

ORIGINAL ARTICLE

Combining Complete Blood Count with Differential Count; C-Reactive Protein and Band Neutrophils in Diagnosis of Early onset Neonatal Sepsis

KHAWAJA ABRAR AHMED¹, MANZOOR ALI KHAN², SYED ZAKIR NAQVI³, ISHTIAQ AHMED MUGHAL⁴, MOHSNA SAEED ZIA⁵, ARZOO IDREES⁶

¹Resident FCPS-II Paediatric Medicine

²Assistant Professor of Paediatric Medicine

³Assistant Professor of Paediatric Surgery

⁴Senior Registrar of Paediatric Medicine

⁵Assistant Professor of Obs & Gynae

⁶Resident FCPS-II Paediatric Medicine

Correspondence to Dr. Khawaja Abrar Ahmed, Email: khawajaabrar786@yahoo.com Cell: 03461904195

ABSTRACT

Aim: To assess the diagnostic accuracy of complete blood count with band versus total neutrophil ratio and C-reactive proteins as an efficient analytical procedure for determining early onset sepsis in neonates.

Study design: Cross sectional analytical study

Place and duration of study: Department of Paediatric Medicine, Abbas Institute of Medical Sciences Muzafarabad, AJ Kashmir from 01-02-2022 to 31-07-2022.

Methodology: Fifty patients were enrolled. Coulter counter was used for analyzing leucocytes of the neonates. Thin film-smears were generated by the laboratory scientist for identifying band neutrophils separately from mature neutrophils. C-reactive proteins level <5mg/dl was considered as negative. Thio-glycate-oxide in liquid form was used for 2ml neonatal blood culture analysis mixed in the 20ml medium at 36 degree celsius.

Results: There were 28 (56%) males and 22 (44%) females. The mean age of the neonates was 1.6 ± 0.77 days. The mean weight of the neonates was 2.4 ± 0.51 kg with a range of 4-1.2kg. A variance of band versus total neutrophil ratio was significantly higher in cultures which were positive than negative such as 70% vs 25%. There was also significant percentage of C-reactive proteins positive in positive sepsis cultures in comparison to negative blood culture.

Conclusion: A combination of complete blood count with differential count, white blood cell analysis with band versus total neutrophil ratio and c-reactive proteins is an efficient early analytical procedure for determining early onset sepsis in neonates as gold standard test blood culture is time taking.

Key Words: Complete blood count, C-reactive protein, Total neutrophils ratio, Early onset neonatal sepsis.

INTRODUCTION

Neonatal sepsis is termed as presumed or confirmed infection formed in new born. It is a systematic-inflammatory response which is attributed with various clinical signs and is caused by pathogens either with bacteria or without¹. The incidence of neonatal sepsis is around 0.008 per live births and as raised as 0.13-0.27 in neonates with a weight less than 1.5kg². Septicemia is responsible for 1.5-2 million morbidities yearly with around 4-5k deaths per day in various countries over the globe³. Asia is highly prevalent in morbidity related with septicemia in neonates. The major reasons behind this high prevalence are either infection, preterm delivery, birth asphyxia which on average accounts for 80% of sepsis cases⁴.

Neonatal sepsis has a high risk for cases in low birth weight (LBW) as well as in newborns which are compromised in their respiratory conditions as well as congenital abnormalities.⁵ Those mothers which are under high risk of developing bacterial infections are pre-screened for development of septicemia in their neonates. Various diagnostic analytical tests are run for assessing the sepsis risk. These tests includes white blood cell analysis as well as immature neutrophils or mature neutrophils and IL⁶.

Blood culturing is the gold standard for assessing the NS within the 3-5 days of the infection⁶. There are some tests which can assess sepsis within 6-8 hours and are really significant is timely prediction of the sepsis. These tests includes C-reactive protein (CRP), band neutrophils as well as mature neutrophils, nitro blue tetrazolium and other as of pro calcitonin⁷⁻¹¹.

The present study was designed for assessing the diagnostic value of CBC with differential count, band neutrophil in ratio with mature neutrophil and C-reactive protein in determining of sepsis in neonates and hence provides an active assessment strategy with timely approach.

Received on 05-04-2022

Accepted on 15-08-2022

MATERIALS AND METHODS

This cross sectional analytical study was performed at Abbas Institute of Medical Sciences Muzafarabad, AJ Kashmir. Permission was granted by ethical committee to start this research. A total of 50 patients were enrolled as study participants depending upon the inclusion criteria. Parent and guardian of each enrolled neonates were requested for their informed consent before being a part of the research. The sample size was generated using WHO sample size calculator where 75% sensitivity, 95% confidence interval, 80% power of test and 5% margin of error was taken in to account. Presumed sepsis was considered in conditions where the blood reports were indicating negative sepsis however all the clinical symptoms were marking towards presence of an infection. On the other hand a complete sepsis picture was defined in the presence of clinical symptoms as well as positive blood test for septicemia. Coulter counter was used for analyzing leucocytes of the neonates. Thin film-smears were generated by the laboratory scientist for identifying band neutrophils separately from mature neutrophils. CRP level <5mg/dl was considered as negative. Thio-glycate-oxide in liquid form was used for 2ml neonatal blood culture analysis mixed in the 20ml medium at 36 degree Celsius. The blood culture was examined daily and report was generated after day seven. Total leucocyte count either < 5000 or >20,000/cumm was screened with BN to TN ratio >0.2 and positivity of c reactive protein. The BN/TN ratio was calculate by dividing the percentage of immature neutrophil over percentage of total neutrophils with having BN and TN. Demographic details as well as clinical characteristics of each patient was recorded. Data was analyzed by using SPSS version 26.0 through using chi square tools and odds ratio.

RESULTS

There were 28 (56%) males and 22(44%) females and mean age of the neonates was 1.6 ± 0.77 days. The mean weight of the neonates was 2.4 ± 0.51 kg with a range of 4-1.2kg. None of the patients was having neutropenia (Table 1). The association of

blood culture with BN/TN showed a probability p value as 0.730 and variance in white blood cells between positive and negative culture reports (Table 2). A variance of BN/TN ratio was significantly higher in cultures which were positive than negative such as 70% vs 25%. The diagnosis accuracy presented for BN/TN for sepsis identification as 70% with specificity as 83% respectively. There was also significant percentage of CRP positive in positive sepsis cultures in comparison to negative blood culture (Table 3). Blood culture relation with BN/TN ratio and C-reactive protein (Table 4). The proven sepsis cases were 10 with culture sensitivity positive report while presumed sepsis cases with

clinical infection symptoms were 7 with culture sensitivity negative (Figure 1)

Table 1: Demographic and Clinical details of neonates

Variable	No.	%
Males	28	56.0
Female	22	44.0
Mean age (days)	1.6± 0.77	
Mean weight (kg)	2.4±0.51	
Mean blood count	18791.18±8610.6	
Ratio of BN/TN	0.1615 ± 0.0423	
Average neutrophil count	64.88 ± 10.12	
BN Count	10.66 ± 2.74	

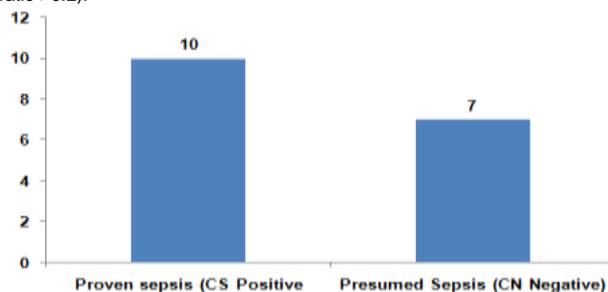
Table 2: Correlation of blood culture with BN/TN ratio days age, weight and total WBC count

Parameter	r _{pb} (p-value)	Blood Culture		P value
		Negative (n=40)	Positive (n=10)	
BN/TN Ratio	0.730 (< 0.001)	0.154±0.035	0.205±0.046	< 0.001
Age (days)	0.282 (0.010)	1.472±0.731	2.012±0.881	0.010
Weight (Kg)	0.022 (0.847)	2.383±0.551	2.415±0.617	0.848
WBC	0.484 (< 0.001)	16688.829±7041.869	27071±9389.220	< 0.001*

Table 4: Blood culture relation with BN/TN ratio and CRP.

Parameters	Blood Culture		P value
	Negative (n=40)	Positive (n=10)	
BN/TN Ratio			
≥ 0.2	10 (25%)	7 (70%)	< 0.001
< 0.2	30 (75%)	3 (30%)	
CRP			
-VE	30 (75%)	3 (30%)	< 0.001
+VE	10 (25%)	7 (70%)	

Figure 1: Proven sepsis cases in comparison with presumed sepsis (BN/TN ratio >0.2).



DISCUSSION

Low birth weight (LBW) was a significant variable in neonates with early onset of sepsis. Various other studies have proven that low birth weight is an important factor in contributing neonatal septicemia.¹²⁻¹³ There was an indirect relationship presented between the birth weight and rate of infection as neonates with LBW had compromised cellular immunity which makes them more vulnerable towards sepsis as documented in the current research and other global studies¹⁴⁻¹⁵.

In majority of the positive cases white blood cell count is found greater than 26000 per cumm whereas cases which are negative have a white blood cell count lower than 15500 per cumm. Studies in this context have elaborated that white blood cell count as an individual predictor has shown to be a poor predictor of septicemia as there are many other infections: viral and bacterial which causes disturbances in the white blood cells count [16]. C reactive proteins have shown a high specificity upto 70% and can be considered as an efficient indicator in sepsis cases as well. A ratio of BN/TN above 2.0 has proven an efficient sepsis predictor¹⁷.

The current study results clearly demonstrates that BN/TN ratio was escalated in negative predictive value than positive which is in solidarity with previously reported literature¹⁸⁻¹⁹. Despite the fact that these tests may assist in decreasing hospital stay and helping in decreasing the patient related anxiety but requires

further assistance through gold standard analysis especially in developing countries with a high rate of septicemia²⁰⁻²¹.

CONCLUSION

A combination of white blood cell analysis with differential count BN/TN ratio and CRP is an efficient analytical procedure for determining early onset sepsis in neonates as a gold standard test blood culture is time taking.

Conflict of interest: None to declare

REFERENCES

- Kliegman R, Stanton B, Geme J St, Schor N. Nelson's textbook of pediatrics: Infections neonatal infant. 20th ed. Philadelphia: Elsevier, 2016:909-23.
- Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care* 2005;6(1):2-8.
- Waseem RI, Khan M, Izhar TS, Qureshi AW. Neonatal sepsis. *Professional Med J* 2005;12(4):451-6.
- Gomella TL, Cunningham D, Eyal FG. Neonatology. 7th ed. London: McGraw-Hill 2013;865-74.
- Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. *Clin Microbiol Rev* 2014;27(1):21-47.
- Hornik CP, Benjamin DK, Becker KC, Jennifer Li, Clark RH, Wolkowicz MC, et al. Use of the complete blood cell count in early-onset neonatal sepsis. *Pediatr Infect Dis J* 2012;31(8):799-802.
- Newman TB, Draper D, Puopolo KM, SooraWi, Escobar GJ. Combining immature and total neutrophil counts to predict early onset sepsis in term and late preterm newborns: use of the I/T2. *Pediatr Infect Dis J* 2014;33(8):798-802.
- Monica L, Riti JS, Amit BK. Role of sepsis screen parameters in early diagnosis of neonatal septicemia. *Int J Curr Microbiol App Sci* 2018;7(1):2410-19.
- Arnon S, Litmanovitz Diagnostic tests in neonatal sepsis. *Curr Opin Infect Dis J* 2008;21(3):223-7.
- Krediet T, Gerards L, Fleer A, van Stekelenburg G. The predictive value of C-reactive protein and I/T-ratio in neonatal infection. *J Perinat Med* 1992;20(6):479.
- Bhandari V. Effective biomarkers for diagnosis of neonatal sepsis. *J Pediatr Infect Dis Soc* 2014;3(3):234-45.
- Ng PC, Lam HS. Diagnostic markers for neonatal sepsis. *Curr Opin Pediatr* 2006;18(2):125-31.
- Stoll BJ, Hansen NI, Sanchez PJ, Faix RG, Poindexter BB, Van Meurs KP, et al. Early onset neonatal sepsis: the burden of group B streptococcal and E. coli disease continues. *Pediatrics* 2011;127(5):817-26.
- Bhutta ZA, Yusuf K. Early-onset neonatal sepsis in Pakistan: A case control study of risk factors in a birth cohort. *Amer J Perinatol* 1997;14(9):577-81.
- Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK, Jr, Smith PB, et al. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. *Early Hum Dev* 2012;88 (Suppl 2):S69-74.
- Hornik CP, Benjamin DK, Becker KC, Benjamin DK, Li J, Clark RH, et al. Use of the complete blood cell count in early-onset neonatal sepsis. *Pediatr Infect Dis J* 2012;31(8):799-802.
- Schmutz N, Henry E, Jopling J, Christensen RD. Expected ranges for blood neutrophil concentration of neonates: The Manroe and Mouzinho charts revisited. *J Perinatol* 2008;28(4):275-81.
- Desai P, Shah AN, Pandya T, Desai P, Pandya T. C-Reactive protein, immature to total neutrophil ratio and micro ESR in early diagnosis of neonatal sepsis. *Int J Biomed Adv Res* 2014;5(8):364-6.
- Gerdes JS. Diagnosis and management of bacterial infections in the neonate. *Pediatr Clin North Am* 2004;51(4):939-59.
- Murphy K, Weiner Use of leukocyte counts in evaluation of early-onset neonatal sepsis. *J Pediatr Infect Dis* 2012;31(1):16-9.
- Camacho-Gonzalez A, Spearman PW, Stoll BJ. Neonatal infectious diseases: evaluation of neonatal sepsis. *Pediatr Clin North Am* 2013;60:367-89