International Journal of Contemporary Pediatrics
Karmaker P et al. Int J Contemp Pediatr. 2024 Nov;11(11):1519-1526
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20243075

Original Research Article

A prospective observational study of neutrophil CD64 as a diagnostic marker in neonatal sepsis

Prohlad Karmaker[1], K. M. Mahbubur Rahman[2], Mohammad Rasel[3], Ummey Tamima Nasrin[4], Shazia Afreen[5], Mohammad Kamrul Hassan Shabuj[6], M. Abdul Mannan[6]*

[1]Department of Paediatrics, Sheikh Sayera Khatun Medical College Hospital, Gopalganj, Bangladesh
[2]Department of Paediatrics, Shaheed M Monsur Ali Medical College and Hospital, Sirajganj, Bangladesh
[3]Department of Paediatrics, Monno Medical College, Manikganj, Bangladesh
[4]Department of Paediatric Neurology and Development, Cumilla Medical College Hospital, Cumilla, Bangladesh
[5]Department of Paediatrics (SCANU), Kurmitola General Hospital Dhaka, Bangladesh
[6]Department of Neonatology, Bangabandhu Sheikh Mujib Medical, University, Dhaka, Bangladesh

Received: 24 August 2024
Revised: 15 October 2024
Accepted: 19 October 2024

***Correspondence:**
Dr. M. Abdul Mannan
E-mail: drmannan64@gmail.com

ABSTRACT

Background: Neonatal sepsis is a major cause of mortality in the developing countries. With current investigations like septic screening and blood culture and sensitivity is not capable to early diagnosis of sepsis and have some limitations.
Methods: This prospective observational study was conducted in the Department of Neonatology and Department of Microbiology and immunology, BSMMU after approval by Institutional review board over a one-year period from May 2021 to April 2022. During the study period, a total of 590 neonates were admitted in NICU of BSMMU. Among them 157 neonates with suspected neonatal sepsis were admitted. Among these 157 newborns, 64 were excluded. Finally, 93 patients were included and analysed in the study.
Results: Total 157 patients with suspected sepsis were admitted during study period. Among them 64 newborns were excluded on basis of different exclusion criteria. Baseline characteristics of enrolled neonates 56(60.2%) were male. Mean gestational age 33.63±3.463 and mean birth weight 1863.23±773.202. Majority of the baby were inborn 68 (73.1%) and mode of delivery was LUCS. Maternal Risk factor for early onset sepsis like fever, UTI, PROM was not statistically significant. Hb and platelet significantly decreased in proven sepsis group. CRP significantly increased in proven sepsis group than clinical sepsis group. Mean nCD64 (%) was 83.62±16.665 and 57±34.277 in proven and clinical sepsis group respectively. It was significantly (P less than 0.001) increased in proven sepsis group. In ROC curve cut-off value for nCD64 in proven sepsis group was 71.5%. For sepsis diagnosis nCD64 showed sensitivity and specificity were 80% and 56% respectively. Calculating PPV and NPV were 71% and 74% respectively. nCD64 has an area under the curve (AUC) of 0.718. So, it is a moderately accurate marker for the diagnosis of neonatal sepsis.
Conclusions: Flow cytometric assessment of neutrophil CD64 was found more in neonates with culture proven sepsis than clinical sepsis. nCD64 has a good sensitivity 80% and specificity 56% and PPV, NPV 71%,74% respectively in culture proven sepsis with a cut-off value 71.5%

Keywords: Neonatal sepsis, Neutrophil CD64, Predictive marker

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life.[1] It has been classified as either early onset (within first 72 hours of life) or late onset sepsis (occurring after 72 hours of age) i.e. infections occurring before and after 72 hours of life.[2] The first 28 days of life the neonatal period are the most vulnerable time for a child's survival.[3] The main causes of newborn deaths are preterm birth related complications (35%) intrapartum related events (24%) and serious infections (21% sepsis or meningitis and pneumonia). These causes account for nearly 80% of deaths in this age group and almost all of these deaths occur in developing countries.[4]

In Bangladesh neonatal death is still high, accounting for more than half of all under-five deaths and more than two-thirds of infant deaths. An estimated 62,000 newborns die every year in Bangladesh and 50% of them die on 1st day of life. The main causes of neonatal deaths are prematurity (29.7 percent), birth asphyxia and trauma (22.9 percent) & sepsis (19.9 percent).[5] Infant Mortality Rate (IMR) is 38/1000 live birth and Neonatal Mortality Rate (NMR) in our country 30/1000 live birth.[6] The overall incidence of primary sepsis (EOS and LOS) is 1 to 2 per 1000 live births. Incidence is strongly influenced by gestational age (GA) at birth.[7]

One study of our country showed 70.38% and 29.62% neonates presented with early onset sepsis (EOS) and late onset sepsis (LOS) respectively.[8] Early diagnosis and treatment of neonatal sepsis may help decreasing neonatal mortality. Neonatal sepsis is considered as one of the major causes of morbidity and mortality. Blood culture has been considered the gold standard diagnostic test but its analysis takes too long time and lacks sensitivity at early stages. It is also thought that total leukocyte count (TLC), total neutrophil count, immature-to-total neutrophil ratio (I/T), micro-ESR and C-reactive protein (CRP) and platelet count also failed to reach the appropriate sensitivity and specificity in this disease.[9]

Early diagnosis, timely administration of appropriate antibiotics and a proper supportive therapy are crucial to improve survival and to reduce long-term sequelae.[10,11] All newborn suspected to have sepsis should undergo a septic screening.[12] These conventional screening tests may help in the diagnosis of septicemias. However, they lack the capacity to predict the severity of sepsis.[13] It's high time to identify a test that is cheap, accurate, and easy to perform with quick availability of reports to enhance the early detection of neonatal sepsis as early diagnosis and treatment reduces the morbidity and mortality.[14] One marker that has shown particular promise as an early marker for infection is neutrophil surface CD64 expression. CD64 is a high affinity Fc receptor expressed on neutrophils. Expression increases when neutrophils are activated by infectious stimuli.[15]

Upregulation of CD64 expression on neutrophils (nCD64) is thought to be a very early step of host's immune response to bacterial infection, increasing approximately one hour after invasion. This upregulated expression is stimulated by inflammatory cytokines during infection, and occurs in a graded manner dependent on the intensity of the cytokine stimulus, and nCD64 expression is stable for more than 24 hours. Advances in flow cytometric technology have made it possible to quantitate nCD64 rapidly for neonates with precision and minimal blood volumes.[16] Resting neutrophils have very low levels of CD64 antigen on their membrane, approximately 1000 molecules per cell. nCD64 expression is increased upon activation of neutrophils by pro-inflammatory cytokines within 4-6 hours and can reach more than 10-fold higher levels than in resting conditions, allowing good discrimination between resting and activated neutrophils.[17]

The objective of this study is to see the performance of neutrophil CD64 as a good and early diagnostic marker for neonatal sepsis.

METHODS

Study type

This was a prospective observational trial.

Study place

The study was done in the Department of Neonatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka.

Study duration

The study duration was from June 2021 to May 2022, after getting the approval from the Institutional Review Board.

Inclusion criteria

All neonates inborn and outborn from birth to 28 days of age with presence of ≥2 clinical feature or ≥2 risk factors for sepsis admitted in the Department of Neonatology, Bangabandhu Sheikh Mujib Medical University during the study period were eligible for enrolment.

Exclusion criteria

Neonates with lethargy (due to H/O PNA), parental refusal to participate the study, parents withdraw consent before sample collection were excluded from study.

Study procedure

Neonates with suspected early or late-onset sepsis satisfying the inclusion criteria were enrolled for the study. In the case of neonates with multiple episodes of

late-onset sepsis, only 1st episode was included. A written informed consent was taken before enrollment. Face-to-face interview with the parents or caregivers was done from all enrolled neonates. Meticulous history regarding the demographic characteristics and clinical features such as hypothermia, fever, lethargy, refusal to suck, respiratory distress, irritability, high pitch cry, seizure etc. were taken from the attendance/mother. Risk factors for sepsis such as prolonged rupture of membrane, prolonged labour, meconium-stained liquor was evaluated and physical examination was done. All required information were recorded in a data collection form during hospital admission. Gestational age was determined by 1st date of last menstrual period, Ultrasonogram in early pregnancy & the New Ballard score. Birth weight was recorded for each baby after admission using an electronic scale having a sensitivity of 10 grams (Model 914, SALTER). For out born babies, birth weight was determined from previous documents. Lubchenco's intrauterine growth chart was used for classification as AGA/ SGA/ LGA. At first cleansing the skin site with 70% isopropyl alcohol for 30 seconds followed by povidone-iodine and isopropyl alcohol again. Four ml (4 ml) venous was collected within 1 hours of onset of sepsis at a time for following purpose. 1.5ml for CBC with PBF, 1 ml for blood C/S,1ml for CRP and 0.5 ml for flow cytometry for nCD64. In EDTA (ethylene diamine tetra acetic acid) tube blood was sent for sepsis screen which was done in Department of Laboratory medicine, BSMMU, by XT-4000I (Japan) or XN-2000 (Japan).

For C-Reactive Protein (CRP) estimation blood was sent in a clot activator tube in Biochemistry Department. Quantitative assay for the estimation of C-reactive protein (CRP) levels were done on an automated Biochemistry analyzer (BECKMAN COULTER, USA). If two or more of the following parameters were positive, it was considered as positive sepsis screen: (i) Total leukocyte count <5000/cu mm or >25,000/cu mm; (ii) Absolute neutrophil count. Low counts (<1500/cu mm); (iii) Immature/total neutrophil >0.2;(iv) Micro ESR >15 mm in 1st hour;(v) C reactive protein ≥ 6 mg/l. Blood samples for C/S were sent to Department of Microbiology and Immunology, BSMMU. The samples were inoculated in the BD BACTEC Peds Plus/F Culture bottle containing 40 ml broth and culture were done by BD BACTEC FX40 (USA) fully automated system. Culture positive baby known as proven sepsis and negative known as clinical sepsis.

Venous blood (0.5 ml) was taken in EDTA tube for neutrophil CD64 expression by Flow Cytometry. This test was done by CYTOMICS FC 500 (USA) in the Department of Microbiology and Immunology, BSMMU. Samples were remained acceptable for up to 24 hours after collection when held at room temperature (18-22˚C) and for 48 hours when will be refrigerated (2-8˚C). At weekend samples were refrigerated and on holiday I kept samples at room temperature. Reports were available within 4 hours after the specimen reached the laboratory. CD64 results were expressed as the percentage of positive cells.

Data analysis

At first, permission was taken from the hospital authority. Then the purpose of the study was explained in detail to the respondents and data were collected from the sampling population through a face-to-face interview. Same questionnaire was used for each respondent for data collection. It was made clear to the respondents that they were at liberty to answer or not to answer any question. The data entry was started immediately after the completion of data collection. The collected data were checked, verified, and coding, post coding, and then entered into the computer. Only a fully completed questionnaire was entered into the computer for final analysis.

Statistical analysis

After collection data were entered into a personal computer and edited, analyzed, and plotted in graphs and tables whenever necessary. Quantitative data were expressed as mean±SD and categorical data were presented as frequency and percentage. All quantitative data were compared by independent sample t test; categorical data were compared by Chi-square test. The predictive power of nCD64 was assessed by receiver operating characteristic (ROC) curve and a cutoff value of nCD64 was determined. Data were analyzed using the statistical package for social sciences (SPSS) version 22. $p<0.05$ was considered as significant.

RESULTS

During the study period, a total of 590 neonates were admitted in NICU of BSMMU. Among them 157 neonates with suspected neonatal sepsis were admitted. Among these 157 newborns, 64 were excluded. Finally, 93 patients were included and analyzed in the study.

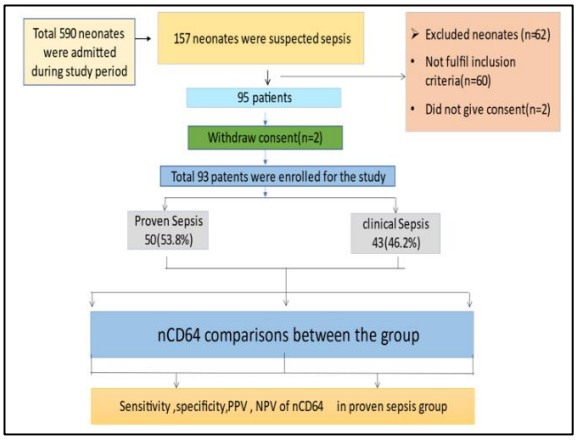

Figure 1: Patient enrollment and their outcome.

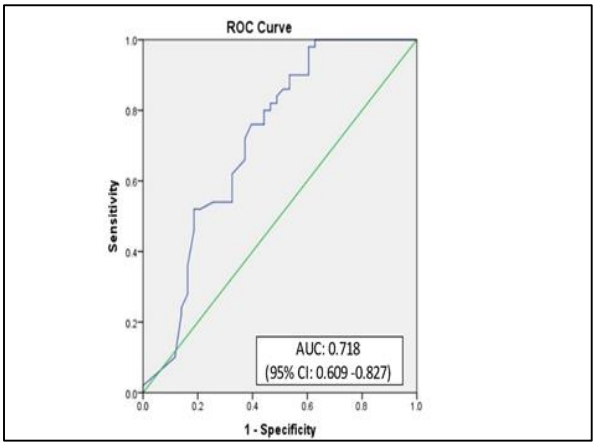

Figure 2: Receiver operating characteristic curve for prediction of culture proven sepsis by nCD64.

Table 2 showed baseline characteristics of the studied infants. Mean gestational age (weeks) 33.63±3.463. Out of 93 enrolled patients, 68 (73.1%) were inborn. Male: Female distribution was 56 (60.2%) and 37 (39.8%) respectively. More than two-thirds of the enrolled patients (74.2%) were Appropriate for gestational age. The predominant mode of delivery was LUCS (73.1%). Preterm and low birth weight baby were born about 76.4% and 71.1% respectively.

Table 1: Baseline maternal characteristics.

Characteristics	Findings
Number of antenatal visits, N (%)	
<4	27 (29%)
≥4	66 (71%)
PROM>18 hours, N (%)	
Yes	16 (17.2%)
No	77 (82.8%)
Maternal fever, N (%)	
Yes	1 (1.1%)
No	92 (98.9%)
H/O maternal UTI, N (%)	
Yes	12 (12.9%)
No	81 (87.1%)
Antenatal corticosteroid, N (%)	
None	49 (52.7%)
Incomplete dose	18 (19.4%)
Complete dose	26 (28%)
Use of antenatal antibiotics, N (%)	
Yes	16 (17.2%)
No	77 (82.8%)

Categorical data are presented as number and percentage (%), PROM:Premature rupture of membrane; UTI:Urinary tract infection

In Table 3 showed mean birth weight less in proven sepsis group. Male and female number and percentage more in proven sepsis group than clinical sepsis group that was 29 (51.8%) and 21 (56.8%) respectively. 5 (100%) infants in clinical sepsis group had meconium stain liquor and was statistically significant. In case of EONS most of the infants 21 (84%) in clinical sepsis group had EONS and in case of LONS 46 (67.6%) infants were in proven sepsis group had LONS and that was statistically significant (p value<0.001).

Table 2: Baseline characteristics of the enrolled neonates (n=93).

Characteristics	Findings
Gestational age (weeks), mean±SD	33.63±3.463
Gestational age category in weeks, N (%)	
<30	13 (14.0)
30-<35	40 (43.0)
35-<37	18 (19.3)
≥ 37	22 (23.7)
Birth weight(g), mean ± SD	1863.23±773.202
<1000	11 (11.8)
1000-<1500	27 (29.0)
1500-<2500	30 (32.3)
≥2500	25 (26.9)
Sex, N (%)	
Male	56 (60.2)
Female	37 (39.8)
Place of birth, N (%)	
Inborn	68 (73.1)
Outborn	25 (26.9)
Mode of delivery, N (%)	
LUCS	68 (73.1)
NVD	25 (26.9)
Fetal growth at birth, N (%)	
SGA	23 (24.7)
AGA	69 (74.2)
LGA	01 (1.1)

Continuous data are presented as mean±SD and categorical data are presented as number and percentage (%), LUCS: Lower segment Caesarean section; NVD: Normal vaginal delivery; SGA: Small for gestational age; AGA: Appropriate for gestational age; LGA: Large for Gestational Age.

Table 4 is showed that the mean of Hb% was lower (13.30±3.429) in proven sepsis group with a statistically significant p value<0.001. The mean CRP level (67.96±59.610) mg/l was significantly raised among proven sepsis in comparison to clinical sepsis group. IT ratio >0.2 in proven sepsis group, 17 (73.9%) and it was statistically significant. Platelet count was significantly lower in proven sepsis group.

We found in Table 5, the mean nCD64% was higher (83.62±16.665) among proven sepsis than clinical sepsis group which was statistically significant (p value<0.001).

The power of nCD64 for diagnosis of culture proven sepsis is demonstrated in table 6 and also Figure 2. In this table shows different cut off values and sensitivity,

specificity and different PPV and NPV. But 71.5 % cut off values shows sensitivity and specificity 80 and 56 respectively and PPV, NPV 71 and 74 respectively and it was statistically significant.

Table 3: Comparison of demographic, clinical data between culture proven and clinical sepsis group (n=93).

Variable	Proven sepsis group (n=50)	Clinical sepsis group (n=43)	P value
Birth weight (g) (mean± SD)	1770.30±714.034	1971.28±832.169	0.213
Gestational age(weeks) (mean ±SD)	33.42±3.517	33.88±3.424	0.523
Sex of the baby, N (%)			
Male	29 (51.8%)	27 (48.2%)	0.638
Female	21 (56.8%)	16 (43.2%)	
Place of delivery, N (%)			
Inborn	35 (51.5)	33 (48.5)	0.465
Outborn	15 (60.0)	10 (40.0)	
PROM>18 hours, N (%)			
Yes	10 (62.5)	6 (37.5)	0.441
No	40 (51.9)	37 (48.1)	
Maternal UTI, N (%)			
Yes	6 (50.0)	6 (50.0)	0.779
No	44 (54.3)	37 (45.7)	
Meconium stain liquor, N (%)			
Yes	0 (0.0)	5 (100)	0.013
No	50 (56.8)	38 (43.2)	
Onset of sepsis, N (%)			
EONS	4 (16.0)	21 (84.0)	0.000
LONS	46 (67.6)	22 (32.4)	

Continuous data are presented as mean ± SD and categorical data are presented as number and percentage. Statistical test: Chi square test, independent sample t test. PROM: premature rupture of membrane. EONS: early onset neonatal sepsis, LONS: late onset neonatal sepsis.

Table 4: Comparison of laboratory parameter between culture proven and clinical sepsis group(n=93).

Variable	Proven sepsis group (n=50)	Clinical sepsis group (n=43)	P value
Hb (%), (mean±SD)	13.30±3.429	15.65±2.393	0.000
WBC count (mean±SD)	14336.00±12689.458	13054.88±8172.026	0.571
ANC (<1500/cumm), N (%)			
Yes	3 (75)	1 (25)	0.621
No	47 (52.8)	42 (47.2)	
IT ratio>0.2, N (%)			
Yes	17(73.9)	6 (26.1)	0.031
No	33 (47.1)	37 (52.9)	
CRP (mg/dl), (mean±SD)	67.96±59.610	29.59±53.376	0.002
Platelet count (mean±SD)	73560.00±87919.295	185674.42±123404.237	0.000

Table 5: Comparison of nCD64 level between culture proven and clinical sepsis group (n=93).

Sepsis on the basis of blood C/S	Variable, nCD64(%), (mean±SD)	P value
Proven sepsis group (n=50)	83.62±16.665	0.000
Clinical sepsis group (n=43)	57±34.277	

Table 6: Cutoff value of nCD64 and Sensitivity, specificity, PPV, NPV of CD64 in Culture proven sepsis group.

Variable	Cutoff value	Sensitivity	Specificity	PPV	NPV	P value
nCD64 (%)	70.5	80	54	72.88	73.52	0.000
	71.5	80	56	71	74	
	72.5	76	56	70.17	69.45	

Figure 2 reveal the result of ROC curve analysis. nCD64 has an area under the curve (AUC) of 0.718. A cutoff value 71.5% of nCD64 had a sensitivity of 80% and a specificity of 56% for diagnosis of culture proven sepsis.

DISCUSSION

Blood culturing is considered the criterion standard for diagnosis of neonatal bacterial sepsis and accurate identification of the bacterial isolates, blood culturing technique is difficult, is time consuming (isolation of causative organism from blood culture takes up to 72 hours), and has unacceptable low sensitivity due to intermittent seeding of low numbers of bacteria within the bloodstream, extremely small blood volume obtained from the infant for culturing, and use of intrapartum antibiotics to mothers of high risk. Many efforts have focused on the use of hematologic parameters to increase the diagnostic yield for neonatal sepsis.

The readily achievable complete blood count and leukocyte differential assays have relatively poor specificity for diagnosing sepsis. The associated band count and leftward shift of myeloid immaturity measurements may improve diagnostic yield, but their subjective measurement is problematic. Therefore, the need persists for improved diagnostic indicators of neonatal sepsis. Acute-phase reactants (e.g., procalcitonin and C-reactive protein) have also been studied as markers of neonatal sepsis. Unfortunately, because these acute-phase reactants have similar diagnostic properties, no single marker has been found to have a significant advantage over the others.

The role of cytokines as a diagnostic aid in neonatal sepsis has been reviewed. Despite the fact that a majority of the cytokine markers have high NPVs (i.e., good for ruling out sepsis), these have not been adopted for general medical use. This is partly attributable to the larger amounts of blood required, the long interval to cytokine results (especially if enzyme-linked immunosorbent assay techniques are used), and the costs involved.[18] So, it is clear that to manage neonates with sepsis properly, a single reliable marker of infection is needed, to avoid unnecessary antibiotic therapy. A rapid laboratory test with high specificity for neonatal sepsis help in making a therapeutic decision and avoiding the unnecessary use of antibiotics in patients with clinical signs and symptoms of sepsis but negative blood cultures.[9]

As sepsis is a major cause of morbidity and death in the neonatal period, early appropriate diagnosis followed by prompt treatment is necessary to improve survival. Thus, this prospective observational study was conducted to see nCD64 is an early diagnostic marker for sepsis. In this study, a total of 93 neonates having risk factors for developing sepsis or clinical features of sepsis were enrolled. Mean gestational age was 33.63±3.463 weeks which is close to a previous study which was done by other authors where mean gestational age was 33.57±2.462.[19] In another study showed the mean gestational age was 38.65±0.81 weeks which was much higher than my study findings.[20] In our study mean birth weight of baby was 1863.23±773.202 g which was close to the previous study.[21] Most of the babies were inborn (73.1%) which is similar (64.7%) to the previous study done in BSMMU.[22] Male:Female distribution is 60.2% and 39.8% respectively which is close to a previous study done in Bangladesh where 67.31% of babies were male.[23] In our study,76.3% babies are preterm and 73.1% babies are low birth weight which is close to a previous study where it was 77.5 % and 77.5% respectively.[9] This findings also close to another previous study where preterm was 82.5% and low birth weight babies was 77.5%.[24]

Higher susceptibility of infection in preterm and low birth weight babies might be due to low level of IgG and lower defense mechanism. In this current study, the percentage of caesarean section was 73.1%. This higher percentage of caesarean section may be explained by the fact, this study was conducted in a tertiary care as well as only university hospital in Bangladesh, where most of the complicated pregnancies are dealt with necessitating caesarean section. In this study 25 (26.88%) babies developed EONS and 68 (73.12%) babies developed LONS. In the previous study done by Paul et al showed EONS was observed more (65%) than LONS (35%).[9]

In my study LONS more possible explanation that preterm low birthweight baby more, out born baby included and congenital anomalies and surgical patient also included. Culture proven sepsis is 50 (53.76%) and clinical sepsis is 43 (46.24%). This finding is close to another previous study where proven and clinical was 50% respectively.[25] The mean Hb% is lower (13.30± 3.429) in proven sepsis group with a statistically significant p value<0.001 as seen in table 4. The mean CRP level, (67.96±59.610) mg/l, is significantly raised among proven sepsis in comparison to clinical sepsis group. IT ratio>0.2 in proven sepsis group is more and it is statistically significant. Platelet count is also significantly lower in proven sepsis group.

These findings were similar in previous studies.[24,18] In my study percentage of expression nCD64 was higher (83.62±16.665) in proven sepsis group than clinical sepsis group. In this study showed statistically significant difference (p=<0.001) between culture proven sepsis and clinical sepsis group regarding percentage of expression of CD64 on neutrophils. This similar finding was found in previous study. There are many advantages of using neutrophil CD64 expression as an indicator of neonatal sepsis, as the quantitation of neutrophil CD64 is rapid (<60 minutes) and only minimal blood volume (100 µl) is used.[24]

The power of nCD64 for diagnosis of culture proven sepsis was done with the result of ROC curve analysis. A

cutoff level of nCD64 is 71.5% and it has a sensitivity of 80% and a specificity of 56% for diagnosis of culture proven sepsis. This finding is correlate with the previous meta-analysis, the sensitivity of nCD64 ranges from 57 to 89%, and the specificity ranges from 62 to 100%, indicating that nCD64 is a reliable marker in the diagnosis of neonatal sepsis.[26] In this study PPV and NPV is 71% and 74% respectively. In previous one study showed PPV and NPV were 83% and 91% respectively and in another study found PPV and NPV were 25% and 100% respectively.[9] In my study PPV and NPV relatively low because of large number of false positive and false negative result. In this current study, nCD64 has an area under the curve (AUC) of 0.718. To check diagnosis accuracy, the following guidelines used based on the AUC level: no informative (0.5), less accurate (0.5<AUC≤0.7), moderately accurate (0.7<AUC≤0.9), and highly accurate (0.9<AUC<1).28 Thus, based on my study results, nCD64 is a moderately accurate marker for the diagnosis of neonatal sepsis.[27]

CONCLUSION

Flow cytometric assessment of neutrophil CD64 increases more in neonates with culture proven sepsis than clinical sepsis. nCD64 has a good sensitivity 80% and specificity 56% and PPV, NPV 71%,74% respectively in culture proven sepsis with a cutoff value 71.5%. nCD64 has an area under the curve (AUC) of 0.718. So, it is a moderately accurate marker for the diagnosis of neonatal sepsis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Charter CE, Gordon B. Preparation for delivery. The Canadian Nurse. 1949;49(2):92-6.
2. Stefanovic M. Inflammation neonatal sepsis. Biochemia Medica. 2011;21(3):276-81.
3. Mannan MA, Iqbal S, Karim SR, Ahmed TU, Khan MHH, Ahmed AU, et al. Bacterial Isolates of Early Onset Neonatal Sepsis and Their Antibiotic Susceptibility Pattern. Chattagram Maa-O-Shishu Hospital Medical College J. 2018;17(1):3–8.
4. Cronan JJ, Yoder IC, Amis ES, Pfister RC. The myth of anechoic renal sinus fat. Radiology. 1982;144(1):149-52.
5. UNICEF. Maternal and Newborn Health Disparities in Bangladesh. New York: UNICEF. 2015:3-4.
6. Ahsan KZ, Jamil K, Islam S, Al-Sabir ACN. Bangladesh demographic and health survey. 2017–18: key indicators report.
7. Gomella TL, Cunningham MD, Eyal FG, Tuttle DJ. Gomella's Neonatology: Management, procedures, on-call problems, Diseases, and Drugs, New York: McGraw Hill education. 2020.
8. Dey S, Mannan MA, Dey SK, Sabina Y, Navila F. Study on Bacteriological Profile and Sensitivity Pattern of the Organisms in Neonatal Sepsis. Bangladesh J Child Health. 2020;44(3):133-8.
9. Paul D, Sattar A, Roy C, Islam S, Ferdousi S, Paul T, et al. 'Role of Neutrophil CD64 as an Emerging Biomarker in the Evaluation of Neonatal Sepsis', International Clinical Pathology Journal. 2017;4(5):114-8.
10. Klinger G, Levy I, Sirota L, Boyko V, Lerner-Geva L, Reichman B, et al. Outcome of early-onset sepsis in a national cohort of very low birth weight infants. Pediatrics. 2010;125(4):736–40.
11. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. 2002. Late-onset sepsis in very low birth weight neonates: the experience of the National Institute of Child Health and Human Dev Neon Res Netw Pedia. 2002;110(2):285-91.
12. Shane AL, Sánchez PJ, Stoll BJ. 'Neonatal sepsis', The Lancet. 2017;390(10104):1770-80.
13. Jajoo M, Kapoor K, Garg LK, Manchanda V, Mittal SK. 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. 2015;4(2):91.
14. Muthukumaran N. 'Mortality profile of neonatal deaths and deaths due to neonatal sepsis in a tertiary care center in southern India: a retrospective study', Int J Contemp Pediat. 2018;5(4):1583.
15. Streimish I, Bizzarro M, Northrup V, Wang C, Renna S, Koval N, et al. Neutrophil CD64 as a diagnostic marker in neonatal sepsis. The Pediatric infectious disease journal. 2012;31(7):777–81.
16. Du J, Li L, Dou Y, Li P, Chen R, Liu H. Diagnostic utility of neutrophil CD64 as a marker for early-onset sepsis in preterm neonates. PloS one. 2019;9(7):1026-47.
17. Hoffmann JJ. Neutrophil CD64 as a sepsis biomarker. Biochemia Medica. 2011;21(3):282-90.
18. Elawady S, Botros SK, Sorour AE, Ghany EA, Elbatran G, Ali R, et al. Neutrophil CD64 as a diagnostic marker of sepsis in neonates. Journal of Investigative Medicine. 2014;62(3):644-9.
19. Bhandari V, Wang C, Rinder C, Rinder H. Hematologic profile of sepsis in neonates: neutrophil CD64 as a diagnostic marker. Pediatrics. 2008;121(1):129-34.
20. Tang Z, Qin D, Tao M, Lv K, Chen S, Zhu X, et al. Examining the utility of the CD64 index compared with other conventional indices for early diagnosis of neonatal infection. Scientific reports. 2018;8(1):1-7.
21. Bhandari V, Wang C, Rinder C, Rinder H. Hematologic profile of sepsis in neonates: neutrophil CD64 as a diagnostic marker. Pediatrics. 2008;121(1):129-34.
22. Dey SK, Shabuj MKH, Jahan I, Akter H, Akhter M. Is Superbug imminent? Findings of a retrospective study in Bangladesh. J Clin Neonatol. 2018;9(1):38.

23. Hafsa A, Fakruddin M, Hakim MA, Sharma JD. Neonatal bacteremia in a neonatal intensive care unit: analysis of causative organisms and antimicrobial susceptibility. Bangladesh J Med Sci. 2011;10(3):187-94.
24. Islam Md, Paul D, Roy C, Rahman Q, Hossain Md, Mortaz R, et al. 'Evaluation of Neutrophil CD64 as a marker in the diagnosis of neonatal sepsis'. Eur Acad Res. 2014;2(7):9290-305.
25. Hashem HE, Halim AEl Masry, S.A., Mokhtar, A.M. and Abdelaal, N.M. The utility of neutrophil CD64 and presepsin as diagnostic, prognostic, and monitoring biomarkers in neonatal sepsis. Int J Microb. 2020:8814892.
26. Dai J, Jiang W, Min Z, Yang J, Tan Y, Ma T, Ge Z. Neutrophil CD64 as a diagnostic marker for neonatal sepsis: Meta-analysis. Adv Clin Exp Med. 2017;26(2):327-32.
27. Choo YK, Cho HS, Seo IB, Lee HS. Comparison of the accuracy of neutrophil CD64 and C-reactive protein as a single test for the early detection of neonatal sepsis. Kor J Pediat. 2012;55(1):11-7.
28. Khadhim, Manal M, Al-Hajjiah, Nasima N, Shaheed, Orass M. 'Detection of the CD64 on Neutrophils and CD69 on Lymphocytes by Flowcytometry as a Marker for Early Diagnosis of Neonatal Sepsis'. J Med Sci Clinical Research. 2017;5:19720-5.

Cite this article as: Karmaker P, Rahman KMM, Rasel M, Nasrin UT, Afreen S, Shabuj MKH. A prospective observational study of neutrophil CD64 as a diagnostic marker in neonatal sepsis. Int J Contemp Pediatr 2024;11:1519-26.