Original Article

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Diagnostic Accuracy of Increased Total Leucocyte Count (TLC) and Decreased Absolute Neutrophil Count (ANC) for Diagnosis of Neonatal Sepsis Taking Culture Sensitivity as Gold Standard

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Author`s Contribution	A B S T R A C T
[1,3]Conception, Synthesis and Planning of the research, final approval of the final draft [2,4,7] data acquisition, revision, Data analysis and interpretation [2,5]Data Collection, Literature review Address of Correspondent Dr. Ayesha Khanum Consultant haematologist The Children Hospital Lahore Ayeshamohsin@gmail.com	**Objective:** To find diagnostic accuracy of increased total leucocyte count (TLC) and decreased absolute neutrophil count (ANC) for diagnosis of neonatal sepsis taking culture and sensitivity as the gold standard **Methodology:** Samples was collected from all the neonates with suspicion of sepsis admitted to neonatal due to severe bad health condition in the Children Hospital, Lahore. Parents were informed for consent. A total 3.5 cc sample was drawn by venipuncture.2.0 cc in CBC voil containing trisodium citrate, this sample was sent to CBC lab for automated CBC on sysmex KX-21 analyzer and peripheral smear. 1.5 cc was taken in specialized containers for blood culture and was sent to the microbiology lab. Neonatal sepsis on TLC, ANC, and blood count were be recorded. Patients with sepsis was managed as per hospital protocol. Data was analyzed using SPSS. **Results:** Neonates in this study was at a mean age of 3.86±1.81 days. There was an almost equal number of males and females neonates. Male were 155(51.7%) and female babies 145(48.3%). It was noted that 182(60.7%) babies were on term while 118(39.3%) were preterm neonates in this study. Neonatal sepsis was positive on TLC in 101(33.7%) cases. in 115(38.3%) on ANC. It was noted that the sensitivity of the TLC was 71% while specificity was 66% with a diagnostic accuracy of 68%. On the other hand, ANC sowed a sensitivity as 65%, specificity as 56%, and diagnostic accuracy of 65%. Conclusion: Conclusively, TLC and ANC is not a good marker for taking a neonate for the consideration of neonatal sepsis. **Keywords:** ANC count, Blood Culture, Neonatal sepsis, TLC count

Introduction

Neonatal Sepsis is known as neonatal septicemia or sepsis neonatorum, most extreme cases present on first day of life. Sepsis in neonates is a disorder portrayed by presentation and manifestations of disease with or without going with bacteremia inside neonatal period.[1, 2]

It is seen that neonates are at most noteworthy danger of bacterial contaminations prompting sepsis. The predominance of neonatal sepsis is 1-10 for each 10000 live births around the world. The occurrence of neonatal sepsis is a lot higher in creating nations than in created countries.[3] In Pakistan the frequency is three folds than in creating countries4. 5,000,000 neonates bite the dust in Asia and Africa every year, out of which 1.6 million (20%) are because of neonatal sepsis.[4]

Clinical highlights of sepsis are for the most part ambiguous and not characterized, general manifestations are changed in bolstering propensities, tachypnea, bradycardia, tachycardia, torpidity, poor cry, missing reflexes, hypo or hyperglycemia and metabolic acidosis.[5]

In created nations Group B streptococcus is the most widely recognized specialist which causes sepsis in neonates while E.coli is believed to be the most well-known reason for mortality. in complexity, creating nations like our own have various information, here gram negative life forms are believed to be the significant reason. According to an investigation led in 2010 at PIMS Islamabad, Pakistan, klebsiella and Acinetobacter are the most well-known organisms.[6, 7]

Blood culture is the highest quality level for making the finding however it takes 48 hours and treatment of septic newborn children can't be postponed that much, so neonatologists need some sensitive lab tests which help in early conclusion of sepsis.[8]

It has been proposed that a mix of hematological tests (all out leucocyte check (TLC), total neutrophil tally (ANC), juvenile to add up to neutrophil ratio(I/T proportion), platelet tally and C-responsive protein (CRP) estimation give early finding of bacteremia.[9]

Neonatologist carefully monitor the reports to any beginning of the anti-microbials, it will prompt worthless deferment in treatment, regular practice is that specialists start treatment with experimental anti-infection agents before the finding is made, it likewise prompts superfluous presentation of anti-toxins and causes multidrug resistance and pulps the gut flora in neonate which is very harmful.so to keep away from these issues, there is a need to do a few tests which help in early conclusion of sepsis.[10]

Already research was engaged in Pakistan, 75 patients were taken, associated with sepsis, TLC indicated a sensitivity of 75% for blood culture positive instances of Neonatal Sepsis. Its sensitivity was 57%. ANC had affectability of 65% and explicitness 78 %.[4]

The importance of our research is that it is carried out at one of the biggest medical clinics for neonates in Pakistan and countless patients report day by day with doubt of sepsis. There is a need to devise a lot of examinations that help in the speedy finding of these patients, and these tests ought to be financially savvy also. So with the assistance of this investigation, we will decide whether this arrangement of investigations (TLC, ANC, blood culture) is useful in early diagnosing these patients, and treatment was begun rapidly, so forestalling superfluous mortality.

Methodology

Samples was collected from all the neonates with suspicion of sepsis admitted to the neonatal emergency ward. Consent was taken from the parents of the child. They were informed about the study. Name, age, gender, history of prematurity was taken. All those neonates (both male and female) are suspected of having sepsis according to the operational definition. While the Neonates with congenital anomalies, parents refused to be part of the research and reported being on therapy for microbes before taking the sample were excluded from the study. The sample size of 300 cases is calculated with 65% sensitivity with 10% margin of error, 78% specificity with 16% margin of error of ANC and 95% confidence interval, and expected percentage of neonatal sepsis as 94%.

A total 3.5 cc sample was drawn by venipuncture.2.0 cc in CBC voil , this sample was sent to CBC lab for automated CBC on sysmex KX-21 analyzer and peripheral smear.1.5 cc was taken in specialized containers for blood culture and was sent to microbiology lab. Neonatal sepsis on TLC, ANC and blood count were be recorded. Patients with sepsis were managed as per hospital protocol. The data was collected using a performa.

Data was entered in the computer and analyzed in SPSS version 23. A 2x2 table was generated to calculate sensitivity, specificity, PPV and NPV of TLC, ANC for taking blood culture as gold standard.

Results

The mean age was 3.86 ± 1.81 days. There was an almost equal number of males and females neonates. Males were 155(51.7%) and female babies 145(48.3%). It was noted that 182(60.7%) babies were on the term. Blood culture showed a high number of neonates with neonatal sepsis. (Table I).

Table I: Distribution of the Demographics in the Study Population

Variable		Mean/Frequency
Age		3.86 ± 1.81
Gender	Male	155(51.7%)
	Female	145(48.3%)
Time of Delivery	Term	182(60.7%)
	Pre-term	118(39.3%)
Neonatal Sepsis	TLC	101(33.7%)
	ANC	115(38.3%)
	Blood Culture	139(46.3%)
Mena TLC count	TLC count	18229.50 ± 4991.67
	Mean ANC count	1866.27 ± 137.35

Table II: Diagnostic Accuracy of Biochemical marker keeping Blood Culture As Gold Standard.

		Sepsis on Blood Culture		
		Yes	No	
Sepsis on TLC	Yes	72(71.3%)	29(28.7%)	Accuracy= 68%
	No	67(33.7%)	132(66.3%)	
Sensitivity=71%	**Specificity=66%**	**PPV=52%**	**NPV=82%**	
Sepsis on ANC	Yes	72(71.3%)	29(28.7%)	Accuracy= 65%
	No	67(33.7%)	132(66.3%)	
Sensitivity=65%	**Specificity=56%**	**PPV=53%**	**NPV=75%**	

It was noted that sensitivity of the TLC was having diagnostic accuracy of 68% , ANC sowed a diagnostic accuracy of 65% . (Table II)

Discussion

Neonatal sepsis with its high death rate despite everything stays an indicative test for the medicinal services suppliers, particularly in creating nations. Early detection of septicemia among neonates supports the clinicians in making the timely decision for start of anti infection medication at the earliest, in this way decreasing the deaths and reliefs in keeping away from the pointless handling of a non-contaminated neonate.[11] Currently, not a single authentic study is there that support a particular method for the determination of neonatal sepsis in creating nations, and in this way, a guideline is needed for such analytical marker.

In this review sepsis increasingly normal in guys which is reliable with the discoveries of Galhotra S et al.[12] It might be connected to the x-connected immune-regulatory quality keeping male neonates ahead progressively helpless to disease. Additionally most likely because of the priority of the guardians who look for restorative administrations more for their male infants. Contamination was progressively normal in babies born with low weight (67.8%) as revealed in different investigations. Prematurely, conceived infants were all the more normally contaminated. It was most likely because of their innate traded off insusceptibility, low supplement levels and hypo-gammaglobulinemia. A significant maternal hazard factor was preterm rupture of membrane (PROM) for early beginning sepsis.[13]

In current study, blood culture was sure in 37.9% cases, practically identical to contemplate in which blood culture was certain in 35% cases.[14] It was promptly feasible to complete blood count, leukocyte count, I/T proportion and small scale ESR in spite of the fact that having high particularity in our investigation, had poor affectability for diagnosing sepsis. Gerdes et al [20] saw in his examination that leucocyte lists (TLC, ANC, and I/T Ratio) were not

exact adequate for early determination of septicemia and their perception was as per our findings.[15]

Complete leukocyte count (TLC) total neutrophil count (ANC) platelet count (PLT). Furthermore, C-receptive protein (CRP) estimation were utilized for the determination of neonatal sepsis. TLC had affectability of 75% for bunch A (demonstrated sepsis) and 76% for bunch B (plausible sepsis), and had a negative prescient worth (NPV) of 80% and 65% individually.[4] The affectability of ANC was 65% and 76% in bunch An and B separately which is comparable as noted right now. Our outcomes affirm and expand those of past examinations. Different investigations have demonstrated that the WBC count and ANC increment quickly during the initial 6 hours, leveling off from that point. Our fifth and 50th percentiles intently coordinate those for term newborn children announced by Schmutz et al, who utilized a comparative plan by utilizing information frameworks at Intermountain Health care. Our finding that the test qualities of the CBC improve with age is in concurrence with contemplates that uncover lackluster showing of the CBC when it is utilized basically in youthful (<4 hours old) babies, including some who explicitly show improvement with later CBCs.[16, 17]

In a research, leukopenia, i.e., absolute WBC checks <5000 cells/cumm, and neutropenia, i.e., ANCs <1850 cells/cumm, were taken as the symptomatic criteria for recognizing neonatal septicemia. Leukopenia has high particularity and positive prescient worth yet low affectability and negative prescient worth.[18] Neutropenia has high explicitness however low affectability in the present investigation which is practically identical with the perception made by Ghosh et al. These varieties appeared by the changed creators might be because of contrasts in the blood examining time, the seriousness of the disease, the age of the neonates, and the diminished affectability of this test in the first seven day stretch of life.[19]

This study has constraint due to being single focused in nature. In addition, restricted time and little example size was likewise solid elements for the little scope consequences of our investigation. An investigation will

different focuses and huge example size is expected to affirm the outcomes and to get them summed up for the whole population.

Conclusion

Both TLC and ANC are poor tools to diagnose neonatal sepsis. Hence it is recommended that blood culture should be advised rather than these tests for confirmation of neonatal sepsis.

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