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Original Article

Absolute Neutrophil Count in Diagnosis of Neonatal Sepsis : A Hospital Based Cross Sectional Study

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Abstract

Background : *Sepsis is the leading cause of neonatal death in developing countries. Delay in initiating treatment can considerably increase the morbidity and mortality. So early diagnosis is important.Traditional methods such as blood culture do not provide a rapid diagnosis. Absolute neutrophil count is one of the important hematological markers for diagnosis of sepsis. The purpose of the study to see the absolute neutrophil count in diognosis of neonatal sepsis.*

Materials and methods: *This is a hospital based cross sectional study conducted from January to June 2014. A total of 100 sick neonates admitted in the Neonatal ward of Chattagram Maa Shishu O General Hospital (CMSOGH) with suspected neonatal sepsis (Based on history and physical examination) constituted the study population. Investigation sent for Absolute neutrophil count, C-reactive Protein (CRP) and blood culture. The collected data was analyzed by statistical software packages SPSS method version 15.*

Results: *A total of 100 sick neonates of both sexes with suspected sepsis were enrolled in this study, out of which most of the patient showed neutropenia (66%), C-reactive protein positive 65% and blood culture positive 33%. Within the C-reactive protein positive patients 78.8% patient had neutropenia (χ^2 =17.711, p= .001). From blood culture positive patients 85% showed neutropenia (χ^2 =8.510, p= 0.014).*

Conclusion: *Neutropenia is a common hematological finding in neonatal sepsis along with other screening test and neutropenia is more significant than neutrophilia.*

Key words : Absolute neutrophil count, C-reactive protein; Neonatal death; Sepsis.

INTRODUCTION

Sepsis is the leading cause of death in developing country. Neonatal sepsis can be defined as "The clinical syndrome of bacteremia characterized by systemic sign and symptom of infection in first twentyeight days of life.[1]" Neonatal sepsis can be early onset – if onset of symptom during 72 hours of life caused by organism present in maternal genital tract or in labour room or in operation theater and late onset – if onset of symptom is after 72 hours of life caused by nosocomial infection.[2,3,4] Common organism those are responsible for early onset sepsis are Group B streptococcus, Escherichia coli, Haemophilus influenzae, Klebsiellasp, Listeria monocytogens and organism those are responsible for late onset sepsis are Staphylococcus aureus, Coagulase negative Staphylococcus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter, Candida sp, Serratia, Acinetobacter.

Sepsis in neonate may be difficult to differentiate from other condition because the clinical signs are non-specific.[5,6] So the identification and treatment of sepsis continuous to be a major health issue.

The incidence of sepsis is particularly high in the neonatal population, where low birth weight and other compromising factors make it a primary cause of morbidity and death. Early identification and treatment are critically important.[7] Timely and correct diagnosis/prediction of neonatal sepsis can reduce the burden of neonatal mortality.[1]

The present trend which is being applied for infants who are suspected to have neonatal sepsis may lead to unnecessary and increased antibiotic consumption, a higher incidence of the side- effects due to their use, increased resistance to the antibiotics, a long hospitalization, the separation of the infants from their mothers and increased health costs.[8] Therefore, using fast diagnostic methods including laboratory markers could be beneficial for the diagnosis of neonatal sepsis.[9]

The most reliable diagnostic tool of neonatal sepsis often referred to a gold standard is a blood culture test for bacteria.[10] While this test is the most reliable available, it can take 48 hrs to obtain the result. An additional complication is fact that the blood culture test can be negative for one in five subjects in sepsis.[11] Delay even a few hours in initiating treatment can considerable increase the morbidity and mortality.

Thus in addition to blood culture different laboratory tests are evaluated in the diagnosis of early neonatal sepsisof which complete blood count with different neutrophil parameters and C-Reactive Protein (CRP) are most frequently used.[12,13]

In the current context, a biomarker is defined as any measurable parameter that provides meaningful information about the diagnosis of neonatal sepsis. An ideal biomarker for neonatal sepsis would not only have a high degree of accuracy in recognizing the presence (or absence) of definite infection at an early stage, but it would also be useful to guide the duration of antibiotic therapy.[14]

Additional diagnostic hematological markers have been studied such as C-reactive proteinandprocalcitonin.[15] Later one is not available in our setup. While these biomarkers have shown to be correlated with sepsis, they have considered to be have limited diagnostic information.[16,17] C-reactive protein is an acute phase protein. Raised serum levels of CRP are found in 50-90% of neonate from 6 hrs. of onset of bacteremia, but raised level are not specific for bacterial infection.[18] CRP values were found to be raised moderately in sepsis but the serum level also found high with asphyxia, shock, and other problems not related to infection.[19]

The hematological responses to inflammation in neonate include change in total white cell count and absolute neutrophil count.[20] The predictive value of high WBC count in sepsis is poor.[21] About 50% of neonate had normal WBC count in culture proven sepsis.[22] Neutrophil is the first line defense against bacterial infection. So circulatory neutrophil count also variable in bacterial infection. Absolute neutrophil count is a more sensitive and specific indicator of bacterial sepsis.[23,24,25] The Absolute Neutrophil Count (ANC) is more sensitive and specific indicator of bacterial sepsis than WBC count, par--ticularly if below the normal range has the greatest specificity of neutrophil indices.[24]

Absolute neutrophil count includes both mature and immature neutrophil count.

Normal absolute neutrophil count varies with postnatal age and weight. Monroe and associates tabulated 905 blood neutrophil counts from 434 neonates and provided range that have been used widely for term and near term.[26] For very low birth weight neonates the neutrophil values reported by Muzinho and colleagues seem more appropriate.[27]

Neutrophil response are initiated as circulating neutrophils flowing through the post capillary vanules detect low level of chemokine and other chemotectic substances released from the site of inflammation.

Neutrophilia is an increase of total number blood neutrophil. It is common findings of inflammation and infection. An increase circulating neutrophil is a result of disturbance of normal equilibrium involving bone marrow neutrophil production, movement out of marrow compartments into the circulation, and neutrophil destruction. Neutrophilia may arise either alone or in combination with enhanced mobilization into the circulating pool from either the bone marrow storage compartment or the peripheral blood marginating pool.[28]

Neutropenia is decrease blood neutrophil count below normal according to age. Neutropenia can be due to decrease production, excessive neutrophil migration, increase destruction or combination of three mechanism.[29] During bacterial infection the redistribution of neutrophil occurs from circulating to marginating pool, so large numbers of neutrophils are used during bacterial infection. The neutrophil storage pool in new born infant is 20-30% of that in adult.[30] So neonates are particularly vulnerable to developing neutropenia. The development of severe neutropenia can reflect the exhaustion of the marrow neutrophil.[31]

The neutrophil count, particularly if below the normal age adjusted range is more sensitive and specific indicator of bacterial sepsis.[32] For many septic neonates, neutropenia is present at the time that sepsis is diagnosed. Funkle and colleagues reported that sepsis related mortality was three fold higher among neonates who develop neutropenia.[33]

The purpose of the study to see the absolute neutrophil count in diognosis of neonatal sepsis.

MATERIALS AND METHODS

The study was designed as a descriptive type of study conducted in the Neonatal ward of ChattogramMaaShishu O General Hospital, a tertiary care hospital from 1st January – 30th June 2014. The study population was 100 patients with suspected neonatal sepsis admitted in this hospital.

Inclusion criteria

i) Patient with suspected neonatal sepsis (Based on history and physical examination)

Exclusion criteria

i) Patient on treatment for sepsis.

ii) Patient without clinical feature and risk factor for sepsis.

Detailed history was recorded in a questionnaire from the mother or other care giver after taking informed written consent and blood sent for Absolute neutrophil count, C- reactive protein and blood culture. The collected data was analyzed by statistical software packages SPSS method version 15.

RESULTS

Total study population was 100, thus the absolute number and percentage were same. Most of the baby was term (73%), Normal birth weight baby (71%) and male (54%). Majority of the patients showed neutropenia (66%).

Table I Absolute neutrophil count in study population (n-100)

Absolute neutrophil count	Frequency	Percentage (%)
Neutropenia	66	66
Normal	28	28
neutrophilia	6	6
Total	100.0	100.0

Table II Association between absolute neutrophil count and clinical diagnosis

Absolute neutrophil count	Neonatal sepsis		χ^2 Test Significance
	Early onset	Late onset	
Neutropenia	51 (78)	15 (43)	$\chi^2 = 14.776$,
Normal	13 (20)	15 (43)	p = .001
Neutrophilia	01 (02)	05 (16)	Significant
Total	65	35	

● *Figures within parentheses indicate percentages.*

Within the study population 65% diagnosed as early onset sepsis and 35% late onset sepsis. From the patients with early onset sepsis 78% and with late onset sepsis 43% showed neutropenia.

Table III Association between absolute neutrophil count and C-reactive protein

Absolute neutrophil count	C- reactive protein		χ^2 Test Significance
	Positive	Negative	
Neutropenia-66	52 (78.8)	14 (21.2)	$\chi^2 = 17.711$
Normal-28	12 (43)	16 (72.7)	p = .001
Neutrophilia-6	01 (16.7)	05 (83.3)	Significant
Total	65	35	

● *Figures within parentheses indicate percentages*

Within the study population 65% patients were C-reactive protein positive, out of which 78.8% showed neutropenia.

Table IV Association between absolute neutrophil count and blood culture

Absolute neutrophil count	Blood culture		χ^2 Test Significance
	Positive	Negative	
Neutropenia	28 (85)	38 (56)	$\chi^2 = 8.510$
Normal	05 (15)	23 (34)	p = .014
Neutrophilia	00(00)	06 (10)	Significant
Total	33	67	

● *Figures within parentheses indicate percentages.*

33% patients had blood culture positive, majority (85%) of them showed neutropenia.

DISCUSSION

In the observed population 54 were male and 46 patients were female. Male female ratio was 1.3:1. So in our study we found male are more affected then female. A.C. Buch et al also showedin the incidence of neonatal sepsis was higher in male (60%) than female neonates.[34]

In this study 73% patients were term, 71% were normal birth weight, 18% low birth weight and 11% were very low birth weight. Among 71 patients with normal birth weight 44 patients showed neutropenia. Among 18 low birth weight baby 11 showed neutropenia. Among 11 very low birth weight baby all showed neutropenia. In developing countries like ours, we think poor antenatal facilities and poverty also plays important role in early onset septicemia. It was found that the incidence of septicemia was higher in preterm neonates (83.33%). Hussein et al and Humayun et al have reported similar finding.[35,36] Waseemet al observed septicemia more common in low birth weight and preterm babies.[37] Higher incidence of sepsis in low birth weight, both Preterm and small for gestational (SGA) is because they have low maternal acquired IgG and inherent susceptibility to infection.[38]

Within the study population 65 patients (65%) clinically diagnosed as early onset neonatal sepsis and 35patients (35%) were late onset neonatal sepsis. One study also reported that frequency of early neonatal sepsis (54.53%) was higher than late onset neonatal sepsis (45.57%), without statistical significance.[14] One study reported that 67% of cases developed neonatal septicemia before seven days.[39] In this study 78% Patient with early onset neonatal sepsis showed neutropenia and 2% neutrophilia, where as 43% patient with late onset sepsis showed neutropenia and 14% patient had neutrophilia. So in our study neutropenia is more common in early onset neonatal, and neutrophilia is more common in late onset sepsis.

In our study, among 100 patients 65 (65%) had C- reactive protein positive. Within these patients 78.8% showed neutropenia. The sensitivity of ANC in comparison to CRP was 78.8%. AqeelaAyub et al showedthe overall diagnostic accuracy of CRP was calculated as 80%.[40]

In this study there were 33 (33%) patients whose blood culture was positive.

Among them 26 patients were with early onset sepsis and 7 with late onset sepsis. 21 term baby and 12 pre term baby showed blood culture positive. Hussein, Sharma and Lee had also lower culture positivity 42%, 20%, and 41.2% respectively.[35] The variation of blood culture positivity may be due to criteria of studied group. Other national and international studies have reported frequency of sepsis with blood culture positive ranging from 20-30%. In this study among these patients 28 (85%) showed neutropenia.

LIMITATIONS

- Small sample size.
- Short duration of study.

CONCLUSIONS

Neutropenia is a common hematological finding in neonatal sepsis along with other screening test and neutropenia is more significant thanneutrophilia. So Absolute Neutrophil Count can be used as a screening test for early diagnosis of neonatal sepsis along with other screening test and neutropenia is more significant thanneutrophilia.

DISCLOSURE

All the authors declared no competing interest.

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