

Diagnostic Value of Neutrophil to Lymphocyte Ratio on Neonatal Sepsis in Full Term and Preterm Neonates

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Abstract

Background: Sepsis is a life-threatening illness with notably high degree of mortality both in preterm and term neonates. Roughly, it may be characterized as a systemic inflammatory response that occurs as a consequence of confirmed or suspected infection in neonatal period. Especially in underdeveloped countries, early detection and treatment of newborns with infections are inadequate. Clinical findings of sepsis in newborns are problematic since many of the symptoms associated to sepsis are unclear and they might be revealed with conditions of other noninfectious disorders. Neonatal sepsis remained a serious concern for neonates across the globe and generates considerable morbidity and death neonates (term and preterm), particularly in underdeveloped nations. It was a clinical illness that defined by systemic infections and characterized by the isolation of bacteria in the blood (bacteremia) that occurs in babies in the first month of life. The cornerstone underlying the development of newborn sepsis is inflammation. Common measures utilized for the effective diagnosis and treatment of newborn sepsis, apart for blood cultures, comprise of inflame inflammatory indicators. Accordingly, the study of inflammatory biomarkers is an essential element of sepsis research. In particular, the influence of inflammation on blood cells such as neutrophils, lymphocytes, and platelets has been a focus of study on the diagnosis of sepsis. The purpose of the study was to establish value of neutrophil to lymphocyte ratio in diagnosis of newborn sepsis in full term and preterm neonates. **Methods:** This was a prospective research was done at neonatal intensive care unit of Benha university hospital; 120 neonates who were split into 2 groups: Group I (patient) :include 60 septic neonates who were separated into 2 subgroups: Group I (A) : 30 full term newborns and Group I (B) : 30 preterm neonates, whereas Group II (control) :include 60 healthy neonates who were broken into 2 subgroups: Group II (A) : 30 full term newborns and Group II (B) : 30 preterm neonates. **Results:** In this research, hemorrhage and fever were considerably greater in pre-term septic neonates than full term and pre-term controls. PROM and UTI were considerably greater in full term septic neonates than full term and pre-term controls. In addition, they were substantially greater in pre-term septic neonates than full term and pre-term controls. In the current investigation, the most prevalent organism was Klebsiella (33.3 percent), followed by E.coli (23.3 percent), pseudomonas (16.7 percent), staph aureus (15.0 percent), Group B streptococcus (6.7 percent), and strept pneumonia (5.0 percent). (5.0 percent). CRP indicated an overall significant difference between research groups (P-value <0.001). Post hoc analysis found that it was considerably higher in full-term septic neonates (24) compared to full-term controls (2.3) and preterm controls (1.8). (1.8). Also, CRP in preterm septic newborns was substantially higher (24) than full-term and preterm controls. In this research, TLC was considerably greater in full-term and preterm septic newborns (18.5 & 17.8, respectively) compared to full-term controls (10.4). (10.4). Our research findings discovered that neutrophils demonstrated that it was considerably greater in full-term septic neonates (11) compared to full-term controls (4.8) and preterm controls (5.8). (5.8). In addition, neutrophils in preterm septic newborns were considerably greater (12) than full-term and preterm controls. In addition, NLR was considerably greater in full-term septic neonates (3.1) compared to full-term and preterm controls (1.3 for each) (1.3 for each). Also, NLR in preterm septic newborns was considerably greater (3.4) than full-term and preterm controls. Our findings indicated that, the lymphocytes count was considerably lower in patients group compared to controls group. In full term our research septic group, NLR exhibited a significant negative connection with Apgar 1 minute ($r = -0.512$ & P-value = 0.004). In contrast, it exhibited a significant positive connection with CRP ($r = 0.362$ & P-value = 0.05). While, in pre-term septic group, NLR exhibited a significant negative connection with Apgar 1 minute ($r = -0.570$ & P-value = 0.001), Apgar 5 minutes ($r = -0.384$ & P-value = 0.036), and platelets ($r = -0.373$ & P-value = 0.042). In this study, NLR higher than 1.6698 showed an excellent AUC with sensitivity and specificity were 90 percent and 91.7, respectively in diagnosing neonatal sepsis and had sensitivity and specificity were 100 percent and 86.7 percent , respectively in diagnosing neonatal sepsis in preterm neonates. While, NLR more than 1.5135 demonstrated a good AUC with sensitivity and specificity were 96.7 percent and 90 percent , respectively in detecting neonatal sepsis in full-term neonates. **Conclusion:** From our research we concluded that we give evidence that NLR may be employed in addition to standard indicators such as CRP in the diagnosis and subsequent therapy of newborn sepsis. In addition, NLR is affordable and widely accessible instrument in contrast to other comparatively more costly technologies.

Key words: Neutrophil, Lymphocyte, Neonatal Sepsis, Full Term Neonates, Preterm Neonates.

1. Introduction

In both preterm and term newborns, sepsis is a life-threatening illness with a high fatality rate. It may be described as a systemic inflammatory response that

occurs during the newborn period as a consequence of an infection that has been proved or suspected [1].

Detection and treatment of neonatal sepsis are critical to a child's survival. Nonspecific clinical

symptoms and the lack of specific biomarkers for diagnosis hamper the detection and treatment of newborn sepsis [2].

A blood culture is the gold standard for diagnosing bacterial sepsis, however pathogens in blood cultures are only found in around 25 percent of the instances the sensitivity of blood culture is considered to be poor, hence clinical evaluation and laboratory indicators such as C-reactive protein (CRP) are typically used to diagnose sepsis [3].

C-reactive protein (CRP) and procalcitonin are two biochemical indicators that have been explored for use in the early detection of newborn sepsis (PCT). Because of this, these markers' specificity and utility cannot be relied upon with any degree of certainty. A constant quest for improved biomarkers of neonatal sepsis is, however, still vitally important [4].

Bacterial infections may be accurately predicted by a ratio of neutrophil and lymphocyte counts known as the NLCR. Easy to get and compute, this marker may be simply incorporated into everyday practise and does not need any additional resources [5].

Neutrophil-to-lymphocyte ratio is an important factor in the diagnosis of neonatal sepsis in both full term and preterm infants.

2. Patients and Methods

This study was conducted in neonatal intensive care unit of Benha university hospital during the period from April 2020 to April 2021.

Study populations:

120 neonates which were divided into 2 groups:

Group I (patient): include 60 septic neonates which were subdivided into 2 subgroups:

- **Group I (A) :** 30 fullterm neonates
- **Group I (B) :** 30 preterm neonates

Group II (control): include 60 healthy neonates which were subdivided into 2 subgroups:

- Group II (A) :** 30 fullterm neonates
- Group II (B) :** 30 preterm neonates

- Full term and preterm neonates with sepsis confirmed by blood culture were considered as disease group.
- Healthy neonates with no symptoms or signs of infection and negative serum CRP were considered as controls.

Inclusion Criteria:

- Full term and preterm neonates with sepsis confirmed by blood culture were considered as disease group.
- Healthy neonates with no symptoms or signs of infection and negative serum CRP were considered as controls.

Exclusion Criteria:

- Neonates with chromosomal abnormalities, birth asphyxia, metabolic disorders and congenital heart disease.

Ethical considerations:

- Approval of the Research Ethics Committee of the Faculty of Medicine was obtained before the study.
- The aim of the study was explained to parents.
- Oral consent from the caregivers was obtained for each patient enrolled in the study before taking blood samples from them.
- Privacy of data was assured.

Study design:

All neonates included in the study were subjected to the following:

History taking:

- Mode of delivery, gestational age, sex, admission diagnosis
- Postnatal age
- Prenatal history of maternal disease as maternal fever and UTI
- Natal history of mode of delivery,maternal fever and PROM
- Present history of most common symptoms of sepsis
- Postnatal history including Apgar score

| SCORE | 0 points | 1 point | 2 points |
|-----------------------------------|----------------------------|---|-------------------------------------|
| Appearance - Skin colour | Cyanotic/ Pale all over | Peripheral cyanosis only | Pink |
| Pulse (Heart rate) | 0 | <100 | 100-140 |
| Grimace - Reflex irritability) | No response to stimulation | Grimace (facial movement)/ weak cry when stimulated | Cry when stimulated |
| Activity - Tone | Floppy | Some flexion | Well flexed and resisting extension |
| Respiration | Apnoeic | Slow, irregular breathing | Strong cry |

General examination of the neonate including:

- Measurements (length, weight, head, abdominal and chest circumference)
- Vital signs (heart rate, respiratory rate, temperature and blood pressure)

- General condition and activity and neonatal reflexes (Moro and Suckling)

• **Clinical examination for detection of clinical signs of sepsis:**

- Hyperthermia or hypothermia.
- Tachycardia, bradycardia or rhythm instability.

- Tachypnea or recurrent apnea.
- Increased oxygen requirement or requirement of ventilator support. 5-feeding intolerance.
- Neurologic alteration (hypotonia, lethargy and seizures).
- Skin and subcutaneous lesions such as mottling and sclerema.

Systemic examination: (chest, heart, abdominal, CNS)

Investigations:

- **Complete blood picture (CBC):** Analysed by sysmex 21-kx cell counter for red blood cell count, hemoglobin level, hematocrit value, white blood cell (WBC) count (Total and differential) and platelet count.
- **Serum CRP:** 1cm of blood was taken, blood was collected in a plain test tube, left to clot, then centrifuged for 10 minutes at 1500 rpm, serum was separated and analyzed using Biosystem A25.
- **Neutrophil** to lymphocyte ratio

Blood culture for confirmation of sepsis:

1- Blood samples collection:

- Under strict aseptic technique we collect blood samples by:
- Using pressure cuff, wearing sterile gloves.
- Locate vein, disinfect vein puncture site.
- Using sterile syringe and needle.
- Should be sure that culture media is not contaminated.
- Insert needle through rubber liver and inject blood into culture bottle.

2- Blood sample incubation:

- Using fresh ethanol ether we swap and wipe the top of each culture bottle.
- Label each bottle with the name, number of patient and date, time of collection.
- Then we incubate the incubated media in BACTEC device.
- Bottle was examined daily (up to 7 days) for microbial growth which was shown at screen of BACTEC instrument which give positive signals for infected cultured bottles.

3- When growth was present we did:

- Subculture on blood agar and chocolate agar.
- Incubate blood agar plates aerobically and Incubate chocolate agar in carbon dioxide atmosphere (anaerobic gas package).
- Examine gram stained smear of colonies depending on bacteria seen and then test the colonies further for coagulase, catalase, oxidase, urease and motility.

Statistical Analysis

Data were checked, entered and analyzed using SPSS version 23 for data processing. The following statistical methods were used for analysis of results of the present study. Data were expressed as number and percentage for qualitative variables and mean ± standard deviation (SD) for quantitative one.

3. Results

- No significant differences were noted regarding sex (P-value = 0.695) and mode of delivery (P value = 0.586).

Table (1) General characteristic in the studied groups.

| | | Septic neonates | | Controls | | P-value |
|--------|--------------|-----------------|-----------|-----------|-----------|---------|
| | | Full-term | Pre-term | Full term | Pre-term | |
| Gender | Males n (%) | 14 (46.7) | 11 (36.7) | 15 (50.0) | 15 (50.0) | 0.695 |
| | Female n (%) | 16 (53.3) | 19 (63.3) | 15 (50.0) | 15 (50.0) | |

One-way ANOVA was used for numerical data. Chi-square test was used for categorical data

Maternal risk factors in the studied groups

- Bleeding, fever, PROM, and UTI showed overall significant differences between study groups (P-values were 0.001, 0.001, < 0.001, and < 0.001, respectively). Post-hoc analysis revealed that bleeding and fever were significantly higher in pre-term septic neonates than full term and pre-term controls. PROM and UTI were significantly higher in full term septic neonates than full term and pre-term controls. In addition, they were significantly higher in pre-term septic neonates than full term and pre-term controls.

Table (2) maternal risk factors in the studied groups.

| | | Septic neonates | | Controls | | P-value |
|----------|-------|-----------------|-----------|-----------|----------|---------|
| | | Full-term | Pre-term | Full term | Pre-term | |
| Bleeding | n (%) | 6 (20.0) | 9 (30.0) | 1 (3.3) | 0 (0.0) | 0.001 |
| Fever | n (%) | 6 (20.0) | 11 (36.7) | 2 (6.7) | 0 (0.0) | 0.001 |
| PROM | n (%) | 14 (46.7) | 14 (46.7) | 2 (6.7) | 2 (6.7) | <0.001 |
| UTI | n (%) | 19 (63.3) | 20 (66.7) | 4 (13.3) | 2 (6.7) | <0.001 |

Clinical manifestations in septic neonates

- The most frequent clinical manifestation was respiratory distress (95.0%), followed by feeding intolerance (75.0%), hypoactivity (56.7%), hypoperfusion (48.3%), tachycardia (46.7%), poor suckling (41.7%), apnea (26.7%), temperature instability (25.0%), and seizures (6.7%).

Table (3) Clinical manifestations in septic neonates

| | n (%) |
|--------------------------------|-----------|
| Respiratory distress | 57 (95) |
| Apnea | 16 (26.7) |
| Temperature instability | 15 (25.0) |
| Hypoactivity | 34 (56.7) |
| Seizures | 4 (6.7) |
| Poor suckling | 25 (41.7) |
| Tachycardia | 28 (46.7) |
| Hypoperfusion | 29 (48.3) |
| Feeding intolerance | 45 (75.0) |

Blood culture in septic neonates

- The most frequent organism was Klebsiella (33.3%), followed by E.coli (23.3%), pseudomonas (16.7%), staph aureus (15.0%), Group B streptococcus (6.7%), and strept pneumonia (5.0%).

Table (4) Blood culture in septic neonates.

| | n (%) |
|------------------------------|-----------|
| Klebsiella | 20 (33.3) |
| E-Coli | 14 (23.3) |
| Pseudomonas | 10 (16.7) |
| Staph aureus | 9 (15.0) |
| Strept pneumonia | 3 (5.0) |
| Group B streptococcus | 4 (6.7) |

Laboratory findings in the studied groups

- TLC showed an overall significant difference between study groups (P-value <0.001). Post hoc analysis revealed that TLC was significantly higher in full-term and preterm septic neonates (18.5 & 17.8, respectively) compared to full-term controls (10.4).
- Neutrophils showed an overall significant difference between study groups (P-value <0.001). Post hoc analysis revealed that it was significantly higher in full-term septic neonates (11) compared to full-term controls (4.8) and preterm controls (5.8). Also, neutrophils in preterm septic neonates were significantly higher (12) than full-term and preterm controls.
- Lymphocytes showed an overall significant difference between study groups (P-value = 0.018). Post hoc analysis revealed that it was significantly lower in full-term and preterm septic neonates (3.7 for each) compared to preterm control neonates (4.8).
- NLR showed an overall significant difference between study groups (P-value < 0.001). Post hoc analysis revealed that it was significantly higher in full-term septic neonates (3.1) compared to full-term and preterm controls (1.3 for each). Also, NLR in preterm septic neonates was significantly higher (3.4) than full-term and preterm controls.
- Platelets showed an overall significant difference between study groups (P-value <0.001). Post hoc analysis revealed that it was significantly lower in full-term septic neonates (130) compared to full-term controls (230) and preterm controls (225). Also, platelets in preterm septic neonates were significantly lower (188) than full-term and preterm controls.
- Hb showed an overall significant difference between study groups (P-value <0.001). Post hoc analysis revealed that it was significantly lower in full-term septic neonates (11.6) compared to full-term controls (16.4) and preterm controls (16). Also, Hb in preterm septic neonates was significantly lower (12.3) than full-term and preterm controls.
- CRP showed an overall significant difference between study groups (P-value <0.001). Post hoc analysis revealed that it was significantly higher in full-term septic neonates (24) compared to full-term controls (2.3) and preterm controls (1.8). Also, CRP in preterm septic neonates was significantly higher (24) than full-term and preterm controls.

Table (5) Laboratory findings in the studied groups

| | | Septic neonates | | Controls | | P-value |
|---|----------------|----------------------|----------------------|----------------------|-----------------------|---------|
| | | Full term | Pre-term | Full term | Pre-term | |
| TLC ($\times 10^3/\mu\text{l}$) | Median (range) | 18.5 (3.4 - 31.7) | 17.8 (4.5 - 37.8) | 10.4 (7.3 - 13.3) | 11.6 (10.1 - 21.5) | <0.001 |
| Neut. ($\times 10^3/\mu\text{l}$) | Median (range) | 11 (2.5 - 21.8) | 12 (3.5 - 30.4) | 4.8 (2.6 - 17.4) | 5.8 (3.5 - 11.2) | <0.001 |
| Lymph. ($\times 10^3/\mu\text{l}$) | Median (range) | 3.7 (0.7 - 7.6) | 3.7 (0.7 - 6.9) | 3.9 (2.6 - 7.6) | 4.8 (2.5 - 7.1) | 0.018 |
| NLR | Median (range) | 3.1 (1.5 - 4.6) | 3.4 (2.1 - 7.8) | 1.3 (0.5 - 2.3) | 1.3 (0.7 - 2.3) | <0.001 |
| Platelets ($\times 10^3/\mu\text{l}$) | Median (range) | 130 (13 - 345) | 188 (22 - 323) | 230 (189 - 579) | 225 (166 - 366) | <0.001 |

Kruskal Wallis test was used. One-way ANOVA was used for hemoglobin

TLC; Total leucocytic count

NLR; neutrophil-to-lymphocyte ratio

CRP; C-reactive protein

NLR correlation with other parameters in full term septic neonates

- In full term septic group, NLR showed a significant negative correlation with Apgar 1 minute ($r = -0.512$ & P-value = 0.004). In contrast, it showed a significant positive correlation with CRP ($r = 0.362$ & P-value = 0.05).

Table (6) NLR correlation with other parameters in full-term septic neonates.

| | NLR | |
|---|---------|---------|
| | r | P-value |
| Gestational age (weeks) | -0.142 | 0.453 |
| Birth weight(kg) | -0.276 | 0.139 |
| Postnatal age(days) | 0.155 | 0.412 |
| Apgar (1minute) | -0.512* | 0.004 |
| Apgar (5minutes) | -0.156 | 0.41 |
| TLC ($\times 10^3/\mu\text{l}$) | -0.205 | 0.278 |
| Neutrophil($\times 10^3/\mu\text{l}$) | 0.125 | 0.511 |
| Lymphocyte($\times 10^3/\mu\text{l}$) | -0.318 | 0.087 |
| Platelets ($\times 10^3/\mu\text{l}$) | 0.245 | 0.193 |
| Hemoglobin (g/dl) | -0.324 | 0.08 |
| CRP (mg/l) | 0.362* | 0.05 |

r; Correlation coefficient

NLR; neutrophil-to-lymphocyte ratio

TLC; Total leucocytic count

CRP; C-reactive protein

* Significant

NLR correlation with other parameters in pre-term septic neonates

- In pre-term septic group, NLR showed a significant negative correlation with Apgar 1 minute ($r = -0.570$ & P-value = 0.001), Apgar 5 minutes ($r = -0.384$ & P-value = 0.036), and platelets ($r = -0.373$ & P-value = 0.042).

Table (7) NLR correlation with other parameters in preterm septic neonates.

| | NLR | |
|--|--------|---------|
| | r | P-value |
| Gestational age (weeks) | 0.293 | 0.116 |
| Birth weight (kg) | 0.259 | 0.168 |
| Postnatal age (days) | 0.08 | 0.675 |
| Apgar (1minute) | -.570* | 0.001 |
| Apgar (5minutes) | -.384* | 0.036 |
| TLC ($\times 10^3/\mu\text{l}$) | 0.282 | 0.131 |
| Neutrophil ($\times 10^3/\mu\text{l}$) | 0.332 | 0.073 |
| Lymphocyte ($\times 10^3/\mu\text{l}$) | -0.215 | 0.254 |
| Platelets ($\times 10^3/\mu\text{l}$) | -.373* | 0.042 |
| HB (g/dl) | 0.101 | 0.595 |
| CRP (mg/l) | -0.234 | 0.213 |

r; Correlation coefficient NLR; neutrophil-to-lymphocyte ratio
 TLC; Total leucocytic count CRP; C-reactive protein
 * Significant

ROC analysis of NLR in diagnosing neonatal sepsis

- ROC analysis was performed for NLR in diagnosing neonatal sepsis. It showed a significant-excellent AUC of 0.975 with a 95% confidence interval ranged from 0.954 to 0.996 (P-value < 0.001). The best cut-off point was > 1.6698, at which sensitivity and specificity were 90% and 91.7%, respectively.

Table (8) ROC analysis of NLR in diagnosing neonatal sepsis.

| ROC characteristics | |
|---------------------|-----------------------|
| AUC (95% CI) | 0.975 (0.954 - 0.996) |
| Best cutoff | > 1.6698 |
| Sensitivity | 90 |
| Specificity | 91.7 |
| P-value | <0.001 |

ROC analysis of NLR in diagnosing neonatal sepsis in full-term neonates

- ROC analysis was performed for NLR in diagnosing neonatal sepsis in full-term neonates. It showed a significant-excellent AUC of 0.988 with a 95% confidence interval ranged from 0.970 to 1 (P-value <0.001). The best cut-off point was > 1.5135, at which sensitivity and specificity were 96.7% and 90%, respectively.

Table (9) ROC analysis of NLR in diagnosing neonatal sepsis in full-term neonates.

| ROC characteristics | |
|---------------------|---------------------|
| AUC (95% CI) | 0.988 (0.970 – 1.0) |
| Best cutoff | > 1.5135 |
| Sensitivity | 96.7% |
| Specificity | 90.0% |
| P-value | <0.001 |

AUC; Area under curve 95% CI; 95% confidence interval

ROC analysis of NLR in diagnosing neonatal sepsis in preterm neonates

- ROC analysis was performed for NLR in diagnosing neonatal sepsis in preterm neonates. It showed an excellent AUC of 0.969 with a 95% confidence interval ranged from 0.933 to 1 (P-value <0.001). The best cut-off point was > 1.6698, at which sensitivity and specificity were 100% and 86.7%, respectively.

Table (10) ROC analysis of NLR in diagnosing neonatal sepsis in preterm neonates.

| ROC characteristics | |
|---------------------|---------------------|
| AUC (95% CI) | 0.969 (0.933 – 1.0) |
| Best cutoff | > 1.6698 |
| Sensitivity | 100% |
| Specificity | 86.7% |
| P-value | <0.001 |

AUC; Area under curve 95% CI; 95% confidence interval

4. Discussion

In our research, there was no discernible difference in gender between the patients and the controls. Xiao et al., [6] observed the same outcome, and this supports their findings. Patients, on the other hand, were mostly male (63.3 percent). The prevalence of male gender in newborn sepsis research, such as the Benitz study, is seen in practically all of those investigations. X chromosome-linked genes may be to blame for the Thymus gland's function or the manufacture of immunoglobulins [7].

Pre-term septic neonates had greater rates of haemorrhage and fever in this research than full-term and pre-term controls. Full-term septic neonates had considerably greater rates of PROM and UTI than did full-term and pre-term controls. Septic neonates, on the

other hand, had considerably greater levels of these markers compared to full- and pre-term controls.

Thirty-five (34.0 percent) of the cases and 472 (59.2 percent) of the controls were included in the research by Adatara et al. Percentage of pregnant women with urinary tract infections (UTI/STI) was found to be somewhat higher in the cases, 4 (3.9%) compared with 29 (29.9%) controls (3.6 percent). Pregnancy-related bleeding disorders were found to be more prevalent in the mothers of controls, 166 (20.8 percent), than in those of patients, 3 (2.9 percent). Premature rupture of membrane (PROM) was more common in the control group, 116 (14.6 percent), than in the case group, 3 (2.9 percent) [8].

There was a high prevalence of respiratory distress (95%) in this research, followed by feeding intolerance

(75%), hypoactivity (56%) hypoperfusion (48%), tachycardia (46.7%) poor suckling (41.7%), apnea (26.7%), temperature instability (25.0%), and seizures (25.0 percent) (6.7 percent).

According to the research, respiratory distress was shown to be the most common clinical indication of EOS (60%) followed by tachycardia [10] and then jaundice (6.7%) and apnea (3.3%) as the last clinical symptoms [9].

Klebsiella (33.3%), followed by E.coli (23.3%), pseudomonas (16.7%), staph aureus (15.0%), Group B streptococcus (6.7%), and strept pneumonia (6.7%) were the most common organisms in this investigation (5.0 percent). There was a statistically significant difference (P-value 0.001) between the study groups in CRP. It was shown to be substantially greater in full-term septic neonates (24) than in full-term controls (2.3) and preterm controls (0.4). (1.8). CRP levels in preterm septic neonates were considerably greater than those of full-term and preterm controls (24) in both groups.

Gram negative bacilli, particularly Klebsiella, have been reported to be the most frequent organisms in various investigations. The bulk of the culture growth was found to be due to staphylococci, gram-positive bacteria, according to previous investigations [10, 11].

Only 23.3 percent of patients had a positive blood culture, with 5 (16.7 percent) showing klebsiella and 2 (6.6 percent) showing Staphylococcus aureus, in accordance with Nasser et al research, in which 76.7 percent of patients had negative blood cultures [9].

Gram-positive organisms were found to be the most prevalent EOS microbes in Korea, according to the Mithal et al. investigation. This illustrates that each newborn unit has its own unique bacteria, which vary from time to time, and antibiotic combinations should be changed based on culture findings [12].

A broad range of results have been reported in several studies on the diagnostic accuracy of blood cultures and traditional markers such as CRP in the diagnosis of sepsis [11, 7].

CRP (with a cut-off value of 1.5–20 -mg/L) has been reported to have a sensitivity of 74 to 98 percent, with an associated specificity of 71 to 94 percent, with respect to blood cultures [13, 14].

An study conducted by Karabulut and Alatas found that variations in gestational age, birth weight, and delivery method might account for the broad cut-off values, sensitivity, and specificity of traditional indicators routinely employed in newborn sepsis diagnosis [15].

When compared to full-term controls, the TLC of septic neonates (18.5 & 17.8) was substantially greater in our research than in the controls (10.4).

Our findings are in accordance with, Can et al., [16], Omran et al., [17] and [6].

Full-term septic neonates had a neutrophil count of 11 compared to full-term controls of 4 and preterm controls of 4 in our research findings (5.8). Preterm septic neonates had neutrophil counts that were

considerably higher (12) than those of full-term or preterm newborns in the study. Full-term septic neonates had considerably greater NLR (3.1) than full-term and preterm control infants (1.3 for each). Septic preterm neonates had considerably greater NLR than full-term and preterm controls, with a value of 3.4.

Some research came to the same conclusion: septic neonates had higher levels of neutrophils and NLR than controls, which was statistically significant [15, 9].

Patients had a much lower lymphocyte count than the control group, according to our findings.

Patients had a considerably lower lymphocyte count than controls, in agreement with our findings, according to Can et al. [16]. The variance in neutrophil and lymphocyte counts between patients and control groups may be described as follows: the natural immunological responses of circulating leukocytes to various stressful events are characterised by elevated neutrophil counts and decreased lymphocyte counts. A microorganism infection triggers an inflammatory response, resulting in higher total leukocyte and neutrophil numbers [18, 19].

There was a statistically significant difference (P-value 0.001) between research groups in platelets. Septic full-term neonates had considerably lower mortality rates (130/230) than controls (230) and preterm controls (130/230). (225). The platelet count was substantially lower in preterm septic newborns (188) than in full- and preterm controls.

In keeping with earlier studies showing a statistically significant drop in platelet count (Plt) in patients compared to controls, this one too shows a similar trend [15, 9].

NLR exhibited a significant negative connection with Apgar 1 minute ($r = -0.512$ & $P\text{-value} = 0.004$) in our full-term research septic group. A substantial positive connection with CRP, however, was found ($r = 0.362$; $P = 0.05$). Preterm septic group NLR revealed a significant negative connection with Apgar 1 minute ($r = -0.570$), Apgar 5 minutes ($r = -0.384$), and platelets ($r = -0.373$).

A similar finding was made by Can et al. [16] and Omran et al. [17] who found that NLR was considerably greater among patients than among controls.

Preterm newborns with an NLR more than 1.6698 had a good AUC of 90% and 91.7 percent, respectively, in diagnosing neonatal sepsis, whereas those with an NLR less than 1.6698 had an AUC of 100% and 86.7 percent. In contrast, NLR greater than 1.5135 exhibited an outstanding AUC with 96.7 percent sensitivity and 90% specificity in identifying neonatal sepsis in full-term newborns, respectively.

There is a 97.4 percent sensitivity and a 100 percent specificity for the neonatal EOS cutoff of NLR 6.76, according to the study by Canet al. [16].

NLR at a cut-off value of 2.7 had 80% specificity and 57.1 specificity, according to Omran and colleagues [17]. NLR at the cut-off value of 1.42

demonstrated 83.3 percent sensitivity and 93.3 percent specificity, according to Xiao et al. [6]. Because there is no precise cut-off point for NLR in EOS, the number of studies was restricted.

NLR's diagnostic usefulness in sepsis has been evaluated in a variety of ways, and the findings have been mixed. A sensitivity of 75.6 percent and a specificity of 38.4 percent were reported by Dursun et al [20].

At the cut-off value of 6.76 (16), Omran et al obtained a sensitivity of 80 percent and specificity of 57.1 percent, while Can et al reported 97.4 percent and 100 percent specificity [17].

NLR's AUCROC, sensitivity, specificity, LR, PPV, NPV, and simplicity of use all support its utility as a diagnostic tool for newborn sepsis, despite a broad variety of cut-off values in previous investigations.

EOS diagnosis may be improved by using NLR, which has a better sensitivity than CRP when compared to other traditional markers [15].

In our investigation, the power of our study was judged to be 100 percent based on a validated reference study with an adequate patient population size. The inclusion of a control group and a prospective design for our research allowed us to compare our findings.

5. Conclusion

We found that NLR may be employed in addition to CRP in the diagnosis and subsequent therapy of newborn sepsis, based on our research. To top it all off, NLR is a low-cost and easy-to-use alternative to more costly tools.

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