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Diagnostic Evaluation of Hematological Sepsis Score and Presepsin in Neonatal Sepsis

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Abstract

Background: Early detection of neonatal sepsis and categorization of patients based on clinical severity is not yet effectively achieved. Some hematological parameters are used to formulate a hematological scoring system (HSS) and a modified hematological scoring system (MHSS) to diagnose neonatal sepsis. A promising biomarker: Presepsin, or Soluble Cluster of Differentiation 14 SubType (sCD14-ST), is a proteolysis product of CD14 produced after immune activation during infections. The purpose of this research is to assess the performance of both hematological sepsis scores and serum presepsin level in neonatal sepsis and compare them to C-reactive protein (CRP) as diagnostic tools and predictors of mortality.

Materials and Methods: This case-control study comprised two groups, one group comprised 51 neonates who were further subgrouped into suspected & proved sepsis, along with 30 uninfected neonates as the control group. Both groups were subjected to the calculation of HSS and MHSS, serum presepsin levels, CRP measurement, and blood culture and assessed for clinical severity and mortality.

Results: Hematological sepsis scores and presepsin levels were significantly higher in the sepsis group (P <0.001). Presepsin showed the best diagnostic performance at > 0.5 ng/ml (AUC 0.979; sensitivity of 94.1% and specificity of 100%). While HSS and MHSS at a cutoff value > 1 achieved comparable specificity, lower sensitivity, 72.6% for the former and 76.5% for the later was noted. Presepsin also was significantly higher in the dead group (P<0.004) with the best predictive performance over CRP at cutoff value >1.9 ng/ml (AUC 0.838; sensitivity of 85.7% and specificity of 79.6%).

Conclusion: Hematological sepsis scores and presepsin were useful diagnostic tools in neonatal sepsis, with presepsin as a good predictor of mortality comparable to CRP.

Keywords: Blood Cell Count, Neonatal Sepsis, Presepsin Protein, Systemic Inflammatory Response Syndrome

Introduction

In developing countries, newborn septicemia is responsible for 30-50% of all neonatal mortality (1). Multicenter studies in Egypt showed that the overall incidence of suspected sepsis was 32.9% at the Neonatal Intensive Care Units (NICUs) of Cairo Hospital, 45.9% at three NICUs in Mansoura with a mortality rate of 42.9% - 51% for proved neonatal sepsis, 38.5% at the NICU of the Zagazig Hospital, and was 8.6% in the NICUs of South Sinai Hospitals with 25% fatality rate (2-5). Considering the high mortality and serious morbidity, a diagnostic marker for neonatal sepsis with high sensitivity and specificity is needed (6). Abnormal hematological counts, acute-phase reactants, and inflammatory cytokines, especially at the outset of illness, are neither sensitive nor specific. Furthermore, microbiological culture findings are typically unavailable for 48 to 72 hours after the sample arrives at the laboratory (7). Consequently, there is a need for a rapid and easy test; a hematological Scoring System (HSS) is a simple, inexpensive, and quick adjunct for diagnosing clinically suspected newborn sepsis (8).The hematological scoring system (HSS) gives a 1 to each of the seven hematologic abnormalities linked to sepsis, except for an aberrant total polymorphonuclear (PMN) count, which gets a two instead of one if no mature PMNs

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are seen in the blood smear (figure1) (9). In 2017, Krishnamurthy hypothesized that while adding nucleated red blood cell count to the HSS would improve its diagnostic ability, removing both band count and the immature to mature ratio, which represents the same pathological mechanism as the immature to total (I/T) neutrophil ratio, would have no effect (10). According to Krishnamurthy's research, neutropenia is highly linked to sepsis and deserves a higher weight. To obtain the modified HSS, the neutropenia score was increased to two (rather than one in HSS) (table I) (10). The cluster of differentiation 14 (CD14) is a pattern recognition receptor that aids in activating the innate immune system in the face of infection and chronic inflammatory disorders (11). Hepatocytes directly secrete the soluble version of CD14 (sCD14). During inflammation, plasma proteases cause sCD14 to be cleaved, resulting in a shortened form known as Soluble CD14-subtype (sCD14- ST), also known as presepsin (12). Depending on the severity of the infection, the concentration of plasma sCD14-ST (Presepsin) has been shown to rise in response to bacterial infections. It is used clinically to diagnose septic shock early (12, 13). Our study aimed to evaluate the performance of hematological sepsis scores and presepsin as diagnostic tools and predictors of mortality in neonatal sepsis.

Materials and Methods

In this case-control study, a total of 81 newborns were studied in this case-control study at the NICU of Ain Shams University Pediatric Hospital, Cairo, Egypt, after informed written consents from their parents. The case group was divided into two subgroups. Proved sepsis group involved 29 newborns, with the following inclusion criteria; C - reactive protein (CRP) >6 mg/L, and abnormal Complete Blood Count (CBC) values, regardless of blood culture result. Suspected Sepsis group involved 22 newborns having features suggestive of systemic inflammatory response syndrome (SIRS), without a source of bacterial infection that can be pinpointed, with the following inclusion criteria; a) Presence of any sign of the following categories: i) an increase in the frequency or duration of apnea or respiratory distress-bradycardia (100/min) that is unrelated to feeding issues or airway blockage and necessitates increased ventilation assistance (intubation and ventilation; nasal intermittent positive pressure ventilation; or increase in continuous positive airway pressure), ii) hypothermia (core body temperature 36.5°C) or hyperthermia (core body temperature >38.5°C), iii) hypotonia, seizures, poor skin color, capillary refilling time longer than two seconds, irritability, and lethargy, b) CRP ≤6 mg/L and c) abnormal CBC parameters regardless of blood culture result. Neonates with congenital malformations or those previously treated with antibiotics were excluded. Control Group included 30 neonates admitted for non-infectious diseases (e.g., neonatal jaundice, hemorrhagic disease of newborn, infant of a diabetic mother, prematurity without sepsis, intrauterine growth retardation, and respiratory distress syndrome). Six ml of blood were collected under complete aseptic conditions; each sample was divided into 1 ml for blood culture, 2 ml in EDTA tube for CBC with a blood film, and 3 ml within the plain tube for serum samples centrifuged for 10 minutes at 3000 rpm. Sera were separated and divided into two tubes, including one for CRP assay and the other stored at -20°C for assessment of presepsin level. All the neonates were subjected to perinatal history taking, full clinical examination, and the lab tests as follows: HSS was calculated from a CBC with differential count using a Coulter® LH 750 cell counter (Coulter Corporation, Florida, USA) and a Leishman-stained peripheral blood film. Rapitex CRP kit for semi-quantitative measurement of CRP in human serum, employing latex agglutination test. CRP values of less than 6 mg/L were considered normal. Using a

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sterile procedure, blood culture samples were collected and inoculated into commercially prepared BD BactecTM Peds PlusTM/F blood culture media (Becton Dickinson Diagnostics, Sparks, MD). A double-antibody sandwich enzyme-linked immunosorbent test (ELISA) with Human soluble cluster of differentiation 14 (sCD14) ELISA Kit from Bioassay Technology Laboratory, Shanghai Korain Biotech Co., Ltd. was used to detect serum Presepsin levels at the time of diagnosis.

Statistical Methodology: The median and interquartile range were used to show skewed numerical data, and the Mann-Whitney test was used to examine between-group differences. The Pearson chi-squared test or Fisher's exact test was used to analyze differences between categorical variables expressed as the number of cases (percentage). The linear-by-linear association method was used to compare ordinal data. The Spearman rank correlation was used to test correlations. The diagnostic (or predictive) utility of biomarkers or clinical scores was investigated using receiver-operating characteristic (ROC) curve analysis. The relationship between presepsin and sepsis was investigated using multivariable linear regression with gestational age adjustment. For subgroup or multiple comparisons, the Bonferroni procedure was employed to alter the significance threshold. So, P-values of less than 0.01 were deemed statistically significant. Data were analyzed using SPSS© Statistics version 22 (SPSS© Corp., Armonk, NY, USA).

Ethical consideration

All procedures were carried out in line with the ethical norms established by the scientific ethics committee of Ain Shams University's Faculty of Medicine in Cairo, Egypt (FWA000017585) as well as the Helsinki Declaration of 1975, as updated in 2008.

Results

Comparison of sepsis cases and controls

Regarding categorical variables, there were 23 males (45.1%) and 28 females (54.9%) among the patients' group. In this study, 39 cases were preterm neonates (76.5%), 14 patients (27.5%) had a prenatal history of premature rupture of membranes (PROM), denoting that neonates with an antenatal history of PROM had a significantly higher risk of sepsis (P=0.001). Respiratory distress syndrome was the most significant presentation in 37 cases (72.5%) (P<0.001). Blood culture was positive for bacterial growth in 35 cases (68.6%) (P<0.001), with Klebsiella being the most common organism (11/35, 31.4%) (P=0.006), followed by coagulase-negative Staph aureus (9/35, 25.7%). Immature/total neutrophil count was significantly higher in the patients' group than the control group (P=0.003). Regarding numerical variables, HSS, modified hematological scoring system (MHSS), Presepsin, and CRP were significantly higher in the patients' group than the control group (P<0.001), however, hemoglobin (Hb) was significantly lower in the patients' group than the control group (P<0.001) (Table II, Figure 1).

Comparison of suspected sepsis and proved sepsis subgroups

Regarding categorical data, both groups showed no significant differences except for the outcome, and the proved sepsis group showed significantly better outcomes than the suspected sepsis group; only 7/29 (24.1%) of proved sepsis cases were deteriorated/died versus 14/22 (63.6%) of suspected sepsis cases (P=0.009).

Regarding numerical variables, apart from CRP on which we relied on, in differentiating proved from suspected sepsis cases, there were no statistically significant differences between both subgroups regarding gestational age, HSS, MHSS, Presepsin, total Leukocytic count (TLC), absolute neutrophil count (ANC), Hb, platelet count, and length of NICU stay. According to ROC curve analysis, cutoff values were established to assess the diagnostic performance of HSS, MHSS, presepsin, CRP, and Hb level in discriminating cases group from the control group.

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As shown in table III and figure 2, presepsin showed the best performance in discriminating sepsis cases from the control group at a cutoff value of > 0.5 ng/ml, followed by HSS and MHSS. It showed good diagnostic performance at a cutoff value > 1 for both, with MHSS slightly better than HSS. CRP and hemoglobin levels showed the least performance.

Comparison between survived (n=44) and dead cases (n=7)

Regarding categorical variables (sepsis subgroup, sex, maturity, antenatal history, the onset of illness, the result of blood culture, isolated organisms from blood culture, Immature/Total neutrophil ratio), no statistically significant differences were found between both groups. Regarding numerical variables, as shown in table IV, presepsin and platelet count were significantly higher in the dead group than in the survived group. However, CRP was lower in the dead group than in the survived group. ROC curve analysis was constructed to assess the predictive performance of presepsin, CRP, and platelet count as predictors of mortality in sepsis cases.

As shown in Table V and figure 4, presepsin at a cutoff >1.9 ng/ml achieved better performance over CRP at a cutoff ≤3 mg/l and platelet count at a cutoff >237 x $10^3/mm^3$.

Correlations of clinical and laboratory variables in studied groups:

Regarding the suspected sepsis group, there was a statistically significant positive correlation between HSS and MHSS (r= 0.862, P<0.001), platelet count and GA (r= 0.432, P= 0.045). Also, there was a statistically significant negative correlation between presepsin and CRP (r= -0.428, P= 0.047), MHSS and GA (r= -0.461, P= 0.031) and NICU Length of stay (r= -0.465, P= 0.029). Regarding the proved sepsis group, there was a statistically significant positive correlation between HSS and MHSS (r= 0.947, P< 0.001), NICU Length of stay and each of presepsin (r= 0.460, P= 0.012) and CRP (r= 0.676, P<0.001). Also, there was a statistically significant negative correlation between platelet count and NICU Length of stay (r= -0.504, P= 0.005), CRP and each of GA (r= -0.402, P= 0.031), and platelet count (r= -0.395, P= 0.034).

Multivariable linear regression to determine the best independent predictors of presepsin (Table VI): After adjustment for the confounding effect of gestational age, both suspected sepsis (B = 1.637, SE =0.219, P-value <0.001) and proved sepsis (B = 1.586, SE = 0.195, P-value <0.001) were independent predictors of the level of presepsin.

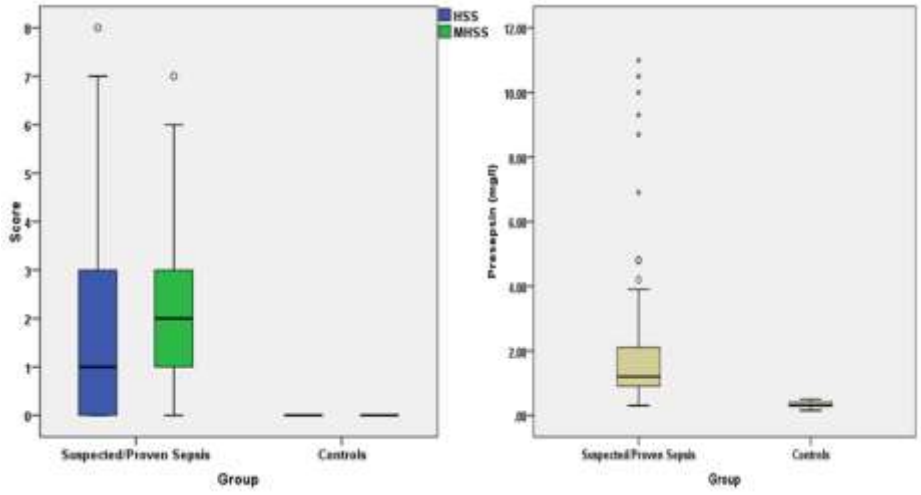

Figure 1. Box plot illustrating HSS, MHSS, and presepsin in cases of suspected or proved sepsis and controls. Box represents the interquartile range. The line inside the box represents the median. Whiskers represent the minimum and maximum values excluding outliers (circles) and extreme values (asterisks).

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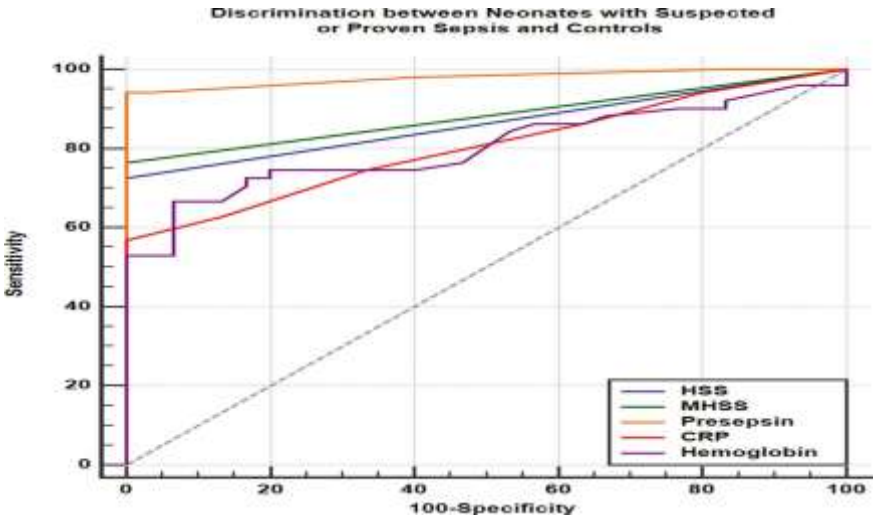

Figure 2. ROC curves for discrimination between cases and controls using HSS, MHSS, presepsin, CRP or hemoglobin.

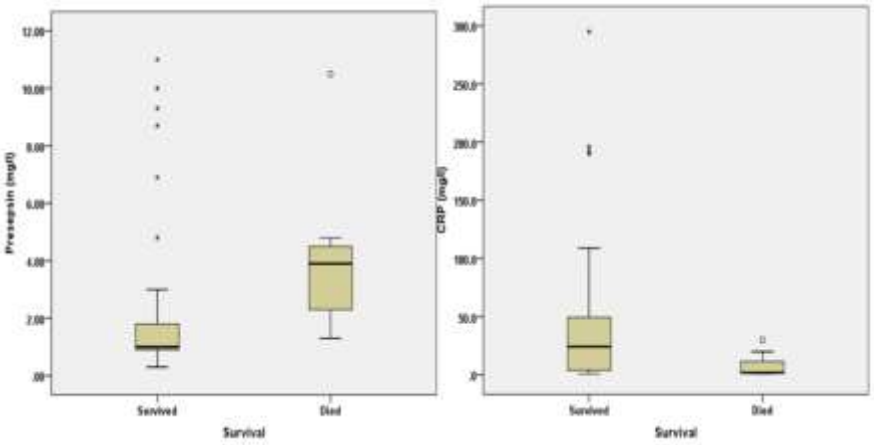

Figure 3. Box plot illustrating presepsin & CRP levels in cases of sepsis that survived or died. Box represents interquartile range. Line inside the box represents the median. Whiskers represent the minimum and maximum values excluding outliers (circles) and extreme values (asterisks).

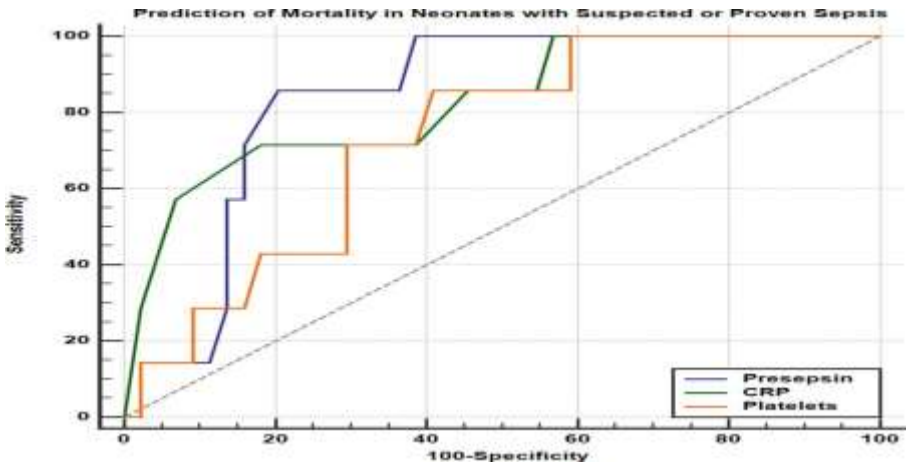

Figure 4. Receiver-operating characteristics (ROC) curves for prediction of mortality in cases of suspected or proven sepsis presepsin, CRP or platelets

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Table I: Components and weightage of hematological septic score (HSS) and modified HSS

Parameter	Value	HSS	Mod HSS
Total leucocyte count	< 5000	1	2
	> 25000 (at birth)	1	1
	> 30000 (12-24 hours)	1	1
	> 21000 (day 2 onwards)	1	1
	Normal	0	0
Total neutrophil count	No neutrophils	2	2
	Increased/ decreased	1	1/2
	Normal (1800 – 5400/mm^3)	0	0
Immature neutrophils	Increased	1	N/A
	Not increased	0	N/A
Immature: total neutrophil ratio (IT ratio)	> 0.2	1	1
	< 0.2	0	0
Immature: mature neutrophil ratio (IM ratio)	> 0.3	1	N/A
	< 0.3	0	N/A
Degenerative changes	Present	1	1
	Absent	0	0
Platelet count	< 150000	1	1
	> 150000	0	0
Nucleated RBC	> 5%	N/A	1
	< 5%	N/A	0

Score Interpretation: < 2 Sepsis is very unlikely, 3 or 4 Sepsis is suspected, > 5 Sepsis or infection is very likely, Minimum score: 0, Maximum score: 8

Table II: Numerical Laboratory variables when comparing patients' group and control group

Variable	Cases (suspected/proved) (n=51)		Controls (n=30)		
	Median	IQR	Median	IQR	P value*
Gestational age (GA) at delivery (weeks)	35	33 - 36	36	34 - 37	0.019
HSS	1	0 - 3	0	0 - 0	**<0.001**
MHSS	2	1 - 3	0	0 - 0	**<0.001**
Presepsin (mg/l)	1.20	0.90 - 2.10	0.30	0.30 - 0.40	**<0.001**
CRP (mg/l)	20.0	3.0 - 48.0	3.0	2.0 - 4.0	**<0.001**
TLC (k/mm^3)	12.9	10.6 - 18.0	13.0	11.6 - 14.2	0.649
Neutrophils (k/mm^3)	55.0	40.0 - 65.0	57.5	49.0 - 63.0	0.186
Platelets (k/mm^3)	231	107 - 370	240	200 - 340	0.248
Hemoglobin (g/dl)	11.1	9.8 - 13.9	14.0	13.6 - 15.0	**<0.001**

Data are median and interquartile range (IQR). *Mann-Whitney test. HSS: hematological scoring system, MHSS: modified hematological scoring system, CRP: C-reactive protein, TLC: total leukocytic count.

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Table III: Receiver-operating characteristics (ROC) curve analysis for discrimination between cases and controls using HSS, MHSS, presepsin, CRP or Hb

ROC curve parameter	Predictor				
	HSS	MHSS	Presepsin	CRP	Hb
AUC	0.863	0.882	0.979	0.803	0.802
SE	0.032	0.030	0.014	0.047	0.049
95% CI	0.768 to 0.929	0.792 to 0.943	0.920 to 0.998	0.699 to 0.883	0.699 to 0.883
z statistic	11.495	12.748	34.992	6.453	6.235
P-value	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
Youden index (J)	0.726	0.765	0.941	0.569	0.600
Cut-off criterion	>1	>1	>0.5	>5	≤12.8
Sensitivity (%)	72.6	76.5	94.1	56.9	66.7
Specificity (%)	100.0	100.0	100.0	100.0	93.3

AUC = area under the curve, SE = standard error, 95% CI = 95% confidence interval. HSS: hematological scoring system, MHSS: modified hematological scoring system, CRP: C-reactive protein, TLC: total leukocytic count, Hb: hemoglobin

Table IV: Comparison of cases of sepsis that survived or died: Numerical variables

Variable	Outcome				
	Survived (n=44)		Dead (n=7)		
	Median	IQR	Median	IQR	P-value*
GA at delivery (weeks)	35	33 - 36	33	32 - 36	0.534
HSS	2	1 - 3	0	0 - 1	0.054
MHSS	2	1 - 3	1	0 - 2	0.229
Presepsin (mg/l)	1.00	0.90 - 1.80	3.90	2.10 - 4.80	**0.004**
CRP (mg/l)	24.4	4.0 - 49.5	2.0	1.0 - 20.0	**0.006**
TLC (k/mm^3)	13.4	10.1 - 19.0	12.5	11.3 - 13.3	0.575
Neutrophils (k/mm3)	52.5	38.3 - 65.5	55.0	41.0 - 65.0	0.556
Platelets (k/mm^3)	209	92 - 339	316	243 - 501	**0.049**
Hemoglobin (g/dl)	11.1	9.9 - 13.7	12.7	9.7 - 14.1	0.732
Time to rise of CRP	3	3 - 4	3	3 - 4	0.963
Time from admission to NICU (days)	5	4 - 8	6	4 - 15	0.277

Data are median and interquartile range (IQR). *Mann-Whitney test. HSS: hematological scoring system, MHSS: modified hematological scoring system, CRP: C-reactive protein, TLC: total leukocytic count.

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Table V: Receiver-operating characteristics (ROC) curve analysis for prediction of mortality in cases using presepsin, CRP or platelets

ROC curve parameter	Predictor		
	Presepsin	CRP	Platelets
AUC	0.838	0.826	0.734
SE	0.060	0.089	0.087
95% CI	0.708 to 0.926	0.694 to 0.918	0.591 to 0.848
z statistic	5.601	3.668	2.692
P-value	<0.0001	0.000	0.007
Youden index (J)	0.653	0.533	0.448
Cut-off criterion	>1.9	≤3	>237
Sensitivity (%)	85.7	71.4	85.7
Specificity (%)	79.6	81.8	59.1

AUC = area under the curve, SE = standard error, 95% CI = 95% confidence interval.

Table VI: Multivariable linear regression for the relation between presepsin and each of sepsis subgroups

Independent variable	Unstandardized Coefficients		Standardized Coefficients			95.0% CI	
	B	SE	Beta	t	P-value	Lower Bound	Upper Bound
(Constant)	0.647	4.630		0.140	0.889	-8.572	9.866
Ln(GA), weeks	-0.514	1.296	-0.032	-0.396	0.693	-3.095	2.067
Suspected sepsis (=1)	1.637	0.219	0.682	7.461	<0.001	1.200	2.074
Proven sepsis (=1)	1.586	0.195	0.712	8.139	<0.001	1.198	1.975
Model diagnostics							
R	0.737						
$_R2$	0.543						
Adjusted R^2	0.525						
F(df 3,77)	30.491						
Significance	<0.001						

Dependent Variable: Ln (Presepsin), mg/l. *95% CI* = 95% confidence interval, *df* = degrees of freedom, *F* = F-statistic, *Ln* = natural logarithm, *R*= multiple correlation coefficient, R^2 = coefficient of determination, *SE* = standard error, *t* = t-statistic.

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Discussion

Given the high mortality rate of newborn sepsis, the best diagnostic tests should have the highest sensitivity and lowest negative predictive value. A diagnostic marker must also have high specificity and a good PPV to reduce the wasteful use of antibiotics in false-positive instances (14).

In our study, neonates with an antenatal history of PROM had a significantly higher risk of sepsis. Other studies found it the commonest maternal risk factor for sepsis (15-18). Also, blood cultures were positive in 68.6% of sepsis cases, compared to a prior study by Pessar (19), who identified positive cultures in 63.3 percent of sepsis cases. Like other studies (20-24), Klebsiella was the most common organism isolated from the blood cultures. In contrast, Mahallei et al. (25) found that coagulase-negative staphylococcus and Staph aureus were the commonest bacteria isolated from blood.

Regarding blood counts in our study, the Hb level was significantly lower in the sepsis group than in the control group. The same was reported by Mohamed et al. (26). However, there were no statistically significant differences between both groups regarding neutrophil count despite abnormal TLC, and neutrophil count was more prevalent in the sepsis group. This could be justified by considering that some newborn infants with proven bacterial infection had normal neutrophil count with increased bands. Also, neutrophilia in the absence of an increase in band forms may occur in patients with no evidence of infection.

Similarly, neutropenia has been more common in association with sepsis, probably due to increased adherence to altered endothelial cells and utilization at the site of infection. However, there are many causes of neutropenia other than infection. In the same context, a study by Myuga & Isleta (27) and Khair et al. (18) found that elevation of neutrophil count in infection is often late and inconsistent. Accordingly, the total neutrophil count was thought to be of limited use for the diagnosis of infection.

We found I/T neutrophil ratio was significantly higher in the sepsis group than in the control group, in agreement with Pessar (19) and Chirico & Loda (14). They found the I/T neutrophil ratio>0.2 to have the best performance over the other hematological parameters denoting that this is the most important CBC parameter for sepsis. Another study by Khair et al. (18) discovered that total PMNs count, immature neutrophil count, and consequently I/T neutrophil ratio have optimal sensitivities and negative predictive values in neonates but are associated with low positive predictive value and specificity, and thus should not be used as a predictor of sepsis in isolation. Contrarily, Payasli et al. (7) and Wojsyk-Banaszak and Szczapa (28) reported poor TLC and I/T ratio sensitivity in the early diagnosis of neonatal sepsis.

Platelet count was significantly lower in proved sepsis than suspected sepsis, suggesting more severe disease in the proved sepsis group, as thrombocytopenia is a well-known biomarker for disease severity, according to Greco et al. (29). This might be attributed to increased platelet destruction, infection-related sequestration, platelet production failure owing to a reduction in megakaryocytes, or endotoxin-induced platelet damage (27).

When tested for diagnostic performance, HSS achieved a diagnostic sensitivity of 72.6% and diagnostic specificity of 100% (AUC 0.863) in discriminating cases from controls at a cutoff value (> 1) in contrast to several studies by Bhalodia et al. (8), Krishnamurthy et al. (10), Khair et al. (18), Pessar (19), Badrawi et al. (21), Elsayed et al. (30), El-Nemer et al. (31), El-Raggal et al. (32), Pramana et al. (33), Jacob et al. (34), and Munazza et al. (35) that showed disparate results at different cutoffs. All these studies concluded that the higher the score, the more likely sepsis was present.

Meanwhile, our research is the first to evaluate the effectiveness of

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Krishnamurthy's suggested MHSS that achieved a diagnostic sensitivity of 76.5% and diagnostic specificity of 100% (AUC: 0.882) at cutoff value > one conforming with Krishnamurthy et al. (10), who found MHSS to achieve a sensitivity of 84% and specificity of 82% at a cutoff value of ≥3.

We found that presepsin and CRP were significantly higher in the sepsis group than in the control group, which came in accordance with Tabl & Abed (36), Ozdemir & Elgormus (37), Mussap et al. (38).

On comparing the suspected sepsis group and proved sepsis group, CBC and hematological sepsis scores showed no significant differences between both subgroups, which conforms with the results of Mussap et al. (38). Presepsin showed no significant difference as well, which came in agreement with Rashwan et al. (24), Ozdemir & Elgormus (37), Mussap et al. (38). Contrarily, Sharma & Sidana (39) found presepsin level was significantly higher in the proved sepsis group than the suspected sepsis group.

Presepsin showed excellent diagnostic performance at a cutoff value > 0.5 ng/ml; at this level, Presepsin reported a diagnostic sensitivity of 94.1% and diagnostic specificity of 100% (AUC: 0.979). This result comes close to Mussap et al. (38), who reported AUC for presepsin 0.995 at a cutoff value of 0.54 ng/ml with a sensitivity of 100% and specificity of 81.2%. In contrast, Liu et al. (40) used a presepsin at a lower cutoff value of 0.317 ng/ml with a sensitivity of 70.8% and specificity of 85.8%. Tabl & Abed (36) found similar results for presepsin with a sensitivity of 95.5% and specificity of 91.7% at a higher cutoff value of 0.8 ng/ml. Also, Pietrasanta et al. (41) found presepsin reported a sensitivity of 72% and a specificity of 87% at a cutoff point of 0.98 ng/mL. Moreover, Poggi et al. (42) asserted that the cutoff value with the best accuracy in their study was 0.88 ng/ml, at which the specificity was 100%, and sensitivity was 94%.

Bellos et al. (43) conducted a meta-analysis that comprised 11 trials and found that the pooled sensitivity and specificity of serum presepsin for the prediction of newborn sepsis were both 0.91, with an AUC of 0.975 for a cutoff of 0.65 ng/ml. The same cutoff with comparable sensitivity of 0.94 was adopted by Yoon et al. (44), who studied sepsis in children and adolescents but with lower specificity 0.71 than CRP in detecting sepsis in children.

According to our study, CRP showed fair diagnostic performance in the discriminating sepsis group from the control group at a cutoff value of > 5 mg/l, with comparable sensitivity to Hisamuddin et al. (45) but with much better specificity.

In this study, the proved sepsis group showed significantly better outcomes than the suspected sepsis group, which emphasizes the importance of early diagnosis of sepsis as it guaranteed proper management.

Both presepsin and platelet count were significantly higher in the dead group than in the survived group. Meanwhile, CRP was found to be lower in the dead group than survived group, which may be related to the late diagnosis of sepsis that led to improper management of the patients. This observation is supported by the higher percentage of mortality in the suspected sepsis group, 22.7%, while the proved sepsis group had only 6.9% mortality.

Presepsin achieved the best performance as a mortality predictor at a cutoff value of > 1.9 ng/ml with a diagnostic sensitivity of 85.7% and diagnostic specificity of 79.6% (AUC: 0.838); this comes in agreement with Spanuth et al. (46), who found the presepsin to be strongly correlated with mortality and had a superior prognostic accuracy when compared to other markers on a ROC curve analysis for the accuracy of 30-day death prediction at a cutoff value of 1.6 ng/ml. In a meta-analysis for mortality prediction by Zhu et al. (47), the AUC of presepsin was 0.77 with a pooled prognostic sensitivity and specificity of 0.83 and 0.69, respectively.

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Consistent with the aim of the study, multivariable linear regression analysis was used to further explore the correlation of different sepsis variables and presepsin while omitting the effect of gestational age. Both sepsis subgroups proved to be independent predictors of presepsin level.

Conclusion

The hematological scoring system and presepsin appear to be reliable tools for detecting sepsis earlier than CRP. Furthermore, presepsin, rather than CRP, is a stronger predictor of illness severity and death.

Conflict of interest

The authors declared no conflict of interest.

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