Journal of Advances in Microbiology

20(1): 80-90, 2020; Article no.JAMB.54569
ISSN: 2456-7116

Presepsin as a New Marker for Early Detection Neonatal Sepsis in Al-Quwayiyah General Hospital Riyadh, KSA

Enas Sh. Khater[1,2*] and Taha M. Al-Hosiny[3,4]

[1]Department of Microbiology and Immunology, Faculty of Medicine, Benha University, Egypt.
[2]Microbiology Laboratory, Al-Quwayiyah General Hospital, Riyadh, KSA.
[3]Department of Pediatrics, Faculty of Medicine, Benha University, Egypt.
[4]Nursery Department, Al-Quwayiyah General Hospital, Riyadh, KSA.

Authors' contributions

This work was performed in cooperation between the two authors. Author ESK planned and designed the study, wrote the protocol, collected the samples, performed the practical laboratory activities, participated in the interpretation of the results and analysis, drafted and critically revised the manuscript. Author TMAH participated in planning and designing the study, clinical evaluation of cases, sample collection, participated in the interpretation of the results. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMB/2020/v20i130210
Editor(s):
(1) Dr. Veysi Okumus, Associate Professor, Department of Biology, Siirt University, Turkey.
Reviewers:
(1) Lorenza Pugni, University of Milan, Italy.
(2) Giuseppe Gregori, Italy.
(3) Jaime Lorduy Gómez, Corporación Universitaria Rafael Núñez, Colombia.
Complete Peer review History: http://www.sdiarticle4.com/review-history/54569

Original Research Article

Received 05 December 2019
Accepted 10 February 2020
Published 18 February 2020

ABSTRACT

Background: Early detection and start of antibiotic therapy neonatal sepsis (N.S) dramatically improves outcomes, so it is important to perform fast, reliable and specific early laboratory biomarkers.
Aim: This study aimed to detect the prevelance, the risk factors, hematology profile, microbial profile of neonatal sepsis patients and also investigate the value of PCT and CRP, in comparison to presepsin in establishing the early diagnosis of neonatal sepsis.
Methods: A cross sectional study was performed from March to September 2019 in Al Quwayiyah General hospital involving 120 neonates who were classified into 3 groups. The patients groups

**Corresponding author: E-mail: drenaskhater@yahoo.com;*

were: Proved N.S, suspected N.S and control healthy neonates, classified depending on Tollner score. Haematology profile and blood culture for each neonate were done. CRP, PCT and presepsin values were analyzed, compared, and their effectiveness as diagnostic markers was determined. Sensitivity, specificity, positive, and negative predictive values of the markers were calculated.
Results: The prevelance of neonatal sepsis was 20.8%. 75 neonates were males and 45 neonates were females. 74 neonates were preterm, while 46 were full term. Gestational age in weeks was 31.1±5.9w for neonates with proved sepsis, 32.4±6.7w for neonates with suspected sepsis and 36.4±4.4w for control group. The mean birth weight was 1740±105.3 g for neonates with proved sepsis, 32.4±6.7 g for neonates with suspected sepsis, 2.650±205.2 g for control group. 36 babies suffered from respiratory distress syndrome, 10 had jaundice, 8 had cough, 28 had fever and 8 complained of other symptoms. Blood cultures were positive for all patients of proved sepsis. The identified bacteria included Gram positive bacteria 22(55%) which were Coagulase negative staph. 13(32.5%) followed by *Staphylococcus aureus* 4(10%) while Gram negative bacteria 15(37.5%) which were *E. coli* 5(12.5%) followed by *Klebsiella peumoniae* and also fungal infection (Candida species) detected in 3(7.5%) cases. There was significant difference between the mean and standared deviation of CRP, PCT and presepsin levels in proved and suspected N.S. groups when compared with healthy controls ($P< 0.05$). CRP sensitivity and specificity (72%, 61% respectively) which were less useful in diagnosis of neonatal sepsis compared to presepsin which has the highest sensitivity and specificity (95%, 81% respectively) followed by procalcitonin with sensitivity and specificity (90%, 69% respectively).
Conclusion: The prevalence of neonatal sepsis among all admitted neonates in Al-Quwayiyah general hospital was 20.8%. Our results also detected higher sensitivity, specificity and positive and negative predictive values for presepsin more than and PCT CRP in the diagnosis of NS.

Keywords: C. reactive protein; prespsin; neonatal sepsis; procalcitonin.

1. INTRODUCTION

Neonatal sepsis (NS) is a common cause of neonatal morbidity and mortality. In neonate, rapid diagnosis and treatment of systemic bacterial infection is necessary as any delay in treatment of serious bacterial infections may lead to inappropriate effects [1]. The clinical signs of NS are unspecific and indistinguishable from non-infectious diseases, so the diagnosis of NS is quite complicated and may be misleading because critically ill neonates frequently experience systemic inflammatory response syndrome without infection [2].

It has been shown that early detection and apprpriate clinical intervention are critical to improve the outcome of sepsis patients [3]. During the first hours of life, reliable infection markers are absent in NS. Therefore, neonatologists usually start early antibiotic treatment in newborn infants who has risk factors for infection, exposing many neonates to unnecessary treatments because of the limitation of the diagnostic tools in early diagnosis of sepsis, as the isolation of causative organisms from microbiological cultures takes up to 3 days and may be negative in newborns. Besides, it is impractical to obtain blood sample for serial blood culture from infants [4]. So, new laboratory methods for early diagnosis of the diseases, evaluation of prognosis and treatment efficiency are needed [5].

C- reactive protein (CRP) is a non specific marker for diagnosis of NS. High levels CRP are seen in infection, in autoimmune disease, in surgery, meconium aspiration and recent vaccination. Also, the CRP levels do not elevate significantly until almost 14-48 hr after the start of infection [6].

Procalcitonin is a calcitonin peptide precursor, and is part of the sepsis inflammatory cascade. Procalcitonin levels tend to rise in bacterial infections, whereas in viral infection they are depressed [7], procalcitonin are a calcitonine peptide precurser, and is a part of the sepsis inflamatory cascade. procalcitonin levels tend to rise in bacterial infections, whereas in viral infections they are depressed [8]. Procalcitonin is appeared in the serum within 4 hours of bacterial infections and has a half-life about 22–26 hours [9]. Sometimes, procalcitonin levels may be increased in patients who do not suffer from sepsis, with levels between 2–10 ng/mL detected in patients with autoimmune diseases [10], trauma [11], cardiac arrest [12], surgery [13], burns [14] and pancreatitis [15].

Presepsin has been emerged as a newer generation of the inflammatory markers with a sensitivity and specificity which is better than other markers. presepsin increased earlier and faster in patients with sepsis, at 2 hours after sepsis model, peaked at 3 hours, and declined at 4–8 hours [16]. It is a CD14 polypeptide, CD14 present in two forms: Membrane-bound CD14 (mCD14) and soluble CD14 (sCD14). The mCD14 has a good affinity to Lipopolysaccarides (LPS), and is mainly expressed on the monocytes/macrophages cell surfaces. The sCD14 is detected in plasma, and is produced by mCD14 fall-off or cell secretion [17,18]. Two types of sCD14 could be detected in the plasma of healthy people at microgram level: 49KD and 55KD. sCD14 have an important role in mediating the immune responses to LPS of CD14-negative cells such as endothelial cells and epithelial cells. sCD14 is cleaved by cathepsin D and some proteases in plasma and the N-terminal fragments of 13kDa constitutes sCD14 subtype (sCD14-ST) which has been named as presepsin recently [19,20].

This study aimed to detect the prevelance, the charachtaristics of newborns, hematology profile, microbial profile of neonatal sepsis patients and also investigate the value of PCT and CRP, in comparison to presepsin in establishing the early diagnosis of neonatal sepsis.

2. MATERIALS AND METHODS

2.1 Study Design

A cross sectional study was performed from March to September 2019 in nursery and neonatal intensive care unit (NICU) in Al Quwayiyah General hospital involving 120 neonates 90 with proved or suspected bacterial infection and 30 control (had no diagnosis of sepsis during hospital stay). The diagnosis of neonatal sepsis was done according to the presence of clinical, laboratory, or culture screen parameters:

a) Clinical signs consistent with infection based on the Tollner score [21] (respiratory distress, fever, cough, abnormal skin color, peripheral circulation impairment, hypotonia or seizures, abdominal distension).
b) Laboratory parameters (leukocyte count, left shift and thrombocytopenia).
c) Positive culture (blood, urine, and cerebrospinal fluid) or pneumonia (chest X-ray findings. Points are given for each parameter: 0, 1, 2, or 3; a higher number of points reflect a greater severity.

Three groups of neonates were investigated;

I. Proved sepsis group included 40 neonates based on clinical and laboratory findings (a Tollner score of ≥10).
II. Suspected sepsis group included 50 neonates based on clinical and laboratory findings (a Tollner score of 5-10).
III. Control group included 30 healthy neonates who had no clinical or laboratory data of infection and who were appeared to be healthy based on a Tollner score of ≤ 5.

Data was collected for each baby who included gender, gestational age, birth weight, age at time of presentation. The study was approved by the hospital ethics committee. Both verbal and written informed consent was given by the parents.

Exclusion criteria included history of antibiotics administration by the mother or the newborn, congenital malformations, TORCH complex related congenital infections, and refusal of parental consent.

2.2 Specimens Collection

- Blood samples were aseptically obtained from each neonate within the 24 hours of NICU admission as follows: 0.5 mL was inoculated immediately into blood culture bottles for blood culture.
- One to two ml venous blood were obtained by peripheral venous puncture and collected in plain tubes to separate serum, Blood samples were centrifuged within 30 min of collection, and the serum was stored at -20°C until analysis until used for assessment of CRP, Presepsin, and PCT.

2.3 Laboratory Methods

2.3.1 Blood culture

1. Peripheral blood culture samples (pediatric bottle) were obtained from each patient as part of their routine evaluation in pediatric and nursery wards before initiation of antibiotic therapy in infants suspected with sepsis.

2. Blood samples collected were inoculated into one aerobic BacT/ALERT PF (BioMérieux) bottle which were incubated in the BacT/ALERT® 3D instrument (BioMérieux) at 35°C for 5 days or until microbial growth was detected.
3. Positive bottles were removed from the BACTEC blood culture system, and a Gram stain was done then sub-cultured on nutrient, MacConkey, blood and chocolate agar media and incubated at 35°C. The isolates were identified by Gram's staining, colony characteristics and biochemical properties. Full identification of microorganisms was done with standard bacteriological and biochemical methods.

2.3.2 CRP

CRP was detected by the semi-quantitative latex agglutination test (AVITEX CRP kits; Catalog No. OD023; supplied by Omega Diagnostics, UK) the CRP kits measured ranges from 0.10 to 20.0 mg/l. cutoff value was 9 mg/ml.

2.3.3 Procalcitonin

Procalcitonin was measured using the PCT sandwich ELISA assay (Bio Vendor R&D, Germany) on evolis machine (biomerieux, France). Absorbance is measured at 450 nm. For the analysis, cutoff value was 5.6 ng/ml.

2.3.4 Presepsin

Presepsin (sCD14 st) level was measured using human sCD 14 ELISA kit (Wuhan Fine Biotech Co., Ltd) on evolis machine (biomerieux, France). This kit was based on sandwich enzyme-linked immune-sorbent assay technology. Read the O.D. absorbance at 450 nm cutoff value was 500 pg/mL.

2.4 Statistical Analysis

Data were entered into SPSS software version 22 (Chicago, IL, USA). Categorical variables were presented as frequencies and percentages. Chi square (X2) test and fisher exact test were used to find the association between the categorical variables. To detect the diagnostic importance of CRP, PCT and presepsin levels, the receiver operating characteristic (ROC) curve was analyzed and the sensitivities, specificities, and positive and negative predictive values were calculated. A P-value< 0.05 was considered as significant.

3. RESULTS

A total 120 neonates were included in our study 90 cases had either proved or suspected sepsis out of 432 admitted babies, which means that the prevalence of neonatal sepsis among all admitted neonates in Al-Quwayiyah general hospital was 20.8%. 75 neonates were males and 45 were females. 74 neonates were preterm, while 46 were full term. Gestational age in weeks was 31.1±5.9 w for neonates with proved sepsis, 32.4±6.7 w for neonates with suspected sepsis and 36.4±4.4w for control group. The mean birth weight was 1740±105.3 g for neonates with proved sepsis, 32.4±6.7 g for neonates with suspected sepsis and 2.650±205.2 g for control group. Moreover, Age at time of presentation was 16.3±18.4d for neonates with proved sepsis, 18.2±15.4d for neonates with suspected sepsis and 3.6±2.3d for control group.

Fig. 1 showed that out of 90 proved and suspected neonatal sepsis, 36(40%) babies had respiratory distress,10(11.1%) had jaundice, 8 (8.88%) had cough, 28(31.1%) had fever and 8 (8.88%) complained of other symptoms.

Table 1. Charachtaristics of newborns with neonatal sepsis

Ch.Ch	Proved sepsis =40		Suspected sepsis=50		Control=30	
	NO	%	NO	%	NO	%
Gender						
Male	25	62.5%	34	68	16	53.3
Female	15	37.5%	16	32	14	46.7
Gestational age						
Preterm <37 weaks	30	75%	39	78	5	16.7
Term≥ 37 weaks	10	25%	11	22	25	83.3
Gestational age in weeks	31.1±5.9		32.4±6.7		36.4±4.4	
Birth weight in grams	1740±105.3		1820±108.5		2.650±205.2	
Age at time of presentation	16.3±18.4		18.2±15.4		3.6±2.3	

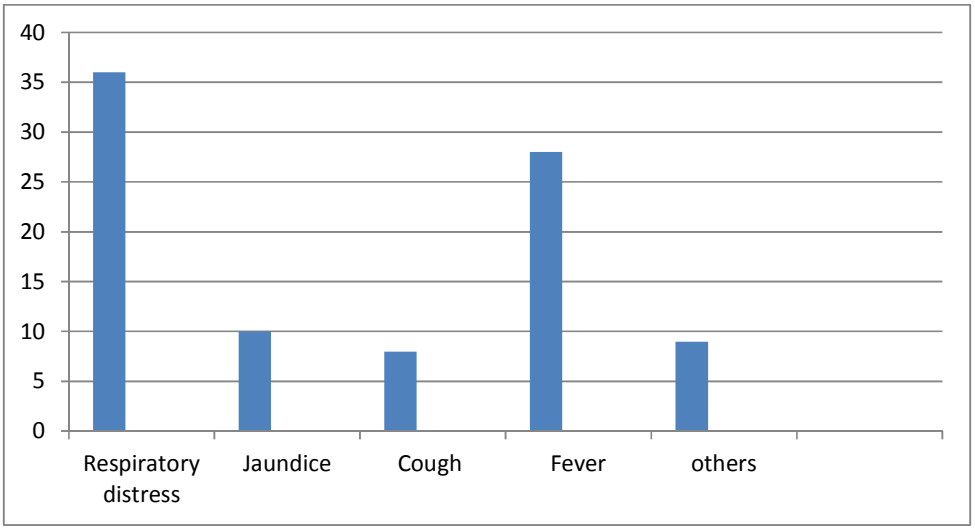

Fig. 1. Clinical manifestation of newborns with proved and suspected neonatal sepsis

Hematology profile and causative organisms of neonatal sepsis were shown in (Table 2). Platelet count/mm^3 was lower for neonates with proved sepsis 458914 ±110305, and for neonates with suspected sepsis 425891±141258 more than for control group 325148±810250. Leukocyte count/mm^3 also was higher for neonates with proved sepsis 18912±9541 and for neonates with suspected sepsis 10912±2451 more than for control group 6417±213. Blood cultures were positive for all patients of proved sepsis. The identified bacteria (Table 2) included Gram positive bacteria 22(55%) which were Coagulase negative staph. 13(32.5%) followed by *Staphylococcus aureus* 4(10%), then *Streptococcus viridans* & MRSA 2(5%) for each), while Gram negative bacteria 15(37.5%) which were *E. coli* 5(12.5%) followed by *Klebsiella peumoniae* 4(10%) then *Pseudomonas aeruginosa* 3(7.5%).also fungal infection (Candida species) detected in 3(7.5%) cases.

Table 2. Shows hematology profile and causative organisms of proved neonatal sepsis

	Proved sepsis =40		**Suspected sepsis=50**	**Control=30**
Platelet count/mm^3 Mean ± SD	458914 ±110305		425891±141258	325148±810250
Leukocyte count/mm^3 Mean ± SD	18912±9541		10912±2451	6417±213
Micro-organisms	**NO**	**%**		
Gram positive bacteria	22	55%		
Coagulase negative staph.	13	32.5%		
Staph.aureus	4	10%		
Strept. viridans	2	5%		
Group B strept.	1	2.5%		
MRSA	2	5%		
Gram negative bacteria	15	37.5%		
E. coli	5	12.5%		
Klebsiella peumoniae	4	10%		
Enterobacter cloacae	1	2.5%		
Pseudomonas aeroginosa	3	7.5%		
Acinetobacter baumanni	2	5%		
Fungal	3	7.5%		
Candida species	3	7.5%		

The mean and standerd deviation of CRP, PCT and presepsin levels in studied groups are shown in (Table 3). There was significant difference between the mean of CRP, PCT and presepsin levels in proved and suspected N.S. groups when compared with healthy controls (P< 0.05). Also, a significant difference was observed between proved and suspected N.S newborns (P< 0.0001).

Table 4 showed that CRP sensitivity and specificity (72%, 61% respectively) which were less useful in diagnosis of neonatal sepsis compared to presepsin which has the highest sensitivity and specificity (95%, 81% respectively) followed by procalcitonin with sensitivity and specificity (90%, 69% respectively). The positive and negative predictive rates were the lowest in CRP (28% and 80% respectively), whereas the positive and negative predictive rate showed high result in case of presepsin and PCT (presepsin positive predictive and negative predictive values were 84% and 95% respectively, while PCT positive predictive and negative predictive values were 55% and 95% respectively).

Table 3. Comparison between serum levels of CRP, procalcitonin and prespsin among studied groups

Test	Proved sepsis	Suspected sepsis	control	F test	P value
	Mean ± SD				
CRP (mg/ml)	38.22±18.74	11.50±5.12	2.65±1.69	45.2	<0.0001
Procalcitonin (ng/ml)	11.45±2.33	6.10±2.55	0.74±0.41	53.4	<0.001
Prespsin (pg/ml)	1892.9±1 487.2	825.9±562.2	325.3±130.2	3.10	<0.001

P-value< 0.05 was considered as significant

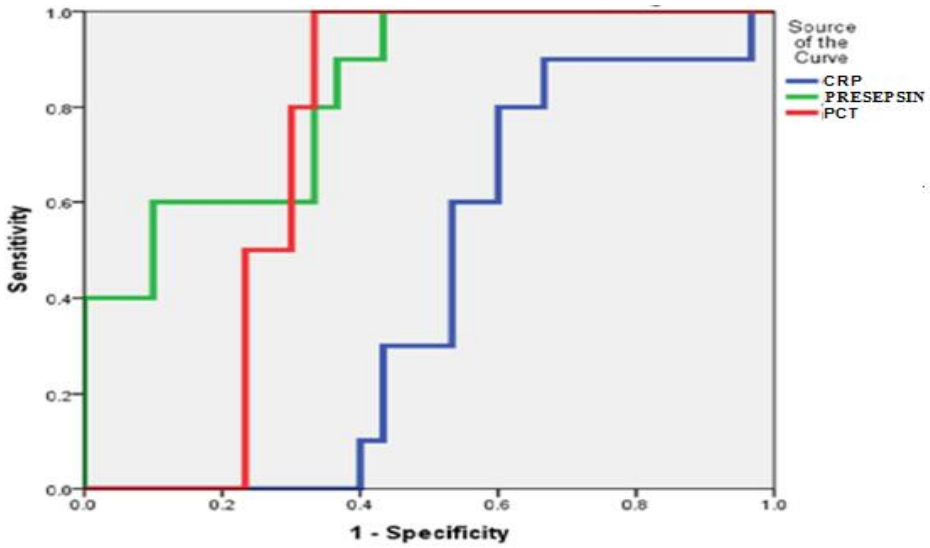

Fig. 2. ROC curve

ROC curves for biomarker, Area under the ROC curve for sepsis patients: CRP =0.43 (0.25 – 0.60), PCT = 0.72 (0.57 – 0.88) and PRE = 0.83 (0.70 – 0.97)

Table 4. Sensitivity, specificity, PPV, NPV of CRP, procalcitonin and prespsin in detection of suspected neonatal sepsis

	CRP	Procalcitonin	Prespsin
Sensitivity	72%	90%	95%
Specificity	61%	69%	81%
PPV	29%	55%	84%
NPV	82%	95%	95%
Cut off	9 mg/ml	5.6 ng/ml	500 pg/ml

PPV: Positive predictive value NPV: Negative predictive value

4. DISCUSSION

The result of this study showed that the prevalence of neonatal sepsis among all admitted neonates in Al-Quwayiyah general hospital was 20.8% which was similar to the incidence of neonatal sepsis among neonates in king Khalid university hospital in 2016 which was 27% [22]. Also agreed with Eman M., et al. [23] who reported a high incidence of neonatal sepsis in three hospitals in Egypt, while this figure was higher than that were reported from Nepal (12.4%) [24] and India (7.6%) [25] as the study focused on admitted neonates in intensive care units in which most of the cases were critically ill and with high probability of sepsis than those admitted to other the general pediatric department as the case of our study.

This study focused on some factors that may precipitate the development of neonatal sepsis like prematurity, Gestational age in weeks, birth weight and age at time of presentation, there was an association being exist between these factors and the neonatal sepsis which agreed with a study in southeastern Mexico at 2012 [26], revealed that, prematurity, and low birth weight are significant contributing factors to the neonatal sepsis. This was similar also to the findings of previous studies on neonatal sepsis conducted internationally and regionally [27-29]. So special attention should be directed to babies with prematurity and low birth weight as they are more prone to develop neonatal sepsis, and appropriate empirical therapy should be started as early as possible.

Reporting the common signs and symptoms associated with neonatal sepsis can be beneficial in the early identification of the affected babies. Our results have showed that most patients with neonatal sepsis presented with respiratory distress 36(40%) babies, 10(11.1%) had jaundice, 8(8.88%) had cough, 28(31.1%) had fever and 8(8.88%) complained of other symptoms, also in a study conducted in Sanaa (Yemen) showed that the most common clinical pictures were Difficulty of breathing (42.2) [30]. Similar findings were reported in India; respiratory distress (44%) [31]. In contrast, Chiabi et al. have found that fever and irritability are more frequent than respiratory distress [32].

In our study platelet count/mm3 was lower (thrombocytopenia) for neonates with proved sepsis 458914±110305 and for neonates with suspected sepsis 425891±141258 more than for control group 325148±810250. Studies by Sartaj A. Bhat et al were revealed that neonates developed thrombocytopenia in cases of neonatal sepsis [33]. Ahmed et al also showed that mortality rate was also higher among children with thrombocytopenia [34]. Leukocyte count/mm^3 also was higher (leukocytosis) for neonates with proved sepsis 18912±9541 and for neonates with suspected sepsis 10912±2451 more than for control group 6417±213. Similar findings by study by Philip et al. [35] showed that leukocytosis and neutrophilia were the two most predominant abnormal WBC results and these abnormalities were predicting neonatal sepsis. Multiple studies have examined total leucocytic count, immature to total neutrophil ratio and platelet count and shown that these routine investigations either have low sensitivity and specificity or varying delayed responses early in the course of infection [36].

The causative organisms of neonatal sepsis are varied from one region to another, and they are changing over time. In this study the blood cultures were positive for all patients of proved sepsis. The identified bacteria included Gram positive bacteria 22(55%) which were Coagulase negative Staph. 13(32.5%) followed by *Staphylococcus aureus* 4(10%), then *Streptococcus viridans* & MRSA 2 (5%) for each), while Gram negative bacteria 15(37.5%) which were *E. coli* 5(12.5%) followed by *Klebsiella peumoniae* 4(10%) then *Pseudomonas aeruginosa* 3(7.5%) also fungal infection (Candida species) detected in 3(7.5%) cases. The reported microbiological etiologies in several studies also showed that CONS is the major causative pathogen [37-40], other studies from other developing countries have reported that gram-negative bacteria constituted the majority of the causative organisms of neonatal sepsis [41,42]. Alrafiaah et al. [43] showed similar results to our study that 35% of neonatal sepsis was caused by different types of gram-negative bacteria, with *E. coli* being the predominant one. *E. coli* is main pathogen causing early sepsis, and this is consistent also with the findings of Kilani and Basamad in a study from Riyadh published in 2000 [44]. Although CONS constitutes the highest percentage of neonatal sepsis in our hospital, it causes less severe disease and it is mostly related to inserted devices e.g. central lines. Alrafiaah et al. [43] showed also similar results of fungal infections that three cases of neonatal sepsis were caused by fungal infections, and all of them occurred exclusively in premature babies. This obviously

related to the immature immune system of those neonates.

In our study there was significant difference between the mean of CRP, PCT and presepsin levels in proved and suspected N.S. groups when compared with healthy controls ($P< 0.05$). Also some authors observed high concentrations of PCT during proved sepsis, [45,46] and comparable low concentrations in suspected sepsis. In a study by Guibourdenche et al. [47], very low PCT concentrations were measured during SIRS, but high concentrations when sepsis was diagnosed. Studies concerning with prespsin marker [48,49] found that the plasma concentration of presepsin was significantly higher in infected patients than in non-infected patients. Shozushima et al. [50] found that the concentration of presepsin was 1 992.9±1 509.2 pg/mL in proved sepsis group, 817.9±572.7 pg/mL in suspected sepsis group and 333.5±130.6 pg/mL in control group so the blood concentration of presepsin among the groups increased sequentially.

A rapid test with the best degree of sensitivity, reliability, and predictability is required for the early diagnosis and treatment of neonatal sepsis [51]. From ROC curve at cut off CRP 9 mg/l the sensitivity and specificity were (72%, 61% respectively) which were less useful in diagnosis of neonatal sepsis compared to presepsin at cut off 500 pg/ml which has the highest sensitivity and specificity (95%, 81% respectively) followed by procalcitonin which at 5.6 ng/ml cut off had sensitivity and specificity (90%, 69% respectively). The positive and negative predictive rates were the lowest in CRP (28% and 80% respectively), whereas the positive and negative predictive rate showed high result in case of presepsin and PCT (presepsin positive predictive and negative predictive values were 84% and 95% respectively, while PCT positive predictive and negative predictive values were 55% and 95% respectively). Hisamuddin E, et al. [52] showed also that CRP estimation does have a role in the diagnosis of neonatal sepsis but the test is not specific enough to be relied upon as the only indicator. Previous studies have reported the sensitivity and specificity of PCT as follows: 66.7%, 94.4% [53]; 75% and 59% [54]; 66.7% and 50%; [55]; 88.9% and 65.2% [56] respectively. These results suggested that PCT is a better clinical marker than CRP—although it is associated with a more expensive cost. Montaldo et al. [57] findings were recorded for presepsin sensitivity and specificity that were 93% and 100% respectively in the study of early-onset sepsis in newborns and showed better sensitivity and specificity of presepsin than PCT and CRP. Bellos et al. [58] reported that Head-to-head comparison with AUC values of C-reactive protein and procalcitonin revealed that presepsin was more sensitive in detecting neonatal sepsis.

5. CONCLUSION

This study showed that the prevalence of neonatal sepsis among all admitted neonates in Al-Quwayiyah general hospital was 20.8%. Our results also detected higher sensitivity, specificity and positive and negative predictive values for presepsin more than and PCT CRP in the diagnosis of NS. Although presepsin has an important role in diagnosing sepsis, we suggest that detection of presepsin be combined with other traditional markers, such as procalcitonin, C-reactive protein, and white blood cells until.

Large scale studies are done to confirm such findings in different Saudi Arabia health care settings.

CONSENT AND ETHICAL APPROVAL

The study was approved by the hospital ethics committee. Both verbal and written informed consent was given by the parents.

ACKNOWLEDGEMENTS

The authors would like to thank infection control, chest department and laboratory personnel for their help during the study work.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hotoura V, Giapros A, Kostoula P, Spyrou, Andronikou S. Pre-inflammatory mediators and lymphocyte subpopulations in preterm neonates with sepsis. Inflammation. 2012;35(3):1094–1101.
2. Schneider HG, Lam QT. Procalcitonin for the clinical laboratory: A review. Pathology. 2007;39:383-390.
3. Garrouste OM, Timsit JF, Tafflet M, Misset B, Zahar JR, Soufir L, Lazard T, Jamali S, Mourvillier B, Cohen Y, De Lassence A,

Azoulay E, Cheval C, Descorps-Declere A, Adrie C, Costa de Beauregard MA, Carlet J. Excess risk of death from intensive care unitacquired nosocomial bloodstream infections: A reappraisal. Clin. Infect. Dis. 2006;42:1118–1126.

4. Yu Z, Liu J, Sun Q, Qiu Y, Han S, Guo X. The accuracy of the procalcitonin test for the diagnosis of neonatal sepsis: A meta-analysis. Scandinavian Journal of Infectious Diseases. 2010;42(10):723–733.
5. Mishra UK, Jacobs SE, Doyle LW, Garland SM. Newer approaches to the diagnosis of early onset neonatal sepsis. Archives of Disease in Childhood. 2006;91(3):F208–F212.
6. Black S, Kushner I, Samols D. C-reactive protein. Minireview. J BiolChem. 2004;279: 48487-48490.
7. Müller F, Christ-Crain M, Bregenzer T, Krause M, Zimmerli W, Mueller B, et al. Procalcitonin levels predict bacteremia in patients with community-acquired pneumonia: A prospective cohort trial. Chest. 2010;138(1):121.
8. Davies J. Procalcitonin. Journal of Clinical Pathology. 2015;9(68):657–679.
9. Becker KL, Snider R, Nylen ES. Procalcitonin assay in systemic inflammation, infection, and sepsis: Clinical utility and limitations. Crit Care Med. 2008;36:941.
10. Meisner M. Update on procalcitonin measurements. Ann Lab Med. 2014;34: 263.
11. Buhaescu I, Yood RA, Izzedine H. Serum procalcitonin in systemic autoimmune diseases—Where are we now? Seminars in Arthritis and Rheumatism. 2010;40(2): 176–183.
12. Mimoz O, Benoist JF, Edouard AR, Assicot M, Bahuon C, Samii K. Procalcitonin and C-reactive protein during the early posttraumatic systemic inflammatory response syndrome. Intensive Care Med. 1998;24:185.
13. Annborn M, Dankiewicz J, Erlinge D, Hertel S, Rundgren M, Smith JG, et al. Procalcitonin after cardiac arrest—an indicator of severity of illness, ischemia-reperfusion injury and outcome. Resuscitation. 2013;84:782.
14. Meisner M, Tschaikowsky K, Hutzler A, Schick C, Schuttler J. Postoperative plasma concentrations of procalcitonin after different types of surgery. Intensive Care Med. 1998;24:680.
15. Carsin H, Assicot M, Feger F, Roy O, Pennacino I, Le Bever H, et al. Evolution and significance of circulating procalcitonin levels compared with IL-6, TNF alpha and endotoxin levels early after thermal injury. Burns. 1997;23:218.
16. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36:296–327.
17. Grunwald U, Krüger C, Westermann J, Lukowsky A, Ehlers M, Schütt C. An enzyme-linked immunosorbent assay for the quantification of solubilized CD14 in biological fluids. J Immunol Methods. 1992;155:225–232.
18. Shirakawa K, Naitou K, Hirose J, Takahashi T, Furusako S. Presepsin (sCD14-ST): Development and evaluation of one-step ELISA with a new standard that is similar to the form of presepsin in septic patients. Clin Chem Lab Med. 2011;49:937–939.
19. Mussap M, Noto A, Fravega M, Fanos V. Soluble CD14 subtype presepsin (sCD14-ST) and lipopolysaccharide binding protein (LBP) in neonatal sepsis: New clinical and analytical perspectives for two old biomarkers. J Matern Fetal Neonatal Med. 2011;24:12–14.
20. Maldeghem I, Nusman C, Visse D. Soluble CD14 subtype (sCD14-ST) as biomarker in neonatal early-onset sepsis and late-onset sepsis: A systematic review and meta-analysis. BMC Immunol. 2019;20:17.
21. Tollner U. Early diagnosis of septicemia in newborn. Clinical studies and sepsis score. Eur J Pediatr. 1982;138:331–7.
22. Abutaleb Arwa A, et al. Clinical epidemiology of neonatal sepsis among neonates admitted to King Khalid University Hospital in Riyadh during the Year 2016. EC Paediatrics. 2018;7(2):48-57.
23. Eman M, et al. Epidemiology of neonatal sepsis and implicated pathogens: A study from Egypt. BioMed Research International; 2015.
24. Ansari S, et al. Neonatal septicemia in Nepal: Early-onset versus late-onset. International Journal of Pediatrics; 2015.
25. Verma P, et al. Neonatal sepsis: Epidemiology, clinical spectrum, recent antimicrobial agents and their antibiotic susceptibility pattern. International Journal

of Contemporary Pediatrics. 2015;2(3): 176-180.
26. Baeza E, et al. Risk factors and prognosis for neonatal sepsis in southeastern Mexico: Analysis of a four-year historic cohort followup. BMC Pregnancy and Childbirth. 2012;12:48.
27. Mehar V, Yadav D, Somani P, Bhatambare G, Mulye S, Singh K. Neonatal sepsis in a tertiary care center in central India: Microbiological profile, antimicrobial sensitivity pattern and outcome. J Neonatal Perinatal Med. 2013;6(2):165-72.
28. Afsharpaiman S, Torkaman M, Saburi A, Farzaampur A, Amirsalari S, Kavehmanesh Z. Trends in incidence of neonatal sepsis and antibiotic susceptibility of causative agents in two neonatal intensive care units in Tehran, I. R. Iran. J Clin Neonatol. 2012;1(3):124-30.
29. Shehab El-Din EM, El-Sokkary MM, Bassiouny MR, Hassan R. Epidemiology of neonatal sepsis and implicated pathogens: A study from Egypt. Biomed Res Int. 2015;50948.
30. Al-Shamahy H, et al. Types of bacteria associated with neonatal sepsis in Al-Thawra University Hospital, Sana'a. Yemen, and their antimicrobial profile. Clinical and Basic Research. 2012;12(1): 48-54.
31. Jajoo M, et al. To study the incidence and risk factors of early onset neonatal sepsis in an out born neonatal intensive care unit of India. Journal of Clinical Neonatology. 2016;4(2):91-95.
32. Chiabi A, Djoupomb M, Mah E, Nguefack S, Mbuagbaw L, Zafack J, et al. The clinical and bacteriogical spectrum of neonatal sepsis in a tertiary hospital in Yaounde, Cameroon. Iran J Pediatr. 2011;21(4):441-8.
33. Sartaj A. Bhat, Suhail A. Naik, Wasim Rafiq, Syed Tariq A. Incident of thrombocytopenia and changes in various platelet parameter in neonates with blood culture positive sepsis. Int J Pediatr. 2015;3(1)757-66.
34. Ahmad MS, Waheed A. Platelet counts, MPV and PDW in culture proven and probable neonatal sepsis and association of platelet counts with mortality rate. J College Physician Surg Pak. 2014;24:340-4.
35. Philip AGS, Hewitt JR. Early diagnosis of neonatal sepsis. Pediatrics. 1980;65(5): 1036–1041.
36. Fowlie PW, Schmidt B. Diagnostic tests for bacterial infection from birth to 90 days: A systematic review. Arch Dis Child Fetal Neonatal Ed. 1998;78:F92–8.
37. Shehab El-Din EM, El-Sokkary MM, Bassiouny MR, Hassan R. Epidemiology of neonatal sepsis and implicated pathogens: A study from Egypt. Biomed Res Int. 2015;45(7):504-10.
38. Chiabi A, Djoupomb M, Mah E, Nguefack S, Mbuagbaw L, Zafack J, et al. The clinical and bacteriogical spectrum of neonatal sepsis in a tertiary hospital in Yaounde, Cameroon. Iran J. Pediatr. 2011;21(4):441-8.
39. Hammoud MS, Al-Taiar A, Thalib L, Al-Sweih N, Pathan S, Isaacs D. Incidence, aetiology and resistance of late-onset neonatal sepsis: A five-year prospective study. J Paediatr Child Health. 2012;48(7): 604-9.
40. Karambin M, Zarkesh M. Entrobacter, the most common pathogen of neonatal septicemia in Rasht, Iran. Iran J Pediatr. 2011;21(1):83-7.
41. Shitaye D, Asrat D, Woldeamanuel Y, Worku B. Risk factors and etiology of neonatal sepsis in Tikur Anbessa University Hospital, Ethiopia. Ethiop Med J. 2010;48(1):11-21.
42. West BA, Peterside O. Sensitivity pattern among bacterial isolates in neonatal septicaemia in Port Harcourt. Ann Clin Microbiol Antimicrob. 2012;11:7.
43. Alrafiaah AS, Al Shaalan M, Alshammari FO, Almohaisani AA, Bawazir AS. Neonatal sepsis in a tertiary care hospital in Saudi Arabia. Int. J. Adv. Res. 2016;4(11):1713-1720.
44. Kilani RA, Basamad M. Pattern of proven bacterial sepsis in a neonatal intensive care unit in Riyadh-Saudi Arabia: A 2-year analysis. J Med Liban. 2000;48(2):77-83.
45. Yu Z, Liu J, Sun Q, Qiu Y, Han S, Guo X. The accuracy of the procalcitonin test for the diagnosis of neonatal sepsis: A meta-analysis. Scandinavian Journal of Infectious Diseases. 2010;42(10):723–733.
46. Park IH, Lee SH, Yu ST, Oh YK. Serum procalcitonin as a diagnostic marker of neonatal sepsis. Korean J Pediatr. 2014;57(10):451-456.
47. Guibourdenche J, Bedu A, Petzold L, et al. Biochemical markers of neonatal sepsis: Value of procalcitonin in the emergency setting. Ann Clin Biochem. 2002;39:130–5.

48. Endo S, Suzuki Y, Takahashi G, Shozushima T, Ishikura H, Murai A, et al. Usefulness of perception in the diagnosis of sepsis in a multicenter prospective study. J Infect Chemother. 2012;18:891–897.
49. Thapa B, Thapa A, Aryal DR, Thapa K, Pun A, Khanal S, et al. Neonatal sepsis as a major cause of morbidity in a tertiary center in Kathmandu. JNMA J Nepal Med Assoc. 2013;52(192):549-56.
50. Shozushima T, Takahashi G, Matsumoto N, Kojika M, Okamura Y, Endo S. Usefulness of presepsin (sCD14-ST) measurements as a marker for the diagnosis and severity of sepsis that satisfied diagnostic criteria of systemic inflammatory response syndrome. J Infect Chemother. 2011;17: 764–769.
51. Park IH, Lee SH, Yu ST, Oh YK. Serum procalcitonin as a diagnostic marker of neonatal sepsis. Korean J Pediatr. 2014;57(10):451-456.
52. Hisamuddin E, Hisam A, Wahid S, Raza G. Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. Pak J Med Sci. 2015;31(3):527–531.
53. Kim EK, Lee BS, Lee JA, Jo HS, Park JD, Kim BI, et al. Clinical availability of serum procalcitonin level in the diagnosis of neonatal bacterial infection. J Korean Soc Neonatol. 2001;8:211-21.
54. Janota J, Stranak Z, Belohlavkova S, Mudra K, Simak J. Postnatal increase of procalcitonin in premature newborns is enhanced by chorioamnionitis and neonatal sepsis. Eur J Clin Invest. 2001;31:978-983.
55. Sakha K, Husseini MB, Seyyedsadri N. The role of the procalcitonin in diagnosis of neonatal sepsis and correlation between procalcitonin and C-reactive protein in these patients. Pak J Biol Sci. 2008;11: 1785-90.
56. Boo NY, Nor Azlina AA, Rohana J. Usefulness of a semi-quantitative procalcitonin test kit for early diagnosis of neonatal sepsis. Singapore Med J. 2008;49:204-8.
57. Montaldo R, Rosso A, Santantonio G, Chello P. Giliberti Presepsin for the detection of early-onset sepsis in newborns. Pediatr. Res. 2017;81(2):329.
58. Bellos I, Fitrou G, Pergialiotis V, Thomakos N, Perrea DN, Daskalakis G. The diagnostic accuracy of presepsin in neonatal sepsis: A meta-analysis. Eur J Pediatr. 2018;177(5):625-632.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/54569