	29.62±2.07	0.417
Length (cm)		43.04 ±3.08	43.56±2.71	42.34±3.38	0.375
Maternal history					
DM		6 (24%)	6 (24%)	5 (20%)	0.926
Fever		3 (12%)	5 (20%)	6 (24%)	0.541
PROM > 18 h		9 (36%)	11 (44%)	13 (52%)	0.522
UTI		8 (32%)	10 (40%)	10 (40%)	0.796
Preeclampsia		10 (40%)	7 (28%)	9 (36%)	0.662
Antibiotics		8 (32%)	4 (16%)	8 (32%)	0.335
Previous sibling death/ NICU		10 (40%)	9 (36%)	8 (32%)	0.841

Data are represented as mean ± SD or frequency (%), NICU: neonatal intensive care unit, GA: gestational age, CS: caesarean section, HC: head circumference. DM: diabetes mellitus, PROM: Premature rupture of membranes, UTI: Urinary tract infection

Table2: Vital signs examination and laboratory investigations of the studied groups

	Group 1 (Infection) (n=25)	Group 2 (Proven Sepsis) (n=25)	Group 3 (Septic shock) (n=25)	P value
Vital signs examination				
Temperature (^{o} C)	36.94 ± 0.6	36.94 ± 0.34	36.92 ± 0.52	0.981
RR (cycle/min)	67.28±13.49	65.84 ± 13.67	67.6 ± 14.34	0.892
HR (beats/min)	154 ± 12.53	145.4 ± 17.16	132.64 ± 33.86	0.006*
	P1	0.049*	0.005*	
	P2		0.099	
CRT (seconds)	3.0 ± 0.82	3.28 ± 1.17	5.92 ± 0.91	<0.001*
	P1	0.332	<0.001*	
	P2		<0.001*	
SBP (mmHg)	55.36±7.85	53.2 ± 9.83	45.88 ± 15.12	0.011*
	P1	0.395	0.008*	
	P2		0.048*	
DBP (mmHg)	34.0 ± 5.44	32.0 ± 6.16	25.32 ± 12.23	0.001*
	P1	0.230	0.002*	
	P2		0.018*	
Laboratory investigations				
Hb (g/dL)	14.8± 3.26	14.52 ± 4.19	13.64 ± 3.55	0.508
TLC (* 10^3/cmm)	11.99 ± 4.7	14.36 ± 6.24	23.55 ± 11.21	<0.001*
	P1	0.136	<0.001*	
	P2		0.001*	
Absolute neutrophil count (Cells/ µl)	4092.4± 1449.4	7332.1 ± 4596.7	11971.3± 8042.5	<0.001*
	P1	0.002*	<0.001*	
	P2		0.016*	
PLT (* 10^9/cmm)	275.9±68.3	180.64 ± 81.06	171.5 ± 112.3	<0.001*
	P1	<0.001*	<0.001*	
	P2		0.742	
CRP (mg/dL)	3.62 ± 1.31	6.4 ± 4.24	39.9 ± 43.7	<0.001*
	P1	0.003*	<0.001*	
	P2		<0.001*	
Blood culture				
Candida albicans	1 (4%)		2 (8%)	0.964
CONS	3 (12%)		3 (12%)	
E. coli	3 (12%)		5 (20%)	
Enterococcus	3 (12%)		1 (4%)	
GBS	4 (16%)		3 (12%)	
Klebsiella	2 (8%)		1 (4%)	
MRSA	1 (4%)		2 (8%)	
Pseudomonas aeruginosa	2 (8%)		2 (8%)	
Staphylococcus Aureus	2 (8%)		3 (12%)	
Streptococcus	--	4 (16%)	3 (12%)	

RR: respiratory rate, HR: heart rate, CRT: capillary refill test, SBP: systolic blood pressure, DBP: diastolic blood pressure, Hb: haemoglobin, TLC: total leukocyte count, PLT: platelet count, CRP: C-reactive protein, CONS: Coagulase-negative staphylococci, MRSA: methicillin-resistant Staphylococcus aureus, IQR: interquartile range, *: statistically significant as P value <0.05, P1: p value compared to group 1, P2: : p value compared to group 2.

Table 3 : Outcome of the studied groups and correlation between Presepsin and different parameters

		Group 1 (Infection) (n=25)	Group 2 (Proven Sepsis) (n=25)	Group 3 (Septic shock) (n=25)	P value
Length of stay in NICU (days)		16.8 ± 8.88	15.76±4.47	18.8±5.3	0.250
Antibiotic therapy (days)		11.16± 3.98	11.6±3.33	13.76±2.7	0.010*
		P1	0.673	0.009*	
		P2		0.015*	
Inotropic drugs		0 (0%)	2 (8%)	25 (100%)	<0.001*
		P1	0.149	<0.001*	
		P2		<0.001*	
Hydrocortisone		0 (0%)	0 (0%)	7 (28%)	0.004*
		P1	1.0	0.004*	
		P2		0.004*	
Outcome	**Improved**	24 (96%)	22 (88%)	19 (76%)	0.117
	Death	1 (4%)	3 (12%)	6 (24%)	
Correlation between Presepsin and different parameters					
			Presepsin (ng/L) at D1		
			r	P	
Gender			-0.220	0.057	
GA at delivery (w)			-0.223	0.054	
Birth weight (Kg)			-0.254	0.280	
Mode of delivery			0.105	0.372	
CRP (mg/dl)			0.264	0.022*	
			Presepsin (ng/L) at D3		
CRP (mg/dl)			0.347	0.002*	
			Presepsin (ng/L) at D5		
CRP (mg/dl)			0.495	< 0.001*	

NICU: neonatal intensive care unit, *: statistically significant as P value <0.05, P1: p value compared to group 1, P2: p value compared to group 2.

Table 4: Diagnostic accuracy of Presepsin

	Cut-off	Sensitivity	95% CI	Specificity	95% CI	PPV	NPV	AUC	P value
In the early diagnosis of infection in group 1 (Infection)									
D1	≤1120	80	59.3 -93.2	70	55.4 -82.1	57.1	87.5	0.869	<0.001*
D3	≤989	80	59.3 -93.2	68	53.3 -80.5	55.6	87.2	0.838	<0.001*
D5	≤685	84	63.9 -95.5	64	49.2 -77.1	53.8	88.9	0.758	<0.001*
In the early diagnosis of neonatal sepsis in group 2 (Proven Sepsis)									
D1	>970	72	50.6 - 87.9	50	24.7 - 52.8	36.7	73.1	0.552	0.450
D3	≤1740	72	50.6 - 87.9	59	34-60	42.5	61.1	0.502	0.977
D5	685	64	42.5 - 82.0	52	37.4 - 66.3	40	74.3	0.549	0.027*
In the early diagnosis of septic shock in group 3 (septic shock)									
D1	>1065	96	79.6 - 99.9	70	45.2 - 73.6	54.5	96.8	0.817	<0.001*
D3	>785	96	79.6 - 99.9	60	35.5 - 74.5	49	96.2	0.840	<0.001*
D5	>677	92	74.0 - 99.0	70	55.4 - 82.1	60.5	94.6	0.900	<0.001*

Table 5: Multiple regression analysis for prediction of neonatal sepsis and septic shock in neonates

	Coefficient	SE	t	P	r partial	r semipartial
Age on admission (days)	0.007	0.024	0.298	0.767	0.048	0.035
Gender	0.107	0.135	0.793	0.433	0.128	0.094
GA at delivery (w)	0.051	0.098	0.517	0.608	0.084	0.062
Birth weight (Kg)	-0.110	0.425	-0.260	0.796	-0.042	0.031
Mode of delivery	0.027	0.171	0.161	0.873	0.026	0.019
APGAR at 1 min	-0.005	0.062	-0.081	0.936	-0.013	0.010
APGAR at 5 min	-0.116	0.086	-1.350	0.185	-0.214	0.161
Hb (g/dL)	0.008	0.017	0.476	0.637	0.077	0.057
TLC (* 10^3/cmm)	-0.001	0.016	-0.076	0.940	-0.012	0.009
Absolute neutrophil count (Cells/ µl)	0.000	0.000	1.860	0.071	0.289	0.221
PLT (* 10^9/cmm)	-0.003	0.001	-3.260	0.002*	-0.468	0.388
CRP (mg/dL)	0.039	0.018	2.165	0.036*	0.307	0.241
Presepsin at D1 (ng/L)	0.001	0.00	2.838	0.007*	0.390	0.316
Presepsin at D3 (ng/L)	0.001	0.000	3.852	<0.001*	0.486	0.486
Presepsin at D5 (ng/L)	0.001	0.000	2.850	0.006*	0.380	0.380
Septic shock in neonates						
Age on admission (days)	-0.028	0.022	-1.298	0.202	-0.206	0.128
Gender	0.092	0.111	0.831	0.411	0.134	0.082
GA at delivery (w)	0.075	0.083	0.912	0.367	0.146	0.090
Birth weight (Kg)	-0.322	0.360	-0.895	0.376	-0.144	0.088
Mode of delivery	-0.101	0.113	-0.889	0.380	-0.143	0.088
APGAR at 1 min	0.011	0.061	0.185	0.855	0.030	0.018
APGAR at 5 min	-0.178	0.057	-3.102	0.004*	-0.450	0.306
Hb (g/dL)	-0.013	0.016	-0.819	0.418	-0.132	0.081
TLC (* 10^3/cmm)	0.015	0.008	1.818	0.077	0.283	0.179
Absolute neutrophil count (Cells/ µl)	0.000	0.000	1.133	0.264	0.181	0.112
PLT (* 10^9/cmm)	-0.002	0.001	-3.044	0.004*	-0.443	0.300
CRP (mg/dL)	0.005	0.002	3.061	0.004*	0.415	0.291
Presepsin at D1 (ng/L)	0.001	0.000	2.255	0.029*	0.319	0.215
Presepsin at D3 (ng/L)	0.000	0.000	2.868	0.006*	0.386	0.306
Presepsin at D5 (ng/L)	0.000	0.000	5.319	<0.001*	0.609	0.609

GA: gestational age, APGAR: appearance, pulse, grimace, activity, and respiration, Hb: haemoglobin, TLC: total leukocyte count, PLT: platelet count, CRP: C-reactive protein, SE: standard error, *: statistically significant as P value <0.05

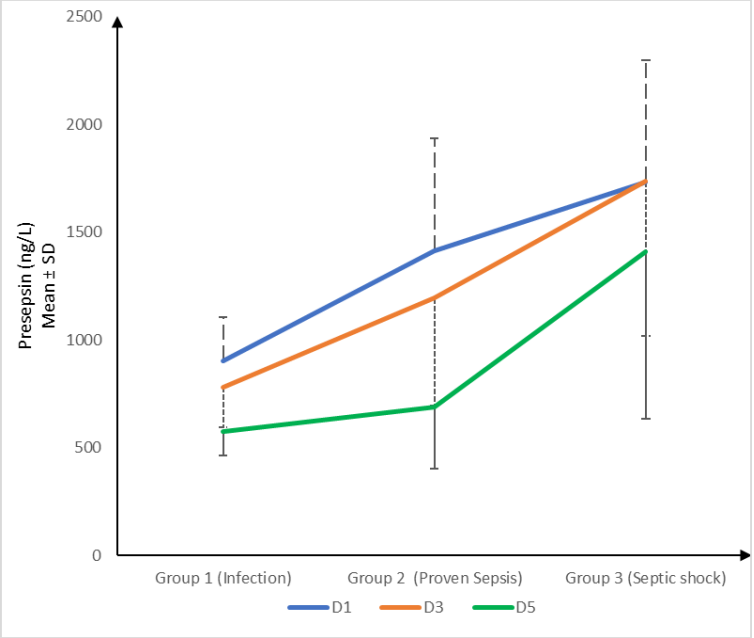
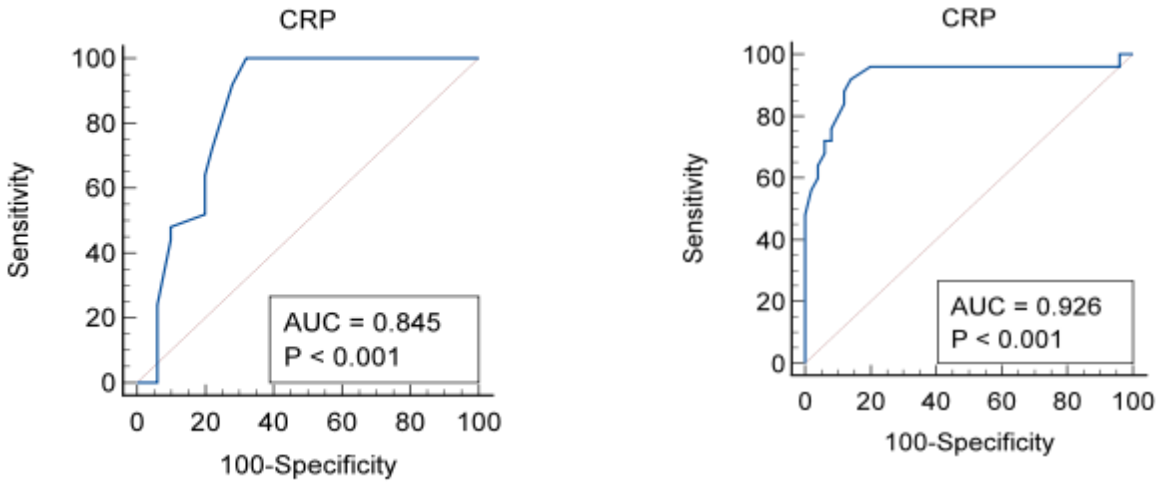


Figure 1: Comparison of Presepsin level of the studied groups



(A) **(B)**

Figure 2: ROC curve of CRP in the early diagnosis of (A) infection in group 1 (Infection), (B) Septic shock in group 3 (Septic shock)

Discussion

Inflammation is an organism's defensive response to damage to its integrity. The hallmark of innate immunity is the ability to recognize and react to a broad spectrum of pathogens mediated by pathogen-associated molecular patterns (8).

In the present study, demographic data of the enrolled neonates were insignificantly different among the studied groups. There was an insignificant difference among the studied groups regarding the maternal history. Our results are similar to prospective study that conducted on 288 pregnant women with preterm infants between 24 + 0 and 36 + 6 weeks of gestation who were classified into two groups sepsis and non- sepsis group. They found that there was no significant difference between sepsis and non-sepsis groups regarding maternal GA, and birth weight. there was no significant difference between sepsis and non-sepsis groups regarding maternal age and fever (9).

Concerning the APGAR score and clinical presentations, our results were in accordance with Pietrasanta et al. who found that the Apgar score at 5 min was significantly lower in sepsis and septic shock compared to the infection group. They demonstrated that the oligoanuria was significantly higher in septic group compared to sepsis and infection groups (10).

In our results, TLC was significantly higher in group 3 compared to group 1 and group 2 ($P<0.001$, 0.001 respectively) and was insignificantly different between group 1 and group 2.

In agreement with our results, a study showed contrasted results as TLC was insignificantly differed between sepsis, septic shock, and infection groups (10).

In the present study, Absolute neutrophil count and CRP were significantly higher in group 3 compared to group 1 and group 2 and were significantly higher in group 2 compared to group 1.

Supporting our results, a prospective study aimed to determine the diagnostic utilities of Presepsin for early detection of neonatal sepsis. The study was conducted on 45neonates; 25 cases and 20 healthy neonates were enrolled as a healthy control group. They found a high statistically significant difference between the studied cases and control as regards total leucocytic count, Immature/Total neutrophils ratios, CRP and platelets count (11).

In the present study, Presepsin level was significantly different among the studied groups at all measurements (D1, D3 and D5). At D1 and D3, Presepsin level was significantly higher in group 3 compared to group 1 and group 2 and was significantly higher in group 2 compared to group 1. At D5, Presepsin level was significantly higher in group 3 compared to group 1 and group 2 and was insignificantly different between group 1 and group 2.

Supporting our results, Pietrasanta et al. showed that the initial presepsin level was significantly higher in septic shock and sepsis group compared to the infection

group, and was significantly higher in the septic shock group compared to the sepsis group (10).

Also, a study reported that the median umbilical cord presepsin was significantly higher in sepsis cases than in those without sepsis 2,231 pg/mL (range, 1,442–3,988 pg/mL) versus 275 pg/mL (range, 116–326 pg/mL; P < 0.000) (9).

In the present study, in all neonates included in group 1 (Infection) showed no growth on the blood culture, whereas the blood culture was positive in both group 2 and group 3, with no significant difference between both groups regarding the culture results.

In another study, 25.8% of cases in the infection group showed positive blood culture growth that was differed from our results, they also showed that there was statistically significant difference between groups regarding the blood culture results. Cases who had blood culture growth were significantly higher in septic shock cases compared to the sepsis group (10).In the current study, there were insignificant correlations between Presepsin at D1and gender, GA at delivery, birth weight and mode of delivery. A study reported that there were no correlations between Presepsin and gestational week (r = 0.178, p = 0.26), postnatal age (r = 0.159, p = 0.315), and birth weight (r = 0.059, p = 0.712) (12).

A study showed that the best cut off for Presepsin inpredicting infection, sepsis, and septic shock were as follow; 687.5 pg/mL for infection (81% sensitivity, 62% specificity), 1013 pg/mL for sepsis (84% sensitivity, 88% specificity), and 971.5 pg/mL for septic shock (92% sensitivity, 86% specificity) (10).

In addition, the cut-off for blood Presepsin to discriminate patients with sepsis from those without is 337 pg/mL, and the manufacturer set a mean Presepsin level of 160 pg/mL (95% CI: 148–171 pg/mL) in healthy individuals (13).

In our results, on multiple regression analysis, we found that only APGAR at 5 min, PLT count, CRP, Presepsin at D1, Presepsin at D3 and Presepsin at D5 were significant predictors of septic shock in neonates.

A study investigated the Presepsin levels of adult patients with severe sepsis and septic shock, and they showed that Presepsin levels have significant associations with parameters reflecting the intensity and severity of sepsis.

They also detected Presepsin as a powerful prognostic biomarker of short- and long-term prognosis in patients with severe sepsis and septic shock (14).

Conclusion

Presepsin is an accurate diagnostic biomarker for early diagnosis of sepsis compared to other acute phase reactant and inflammatory markers. Presepsin is a strong predictive marker for sepsis and septic shock from day1 to day 5 with high sensitivity and specificity.

References

1. Odabasi IO, Bulbul A. Neonatal Sepsis. Sisli Etfal Hastan Tip Bul. 2020;54:142-58.
2. Spaggiari V, Passini E, Crestani S, Roversi MF, Bedetti L, Rossi K, et al. Neonatal septic shock, a focus on first line interventions. Acta Biomed. 2022;93:e2022141.
3. Celik IH, Hanna M, Canpolat FE, Mohan P. Diagnosis of neonatal sepsis: the past, present and future. Pediatr Res. 2022;91:337-50.
4. Zea-Vera A, Ochoa TJ. Challenges in the diagnosis and management of neonatal sepsis. J Trop Pediatr. 2015;61:1-13.
5. Eichberger J, Resch E, Resch B. Diagnosis of Neonatal Sepsis: The Role of Inflammatory Markers. Front Pediatr. 2022;10:840288.
6. El-Madbouly AA, El Sehemawy AA, Eldesoky NA, Abd Elgalil HM, Ahmed AM. Utility of presepsin, soluble triggering receptor expressed on myeloid cells-1, and neutrophil CD64 for early detection of neonatal sepsis. Infect Drug Resist. 2019;12:311-9.
7. Kieliszek M, Pobiega K, Piwowarek K, Kot AM. Characteristics of the Proteolytic Enzymes Produced by Lactic Acid Bacteria. Molecules. 2021;26.
8. Paludan SR, Pradeu T, Masters SL, Mogensen TH. Constitutive immune mechanisms: mediators of host defence and immune regulation. Nature Reviews Immunology. 2021;21:137-50.
9. Seliem W, Sultan AM. Presepsin as a predictor of early onset neonatal sepsis in the umbilical cord blood of premature infants with premature rupture of membranes. Pediatrics International. 2018;60:428-32.
10. Pietrasanta C, Ronchi A, Vener C, Poggi C, Ballerini C, Testa L, et al. Presepsin (Soluble CD14 Subtype) as an Early Marker of Neonatal Sepsis and Septic Shock: A Prospective Diagnostic Trial. Antibiotics (Basel). 2021;10.
11. Mahmoud Zayed K, Abd ELmoez Ali Saad A, Mohamed Amin W, Gamal Abo El-Nasr M. Diagnostic value of presepsin in detection of early-onset neonatal sepsis. Al-Azhar Journal of Pediatrics. 2020;23:825-51.
12. Topcuoglu S, Arslanbuga C, Gursoy T, Aktas A, Karatekin G, Uluhan R, et al. Role of presepsin in the diagnosis of late-onset neonatal sepsis in preterm infants. The Journal of Maternal-Fetal & Neonatal Medicine. 2016;29:1834-9.
13. Giavarina D, Carta M. Determination of reference interval for presepsin, an early marker for sepsis. Biochem Med (Zagreb). 2015;25:64-8.
14. 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. Critical Care. 2016;18:1-13.

To cite this article: Ashraf M. Shahin, Omima M. Abdel Haie, Sahar M. Fayed, Rime A. Radwan. Presepsin as an Early Diagnostic Marker in Premature Infants with Neonatal Sepsis and Septic Shock. BMFJ 2024;41(2):1-13.