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STUDY OF ABSOLUTE, IMMATURE NEUTROPHIL COUNT AND CRP AS DIAGNOSTIC MARKERS FOR EARLY ONSET NEONATAL SEPSIS.

Pathology

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ABSTRACT

Introduction: Neonatal Sepsis is difficult to differentiate from other conditions due to non- specific clinical signs and symptoms. Inflammation in neonates shows variations in hematological parameters. Our study is to evaluate the hematological parameters and C-reactive protein estimation in neonatal sepsis for early diagnosis.

Material And Methods: It was a cross-sectional study including 80 neonates admitted in the neonatal care unit, 40 (proven sepsis) and 40 probable cases); blood culture being the gold standard. Hematological parameters, immature to total neutrophil ratio (I/T ratio), Absolute neutrophil count (ANC), CRP and Blood culture were done as per standard protocols.

Results: ANC had highest sensitivity of 90% followed by I/T ratio (87.5%) and CRP (77.5%). The sensitivity and specificity for the combination of ANC and I/T ratio was 78.3% and 83.6% respectively.

Conclusion: ANC, I/T Ratio and CRP are quick, simple and cost-effective routine laboratory tests which help in neonatal sepsis prediction and to start proper and timely antibiotic therapy.

KEYWORDS

ANC; Blood Culture; CRP; Hematological Score System; Neonatal Sepsis.

INTRODUCTION

According to WHO, perinatal deaths are responsible for maximum cases of the childhood mortality in children aged below 5 years especially in developing countries like India.[1] Neonatal sepsis is a common occurrence in our part of the world characterized by signs and symptoms of bacterial infection during first 28 days of life. It is the most common cause of perinatal mortality. [2,3] According to UNICEF data neonatal mortality rate is 21.7 per 1000 live births in 2019-2020. Neonatal septicaemia is a clinical syndrome characterized by classical signs and symptoms associated with bacteraemia.[4] Initial warning signs and symptoms of sepsis are mostly non-specific [5] and have different presentation in various gestational ages [6] making it difficult in establishing an early clinical diagnosis. Therefore an early diagnosis is critical for timely treatment.

In Europe and North America, Group B Streptococcal disease is the leading cause of neonatal sepsis, but in tropical and developing countries gram negative organisms predominate in majority of cases.[7] According to NNDP data, in India the disease is most frequently caused by Klebsiella pneumoniae followed by Staphylococcus aureus.[8] Although Blood Culture is considered as the "Gold Standard" for its diagnosis, but it has some associated limitations like it is time consuming, has low positivity and false positive results due to sample contamination.[9] Cheap, easily performed, quick and reliable tests like complete blood count (CBC) with different neutrophil parameters and C-reactive protein (CRP) are frequently used. [10] A combination of haematological parameters can help in providing an early diagnosis of bacteremia. This helps in avoiding the overtreatment and development of antibiotic resistance thus reducing burden of high cost in underprivileged settings .[11]

MATERIAL AND METHODS

In the present cross-sectional study, we intent to analyse various hematologic parameters in 80 neonates admitted in the neonatal care unit of a tertiary care hospital in Gurugram. Infants with predisposing perinatal factors or with clinical suspicion of sepsis were included. The study included two groups: Group 1—Infants with sepsis with positive blood cultures and Group 2—Normal infants with negative blood cultures.

We obtained data from the records of blood culture and complete blood counts of the new born, from the departments of Pathology and Microbiology of the hospital. Out of 80 admitted neonates, 40 were taken as cases and remaining 40 were taken as controls. Medical records were studied to identify infants born at ≥ 34 weeks gestation. Only those infants were included who had a CBC done at <72 hours of age and within 1 hour of a blood culture. CBCs was analysed using Sysmex haematology analysers in haematology laboratory. Blood cultures and CRP were done in department of Microbiology by Bactec method and automated analyser respectively.

CBC, CRP and Blood culture was done as per standard protocols and clinical assessment was done by the paediatrician. The differential WBC counts and peripheral blood examination was done manually for identification of band forms. The ANC and I/T ratio were calculated as per the formulae.

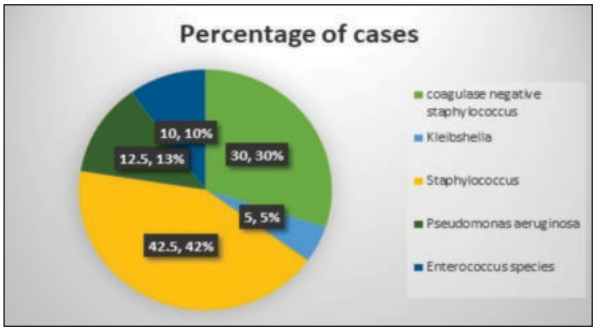
Statistical Analysis:

Sensitivity, specificity and positive and negative predictive values were evaluated using standard statistical methods. P<0.05 was considered as statistically significant difference. The statistical analyses were performed using SPSS version 26 for windows.

RESULTS

Among 40 neonates, who were in early neonatal sepsis, 22 cases (55%) were females, and 18 (45%) were males. In the non-septic group, 25 neonates (62.5%) were females and 15 (37.5%) were males.

Microbiological profile of 40 septic neonates showed, 12 cases (30%) were coagulase negative staphylococcus, 02 (5%) were Klebsiella pneumoniae, 17 (42.5%) were Staphylococcus aureus, 05(12.5%) were Pseudomonas aeruginosa and 4 (10%) were Enterococcus (Figure 1).



Among 40 septic neonates (cases), 15 (37.5%) were having normal ANC while 25(62.5%) were having increased ANC. In the non-septic group (control), 36 neonates (90%) were normal ANC and 04 (10%) were having high ANC .

Among 40 septic neonates (cases), 17 (42.5%) were having normal I:T ratio while 23(57.5%) were having increased I:T ratio. In the non-septic group (control), 35 neonates (87.5%) were normal and 05 (12.5%) were having high I:T ratio.

Out of 40 septic neonates (cases), 09 (22.5%) were having normal CRP while 31(77.5%) were having increased CRP. In the non-septic group (control), 14 neonates (35%) were having normal CRP and 26 (65%) were having high CRP .

According to the findings, I/T value, ANC and CRP values were significantly higher in the septic neonates compared to the control group.

Sensitivity, Specificity, and Negative and Positive Predictive Values of Evaluated Parameters (%) in Sepsis Proven Population (N=40) (Table1).

Parameter	ANC	I/T ratio	CRP
Senstivity(%)	90.00	87.50	77.5
Specificity(%)	62.50	57.50	65.0
PPV(%)	70.59	67.31	54.4
NPV(%)	86.21	82.14	60.9
Accuracy (%)	76.25	72.50	73.40

Combined Sensitivity and Specificity of both ANC and I/T ratio evaluated in Sepsis Proven Population (N=40) (Table 2).

Parameters	ANC + I/T ratio
Sensitivity (%)	78.3
Specificity (%)	83.6

DISCUSSION

The high mortality and morbidity associated with neonatal sepsis prompts for an early diagnosis which is very crucial for the management of these neonates. Risk factors include maternal factors like maternal infections, premature rupture of membranes, various procedures etc. and risk factors in infants include, poor cord care, low birth weight, various congenital anomalies, low APGAR score etc.[1,2] Patients may present with complaints of respiratory distress, hypothermia, irritability, hypo or hyperglycaemia, vomiting, poor feeding, seizures and shock.[5]

Our study re-evaluated various screening tests for neonatal sepsis, which is an absolute necessity to prevent a serious threat to the baby. Neonates which are non-infected should also be identified so as to avoid antibiotic administration and to prevent the emergence of resistant microorganisms. [12,13,14] Ideally a screening test must have high sensitivity and high negative predictive values. Risk of missing a sepsis prone patient with a certain infection is higher than the risk of antibiotics over treatment, so a low specificity and low positive predictive value are acceptable.[5] Also the technique requires a well-equipped laboratory setup which is mostly non available in most of the community hospitals.[15-16] Blood culture can be falsely negative also, because of intermittent or low-density bacteremia, suppression of bacterial growth by intrapartum antibiotic administration,[17] improper inoculation and incubation of blood culture.

C-reactive protein (CRP) is a non-specific acute phase protein, released in response to sepsis. Good evidence exists to support the use of CRP measurement in conjunction with other diagnostic tests such as TLC, ANC, platelet count and blood culture to establish or exclude the diagnosis of sepsis in full term or near term infants. [18]

In the present study, we also analyzed the combination of ANC and I/T ratio was having significantly high sensitivity. The tests used, were readily available, reliable and in combination found to be highly sensitive for the detection of NS.

LIMITATION

Limitations of this study were that correlation with laboratory data like micro ESR , procalcitonin etc., could not be done due to some technical difficulties, which otherwise if done would have increased the validity of the study.

CONCLUSION

ANC, I/T Ratio and CRP are quick, simple and cost-effective routine laboratory tests which help in neonatal sepsis prediction. Although there are many serological markers available, ANC and I/T Ratio serves as a reliable predictor of neonatal sepsis. With a good sensitivity, rather than high specificity and a good negative predictive value these parameters can therefore help in timely and early identification of neonatal sepsis.

REFERENCES

1. WHO. World Health Report. Geneva: World Health Organisation; 2005.
2. Lagro MG, Stekelenburg J. The Millennium project of the United Nations, focusing on adequate postpartum care to reduce maternal and neonatal mortality world-wide. Nederlands Tijdschrift Voor Geneeskunde. 2006 May 1;150(20):1143-7.
3. Mufti P, Setna F, Nazir K. Early neonatal mortality: effects of interventions on survival of low birth babies weighing 1000-2000g. JOURNAL-PAKISTAN MEDICAL ASSOCIATION. 2006 Apr;56(4):174.
4. Barbara JS. Infections of neonatal infant. In:Behrman RE, Kleigman RM, Jenson HB, Stanton BF, editors. Nelson Textbook of Pediatrics. 18th edition. Philadelphia; Saunders Company; 2008: 794-811.
5. Adams-Chapman I, Stoll BJ. Neonatal infection and long-term neurodevelopmental outcome in the preterm infant. Current opinion in infectious diseases. 2006 Jun 1;19(3):290-7.
6. Duhan A, Berwal A, Raikwar P, Punia A, Beniwal K, Kamra HT. Utility of Hematological Parameters in Detection of Neonatal Sepsis. Journal of Krishna Institute of Medical Sciences (JKIMSU). 2016 Jul 1;5(3).
7. Dawodu A, Al Umran K, Twum-Danso K. A case control study of neonatal sepsis: experience from Saudi Arabia. Journal of tropical pediatrics. 1997 Apr 1;43(2):84-8.
8. Tripathi S, Malik GK. Neonatal Sepsis: past, present and future; a review article. Internet Journal of Medical Update-EJOURNAL. 2010;5(2): 45-54.
9. Buttery JP. Blood cultures in newborns and children: optimising an everyday test. Archives of Disease in Childhood-Fetal and Neonatal Edition. 2002 Jul 1;87(1):F25-8.
10. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for neutrophilic cells. The Journal of pediatrics. 1979 Jul 1;95(1):89-98.
11. Shirazi H, Riaz S, Tahir R. Role of the hematological profile in early diagnosis of neonatal sepsis. Ann Pak Inst Med Sci. 2010;6(3):152-6.
12. Zipursky AJ, Palko J, Milner R, Akenzua GI. The hematology of bacterial infections in premature infants. J Pediatrics. 1976 Jun 1;57(6):839-53.
13. Rodwell RL, Leslie AL, Tudehope DI. Early diagnosis of neonatal sepsis using a hematologic scoring system. The Journal of pediatrics. 1988 May 1;112(5):761. -7.
14. Aggarwal R, Sarkar N, Deorari AK, Paul VK. Sepsis in the newborn. The Indian Journal of Pediatrics. 2001 Dec 1;68(12):1143-7.
15. Patel U, Patel VK, Patel NP, Verma J, Ratre BK, Verma SP. C-Reactive protein and other hematological parameters for diagnosis of neonatal sepsis. Int J of Med Res Rev 2014July-Aug:2:311-8.
16. Mondal SK, Nag DR, Bandyopadhyay R, Chakraborty D, Sinha SK. Neonatal sepsis: Role of a battery of immunohematological tests in early diagnosis. International Journal of Applied and Basic Medical Research. 2012 Jan;2(1):43.
17. Pourcyrous M, Bada HS, Korones SB, Baselski V, Wong SP. Significance of serial C-reactive protein responses in neonatal infection and other disorders. Pediatrics. 1993 Sep 1;92(3):431-5.
18. Hengst JM. The role of C-reactive protein in the evaluation and management of infants with suspected sepsis. Advances in neonatal care: official journal of the National Association of Neonatal Nurses. 2003 Feb;3(1):3-13.