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The Role of CD64 and CRP in the Diagnosis of Sepsis in Neonates

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ABSTRACT

Sepsis is the body's extensive reaction to an infection. It is a severe medical emergency. Without prompt treatment, sepsis can quickly lead to tissue damage, organ failure, and death. Neonatal sepsis is defined as a syndrome of clinical features of the spread of infection and the presence of bacteremia increase access to the bloodstream. Bacteria most often cause infantile septicemia. An infant may be exposed to infections in the hospital or at home. This work came to assess the role of CRP and neutrophil CD64 in the diagnosis of sepsis in neonates and infants. This study is a case-control study, it involved two groups (60) patients and (20) controls of one day to one year of age during the period from May 2019 to September 2020 of neonates and infants admitted in Kerbala pediatric teaching hospital and Kerbala Primary health care centers. For a total of 80 children, two categories have been included and classified. the study showed the mean age for neonates of sepsis was (7.40±13) days while the mean age for neonates of control was (5.58±6.75)days, The mean age for infants of sepsis was (4.1±7.971) months while the mean age for infants of control was (4.01±5.66) months. in this research, CRP, PCT, and nCD64 are well-diagnostic biomarkers for early detection of neonatal and infantile sepsis. The combination of these biomarkers the diagnosis of suspected early and late-onset neonatal sepsis based on ROC curve analysis.

INTRODUCTION

Sepsis is a life-threatening malfunction of the organ due to a deregulated host reaction to infection (Singer *et al.*, 2016; Shankar-Hari *et al.*, 2016; Seymour *et al.*, 2016). It is one of the very important Causes of fatality for neonates and infants. If left organic, Gram-negative sepsis is commonly correlated with rather greater death than gram-positive death (Moradi *et al.*, 2015). One of the major causes of neonatal disease and death is bacterial sepsis with a prevalence of 1-5 Live births in 1000. free exposure to infection can occur during delivery, and its clinical presence can appear at birth or during the first days of life (Sharma *et al.*, 2020). Sepsis is the predominant cause of neonatal and infantile death in developing countries, accounting for 30-50 percent of total neonatal deaths annually (Gupta *et al.*, 2014; Al-Karaw *et al.*, 2024). Neonatal sepsis (NS) is a systemic infection that occurs at ≤28 days of life in neonates and is a significant cause of neonate disease and death (Sankar *et al.*, 2008). Neonatal sepsis is a clinical condition characterized by systemic signs of bacterial invasion of the bloodstream that causes circulatory reduction (Edmond & Zaidi, 2010; Kadhim *et al.*, 2023).

Sepsis refers to the dispersed inflammatory response caused by microbial infections, in which the patient typically develops fever, tachycardia, and tachypnea. Severe sepsis is linked to at least one organ's dysfunction. When extreme sepsis is supplemented by multiple organ system failures, the disease is called septic shock.

In clinical practice, a common problem is that the signs and symptoms of bacterial infections typically overlap, particularly in the case of respiratory tract infections, even after laboratory tests have been detected. In these circumstances, therefore, a laboratory test with more precision would expressively enhance the clinical differential diagnosis.

Neonatal sepsis (NS)

Neonatal sepsis is stated to be an infection involving the bloodstream in neonates less than 28 days old. Many systemic neonatal infections, such as meningitis, pneumonia, arthritis, and osteomyelitis, include neonatal sepsis. (Vergnano *et al.*, 2005). Neonatal sepsis is one of the major causes of disease and death among neonates in the developing world (Edmond & Zaidi, 2010). It has been well known that neonatal sepsis causes over 520,000 deaths of neonates yearly (Lawn *et al.*, 2010).

Mode of transmission of early-onset sepsis and late-onset sepsis

There are some routes of infection for the neonates such as the ascending route that allows bacteria from the parental vaginal tract and cervix to enter the uterus before delivery, usually due to ruptured membranes or through the maternal-fetal vasculature. This is the most popular infection path in neonates, Descendent route the fetus acquires the pathogen as the neonates descends through the vagina at birth. Early-onset sepsis (EOS) is generally caused by vertically transferred by the mother to neonates before or after birth (Hornik *et al.*, 2012; Abdullah *et al.*, 2021), these pathogens can rise the vagina, cervix, uterus, and amniotic fluid may be infected.

Treatment of Neonatal sepsis: The World Health Organization (WHO) now recommends ampicillin or penicillin with gentamicin for both EOS and LOS as first-line antimicrobials (Organization, 2013).

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Prevention of Neonatal sepsis

The prevention of neonatal sepsis requires the continuation of what is understood and new prevention plans are being created. Parental treatment with the detection of protective carriage of GBS via universal screening for all prenatal women remains critical for the prevention of early-onset sepsis group B Streptococcus (GBS). The guidelines for the prevention of topical group B Streptococcus (GBS) emphasize the need for complete parental GBS screening at 37 weeks of gestation and include nucleic amplification tests (NAATs) as new diagnostic techniques that can be used to improve the identification of group B Streptococcus (GBS) production.

Infantile septicemia (IS)

Bacteria most commonly cause infantile septicemia (IS). However, it can be triggered by other microorganisms too. Infants can be exposed in the hospital or at home to infections. The best ways to avoid sepsis are by early diagnosis and treatment. Antibiotic medicine begins as early as possible.

Treatment of infantile sepsis

Early diagnosis and care is the only way to avoid sepsis. Importantly, the epidemiology of aggressive infections is subject to change as a result of injection drives (Henderson *et al*., 2010) and the increasing number of infants at risk of getting healthcare-associated infections, including premature infants, the infant with a hateful disease, or after transplantation (Levy *et al*., 2012).

Prevention of infantile septicemia

Prevention of infantile septicemia, the start of the 20th century, and the toll of infectious diseases on the United States (US) population was high.

Risk factors of sepsis

Risk Factors of Neonatal Sepsis

Events that disrupt the amniotic cavity during pregnancy, such as cervical and amniocentesis, can increase the rate of intra-amniotic infection and subsequent neonatal sepsis. Parental risk variables during effort include fever, infected placenta, Elongated rupture of membranes (> 18 h), premature birth, Preterm birth (< 37 weeks), and frequent vaginal checkups during pregnancy. While risk factors for late-onset neonatal sepsis (LOS) include an Infected hospital environment, Staying in the hospital for a long period, Low birth weight, Birth before 37 weeks, or birth more than 18 hours after the Amniotic sac for the mother (water) insolvent and long automatic drying.

Risk factors of Infantile septicemia

The risk factors include the absence of pregnancy care, unconfirmed or sick oversaw home deliveries, unclean and unsafe delivery observes and cord care, prematurity, low birth weight of the infant, More than 18 hours before birth, the amniotic sac splits (ruptures), lack of special breastfeeding, and delays in respect of danger signs in both mother and infants (Lawn *et al*., 2005; Barnett *et al*., 2006).

MATERIAL AND METHODS

Patients

This study involved two groups (60) patients and (20) controls of one day to one year of age during the period from May 2019 to September 2020 of neonates and infants admitted to Kerbala Pediatric Teaching Hospital and Kerbala Primary Health Care Centers. A total of 80 children in two categories have been included and classified. The first group was neonates and infants (a group of sepsis), which consisted of 60 patients (40 males and 20 females) who attend Kerbala teaching hospital during the period from May 2019 to September 2020. The second group was a healthy control group, which consisted of 20 healthy control (12 males and 8 females) who attend Kerbala primary health care centers. They are of age and sex matching with patients who were diagnosed based on the clinical features and laboratory findings.

Inclusion criteria for neonates

- Fever (>38°C).
- Breathing problems.
- Reduced movements.
- Seizures.
- Bradycardia
- Tachycardia

Signs of pain, such as a very fast heart rate during work or delivery.

- High fever (temperature above 38.1.
- Breathing issues, such as very rapid breathing.
- Digestive concerns, such as low appetite.

Sample Collection

Approximately 3cc of venous blood was obtained from each child (patient and control) preceded by sterilization of the area with 60% ethanol. 2cc of blood was dispensed into an EDTA tube (for Complete Blood Count (CBC) and neutrophil CD64), 1 cc of blood (for CRP), Dispensed into a plain tube, the serum was separated by centrifugation and allowed to coagulate 4,000 round per minutes (RPM) for 10 minutes.

Serum inflammatory biomarker detection:

Venous blood sample for biomarkers was evaluated before exposure to antibiotics. The samples are placed in a plain tube and were separated by centrifugation at 4,000 rounds per minute (RPM) for 10 minutes, CRP are detected by enzymatic immunoassay (EIA).

Statistical Analysis

Using the statistical SPSS v 22.0. Statistical analyses were performed to determine the optimal laboratory diagnostic parameters (CRP, CD64, and WBC) for predicting neonates and infants with sepsis, the receiver operating

characteristic (ROC) curve was developed to calculate the diagnostic importance of blood biomarkers for predicting neonates and infants with sepsis. A ROC curve showed the false-positive rate on the x-axis (specificity) and the true-positive rate on the y-axis (sensitivity) for variable test cut-off values.

RESULTS AND DISCUSSIONS

The clinical patterns of the study groups

This study involved two groups (60) patients and (20) controls of one day to one year of age, The clinical patterns of the study groups are summarized in Table 1.

Table 1: Clinical patterns (sepsis and control group) of the study.

Clinical patterns	Sepsis group (n=60)		Control group (n=20)	
	(neonates)	(infants)	(neonates)	(infants)
Age days	7.40±13	124.70±239.13	5.58±6.75	120.4±170
Temperature	0.78±39.3	0.75±39.004	0.518±37.04	0.1±37
Gestational age (months)	0.91±9.4	0.65±8.94	0.40±9	0.66±8.75
Birth weight (kg)	0.84±3.35	2.56±8.25	0.39±3.01	2.94±6.42
Total leukocyte count (mean±SD)	9.04±15.45	7.71±17.38	4.94±9.04	3.06±9.32
CRP, mg/L (mean±SD)	22.21±24.64	36.08±28.65	0.29±0.36	0.46±0.59
nCD64 (mean±SD)	53.90±18.49	66.33±15.63	14.79±19.65	11.85±16.51

Table 2: Comparison between the means and Std. the deviation between the Sepsis and controls of the total sample (n=80).

Group		Mean	Std. Deviation	Significance
CD64	Control	18.39500	14.14	<0.001*
	Sepsis	64.5933	16.63	
WBC	Control	9.1530	4.41	<0.001*
	Sepsis	17.0419	7.97	
Age(days)	Control	72.050	113.39	<0.001*
	Sepsis	209.375	139.09	
Temp	Control	37.025	.41	<0.001*
	Sepsis	39.066	.763	

**=significant difference.*

Types of Delivery

The percentage of the delivery of neonatal and infantile of the total samples patients and healthy control was 37 out of 80 (37%) cesarean and 63 out of 80(63%) nature as in Figure 1.

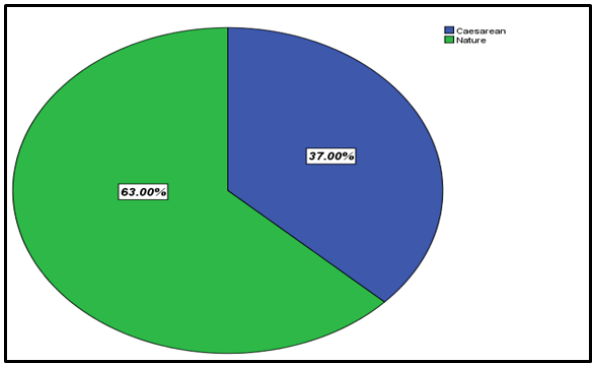

Figure 1: Types of delivery

Bleeding during pregnancy

The percentage of bleeding during pregnancy in the total samples patients and healthy control were 19 out of 80(19%) mothers they get bleeding and 81 out of 80 (81%) they have no bleeding. as in Figure 2.

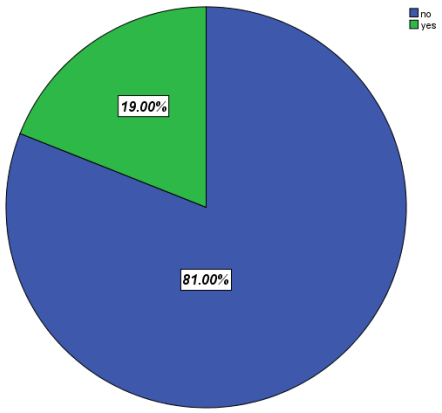

Figure 2: The distribution of Bleeding during pregnancy of the mother among the total sample

Use of Optimum inflammatory biomarker cut-off values for sepsis diagnosis

ROC analysis has been used to recognize the sensitivity, specificity, positive predictive value (PPV), negative

predictive value (NPV), and AUC of the tests for the optimal cut-off values select, Comparison of the nCD64, CRP, and WBC receiving operating characteristic (ROC) curves as markers for diagnosis of neonatal and infantile sepsis as in Figure 3.

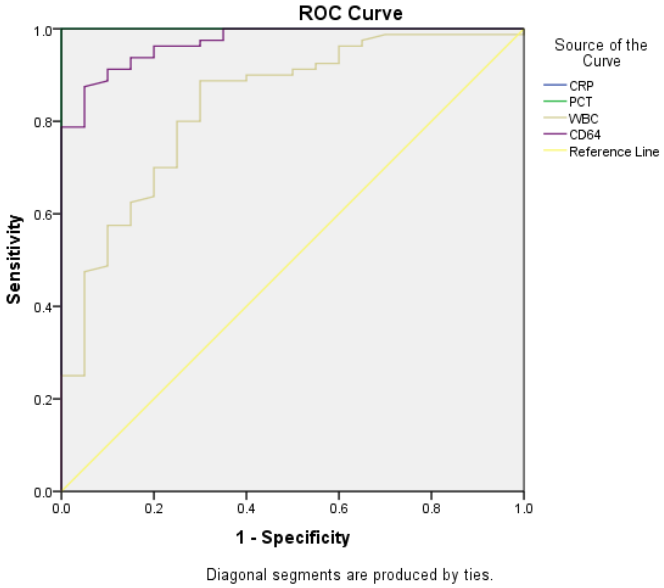

Figure 3: Comparison of the nCD64, CRP, and WBC receiving operating characteristic (ROC) curves as markers for diagnosis of neonatal and infantile sepsis.

Table 3: Area under the curve

Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
CRP	1.000	.000	.000	1.000	1.000
WBC	.836	.050	.000	.738	.934
CD64	.971	.015	.000	.942	1.000

The test outcome variable(s): WBC, CD64 has at least one relationship between the group of positive real states and the group of negative real states.
The optimum cut-off value was (10) mg/L for CRP, (8.70) for WBC and (2.21) for CD64 in the diagnosis of neonatal and infantile sepsis

The Receiver Operating Characteristic (ROC) for CD64 as a diagnostic marker to detect neonatal and infantile sepsis in (sepsis and control) and area under the curve (AUC) were (0.971) this indicates an excellent distinctive nature of WBC count as a classifying index as in Figure 4.

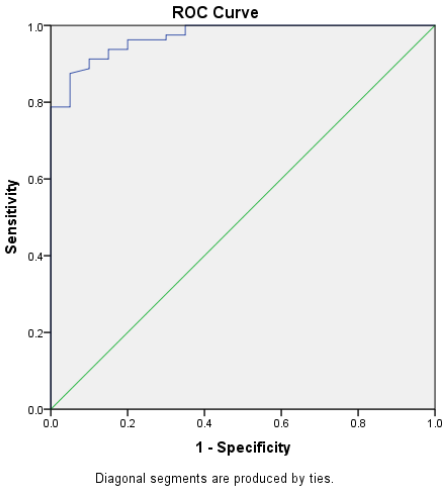

Figure 4: The Receiver Operating Characteristic for CD64 as a diagnostic marker to detect neonatal and infantile sepsis in (case and control) among the total sample (n=80).

Discussion

Due to high morbidity and mortality, despite developments in medical therapeutics, sepsis remains a major global health issue (Angus *et al.*, 2001; Todi *et al.*, 2007). Neonatal sepsis (NS) is a clinical condition that is potentially life-threatening and requires early intervention.

In this study, the mean CRP for neonates of the sepsis group was (22.21±24.64) mg/L, and the control group was (0.29±0.36) mg/L. While in Another study found that the mean CRP for the sepsis group was (9.31±13.60) mg/L, and the control group was (4.22 ± 2.66) mg/L (Adib *et al.*, 2012).

as the cut-off value by using ROC curves is the range of reported statistical outcomes are as follows: sensitivity (100%), specificity (52.66%), positive predictive value (82.2%) negative predictive value (95 %), and AUC value are (0.951) (Sakha *et al.*, 2008). Most studies have completed the importance of CRP as an early marker of neonatal and infant sepsis. From other studies, we know CRP is a very early marker, but levels can become normal even if the infection continues.

Serum CRP and PCT measures can help look at neonatal and infant sepsis. There must also be a rationally high sensitivity and specificity of a capable diagnostic marker the test is negative if the infection is absent) and a good PPV (infection is present when the test is positive),

Thus, both markers had a large diagnostic value more usefulness was shown by CRP levels. We used the following criteria based on the AUC level to verify diagnosis accuracy (Greiner *et al.*, 2000).

Neutrophil CD64 (nCD64) is a receptor of high affinity for monomeric IgG antibodies, which is so complex in the opsonized bacteria phagocytosis process. Since receptor expression on neutrophil surfaces increases approximately one hour after the invasion, infectious complications may be a relatively early marker. The neutrophil CD64 index is a potential hematologic marker of sepsis. First, many studies have tested the utility of this index in the NICU community, yet with good results in both the preterm and term populations, as well as in both EOS and LOS cases (Bhandari *et al.*, 2008; Morsy *et al.*, 2008). In this study, The mean CD64 for neonates of the sepsis group was (53.90±18.49), and the control group was (14.79±19.65). While in Another study found that the mean CD46 for the sepsis group was (4.08±28.65) and the control group was (3.01±13.42) (Ng *et al.*, 2004).

CONCLUSIONS

As compared to CRP, PCT, and nCD64 are well-diagnostic biomarkers for early detection of neonatal and infantile sepsis. The combination of these biomarkers could increase sensitivity for the diagnosis of suspected early and late-onset neonatal sepsis based on common serum biomarkers with the aid of optimal cut-off value based on ROC curve analysis.

Recommendations

Further study is to find out or to highlight the association biomarkers CRP, PCT, CD64, and other clinical diagnoses or cases. Make other research to study other biomarkers in the diagnosis of sepsis or septicemia.

REFERENCES

Abdullah, Y. J., Kadhim, A. S., Khallaf, S. A., & Alsaedi, R. Z. J. (2021). Serum levels of interleukin–6, ferritin, C-reactive protein, lactate dehydrogenase, D-dimer and count of lymphocytes and neutrophils in COVID-19 patients. Its correlation to the disease severity. *Annals of the Romanian Society for Cell Biology, 25*(2), 2220-2228.

Adib, M., Bakhshiani, Z., Navaei, F., Fosoul, F. S., Fouladi, S., & Kazemzadeh, H. (2012). Procalcitonin: a reliable marker for the diagnosis of neonatal sepsis. *Iranian journal of basic medical sciences, 15*(2), 777.

Al-Karawi, A. S., & Kadhim, A. S. (2024). Exploring the role of autoantibodies in Iraqi females with polycystic ovary syndrome. *J Adv Biotechnol Exp Ther, 2024*(7), 147-56.

Angus, D. C., Linde-Zwirble, W. T., Lidicker, J., Clermont, G., Carcillo, J., & Pinsky, M. R. (2001). Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Critical care medicine, 29*(7), 1303-1310.

Bhandari, V., Wang, C., Rinder, C., & Rinder, H. (2008). Hematologic profile of sepsis in neonates: neutrophil CD64 as a diagnostic marker. *Pediatrics, 121*(1), 129-134.

Edmond, K., & Zaidi, A. (2010). New approaches to preventing, diagnosing, and treating neonatal sepsis. *PLoS medicine, 7*(3), e1000213.

Greiner, M., Pfeiffer, D., & Smith, R. D. (2000). *Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. Preventive veterinary medicine, 45*(1-2), 23-41.

Gupta, N., Kabra, M., & Kapoor, S. (2014). Establishing national neonatal perinatal database and birth defects registry network—Need of the hour!. *Indian pediatrics, 51*, 693-696.

Henderson, K. L., Johnson, A. P., Muller-Pebody, B., Charlett, A., Gilbert, R., & Sharland, M. (2010). The changing aetiology of paediatric bacteraemia in England and Wales, 1998–2007. *Journal of medical microbiology, 59*(2), 213-219.

Hornik, C. P., Fort, P., Clark, R. H., Watt, K., Benjamin Jr, D. K., Smith, P. B., ... & Cohen-Wolkowiez, M. (2012). Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. *Early human development, 88,* S69-S74.

Kadhim, A. S., Abdullah, Y. J., & Hasan, N. F. (2023). Asymptomatic individuals with coronavirus disease-19 as infectious cases and encouragement immunity hypothesis. *Journal of Preventive, Diagnostic and Treatment Strategies in Medicine, 2*(2), 74-79.

Lawn, J. E., Kerber, K., Enweronu-Laryea, C., & Cousens, S. (2010, December). 3.6 million neonatal deaths—what is progressing and what is not?. In *Seminars in*

perinatology (Vol. 34, No. 6, pp. 371-386). WB Saunders.

Levy, M. M., Artigas, A., Phillips, G. S., Rhodes, A., Beale, R., Osborn, T., ... & Dellinger, R. P. (2012). Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study. *The Lancet infectious diseases, 12(*12), 919-924.

Moradi, N., Javadpoor, S., & Vahdani, M. (2015). Prevalence and antibiogram pattern of gram negative bacteria isolated from blood cultures in Shahid mohammadi hospital Bandar Abbas. *Journal of Preventive Medicine, 2*(2), 55-61.

Ng, P. C., Li, G., Chui, K. M., Chu, W. C., Li, K., Wong, R. P., ... & Fok, T. F. (2004). Neutrophil CD64 is a sensitive diagnostic marker for early-onset neonatal infection. *Pediatric research, 56*(5), 796-803.

Sankar, M. J., Agarwal, R., Deorari, A. K., & Paul, V. K. (2008). Sepsis in the newborn. *The Indian Journal of Pediatrics, 75,* 261-266.

Sharma, A., Thakur, A., Bhardwaj, C., Kler, N., Garg, P., Singh, M., & Choudhury, S. (2020). Potential biomarkers for diagnosing neonatal sepsis. *Current Medicine Research and Practice, 10*(1), 12-17.

Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., ... & Angus, D. C. (2016). The third international consensus definitions for sepsis and septic shock (Sepsis-3). *Jama, 315*(8), 801-810.

Vergnano, S., Sharland, M., Kazembe, P., Mwansambo, C., & Heath, P. T. (2005). Neonatal sepsis: an international perspective. *Archives of Disease in Childhood-Fetal and Neonatal Edition, 90*(3), F220-FF224.