Platelet to Lymphocyte Ratio and Neutrophil to Lymphocyte Ratio as New Diagnostic Markers for Detection of Early-onset Neonatal Sepsis in Full-term Newborns.

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Research

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Abstract

Objective: The purpose of this study was to investigate the clinical significance of the platelet to lymphocyte ratio (PLR) and the neutrophil to lymphocyte ratio (NLR) in term neonates and its impact on management of Early-Onset Neonatal Sepsis (EOS).

Materials and Methods: This prospective cross-sectional observational study was conducted with 40 term neonates diagnosed with EOS compared with 40 healthy controls. Exclusion criteria were prematurity, post-maturity, small or large for gestational age according to week of pregnancy, preeclampsia, gestational diabetes mellitus, chorioamnionitis, congenital major anomalies, and cyanotic congenital heart disease.

Results: A total of 80 term neonates were included in the study. Of these, 40 were diagnosed with EOS and 40 were healthy controls. NLR and PLR as predictors of early-onset neonatal sepsis, sensitivity of NLR was 67% and PLR was 70% and specificity of NLR was 99% and PLR was 73% and PPV of NLR was 98%, PLR was 72%. There is a significant weak positive correlation between platelets and sepsis, significant fair positive correlation between WBCs and PLR with sepsis, significant moderate positive correlation between immature neutrophils, I.T and NLR with sepsis, finally a significant negative fair correlation between lymphocytes and sepsis.

Conclusions: NLRs and PLRs were positively correlated with EOS in term neonates, and these ratios can be used as diagnostic adjunct tests for neonate EOS workups.

Introduction

Neonatal Sepsis is an important cause of morbidity and mortality among newborn infants. Although the incidence of sepsis in term and late preterm infants is low, the potential for serious adverse outcomes is of such great consequence that caregivers should have a low threshold for evaluation and treatment for possible sepsis in neonates (1).

Neonatal sepsis a systemic condition of bacterial, viral, or fungal (yeast) origin that is associated with hemodynamic changes in an infant 28 days of life or younger, the definition of sepsis has included isolation of a pathogen from a normally sterile body fluid such as blood or cerebrospinal fluid (CSF). However, as the clinical features of sepsis can be induced by potent pro-inflammatory cytokines, the term systemic inflammatory response syndrome (SIRS) has also been used when describing neonatal sepsis (2). the presence of sequential organ dysfunction (objectively determined by the sequential organ failure assessment (SOFA score) predicts mortality (e.g., sofa score > 4 predicts mortality) and admission to the intensive care unit with death as a final outcome measure. The presence of organ dysfunction indicates a more complex pathobiology than simply infection with an accompanying inflammatory response (3).

Table (I) Hypothetical neonatal SOFA score 2018
| System          | 0                                           | 1                                           | 2                                           | 3                                           |
|-----------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| Respiratory     | No support or OI < 2, PaO₂/FiO₂ > 330 (70/0.21) | CPAP/HFNC or OI-2-8 (max of 40% O₂, max MAP 14, PaO₂ 70) | NIPPV or OI-8–14 (max 60% O₂, max MAP 16, PaO₂ 70) | Intubated: CMV/HFV or OI-14–20 PaO₂/FiO₂ <140 (70/0.6) or any iNO Score of 4: ECMO (if eligible), OI > 20 if ineligible |
| Cardiovascular  | MAP > GA and < 3 s capillary refill          | Two measurements of: (i) SBP decrease > 10 mmHg or (ii) capillary refill > 3 s 1–6 h apart | Vasopressor requirement | Vasopressor refractory state (requirement for post-vasoactive meds, e.g., corticosteroids) |
| Platelets (10^3/µl) | ≥ 100                                      | < 100                                      | < 50                                      | < 50 in ≤ 24 h after transfusion |
| ANC (cells/µl)  | > 1,500                                     | 1,001–1,500                               | 500–1,000                                 | < 500                                      |
| Renal           | UOP > 0.5 and no change in sCr or rise < 0.3 | UOP < 0.5 for 6–12 h and sCr increase > 0.3 in 48 h or > 1.5–1.9 × LPC value within 7 days | UOP < 0.5 for ≥ 12 h and ≥ 2.0-2.9 × LPC value | UOP < 0.5 for ≥ 12 h and ≥ 3 × LPC value or sCr > 2.5 or dialysis |
| CNS             | Baseline responsiveness                    | Any change in status                      | Lethargic or hypotonic                    | Unresponsive                               |

CMV, conventional mechanical ventilation; CPAP, continuous positive airway pressure; ECLS, extracorporeal life support; GA, gestational age; HFNC, high-flow nasal cannula; HFV, high-frequency ventilation; LPC, lowest previous sCr; MAP, mean arterial pressure; NIPPV, non-invasive positive pressure ventilation; OI, oxygenation index; SBP, systolic blood pressure; sCr, serum creatinine; UOP, urine output.
Sepsis is classified according to the infant's age at the onset of symptoms to: Early-onset sepsis defined as the onset of symptoms before 7 days of age, although some experts limit the definition to infections occurring within the first 72 hours of life (Wynn et al., 2014)(2) and Late-onset sepsis that defined as the onset of symptoms at ≥ 7 days of age similar to early-onset sepsis, there is variability in the definition, ranging from an onset at > 72 hours of life to ≥ 7 days of age (Edwards MS, 2004)(4).

Early-onset neonatal sepsis occurs in utero from either transplacental or, more commonly, ascending bacteria entering the uterus from the vaginal environment following membrane rupture.. (5). Premature rupture of membranes (PROM) is a common event in obstetrics that has a major impact in pregnancy outcome. (6).

The overall incidence of neonatal sepsis ranges from one to five cases per 1000 live births. Estimated incidence rates vary based on the case definition and the population studied. Globally, neonatal sepsis and other severe infections were responsible for an estimated 430,000 neonatal deaths in 2013, accounting for approximately 15 percent of all neonatal deaths (7). Rates of neonatal sepsis increase with decreasing gestational age(8). The estimated incidence of sepsis (both early- and late-onset) in term neonates is one to two cases per 1000 live births (9).

Group B Streptococcus (GBS) and Escherichia coli are the most common causes of both early- and late-onset sepsis, accounting for approximately two-thirds of early-onset infection (10). Other bacterial agents associated with neonatal sepsis include: Listeria monocytogenes accounts for rare sporadic cases of neonatal sepsis, usually acquired transplacentally (11)). Staphylococcus aureus, including community-acquired methicillin-resistant S. aureus, is a potential pathogen in neonatal sepsis (12). Bacteremic staphylococcal infections in term infants usually occur in association with skin, bone, or joint sites of involvement. Enterococcus is a commonly encountered pathogen among preterm infants. The most common viral causes of sepsis are: Herpes simplex virus associated with substantial morbidity and mortality. Manifestations of viral infections can result in presentations similar to sepsis and might be localised to the skin, eyes, and mouth, involve the CNS, with onset between days 5–9 of life (13). Enterovirus infections might develop meningoencephalitis, myocarditis, and hepatitis, following poor feeding, lethargy, fever, irritability, hypoperfusion, and jaundice (14).

Preterm low birthweight infants have a 3–10 times higher incidence of infection than full-term normal birthweight infants. Immune dysfunction and an absence of transplacentally acquired maternal IgG antibodies in premature infants might increase risk of infection. (15).

Maternal factors are associated with an increased risk of sepsis, particularly group B Streptococcus (GBS) infection (2) include Chorioamnionitis and urinary tract infections, Aspiration or ingestion of bacteria in amniotic fluid might lead to congenital pneumonia or systemic infection (16), Intrapartum maternal temperature ≥ 38°C (100.4°F), Delivery at < 37 weeks’ gestation, Maternal GBS colonization, Membrane rupture ≥ 18 hours – The risk of proven sepsis increases 10-fold to 1 percent when membranes are ruptured beyond 18 hours (17).
Clinical manifestations range from subtle symptoms to profound septic shock, (16).

Hematological indices such as total white blood cell count, absolute neutrophil count (ANC), absolute band count (ABC), immature to total white blood cell ratio (I:T ratio) and platelet count are commonly used in the evaluation of neonatal sepsis (18). More recently, advanced white blood cell indices such as mean neutrophil volume (MNV), mean monocyte volume (MMV), and distribution width (NDW; MDW) are emerging as possible additional markers of NS (19). WBC count of < 5000 to 7500/mm³ have been used for the diagnosis of neonatal sepsis. Leucopenia has shown to have low sensitivity (29%) but high specificity (91%) for the diagnosis of neonatal sepsis, Neutropenia has shown to be more predictive of neonatal sepsis than neutrophilia (20). Biomarkers for diagnosis of neonatal sepsis have been discovered that help in the early diagnosis of neonatal sepsis, before the onset of clinical manifestation so that early treatment of sepsis can be started and neonate can be properly managed (21).

Materials And Methods

The present study is a prospective cross-sectional study, was conducted on 40 neonates delivered in Obstetrics and Gynecology department, Minia University Children and Maternal hospital. A total of 80 neonates were included in the study, 40 of them had been admitted in our neonatal intensive care unit have been taken as a study group, in addition to 40 healthy control newborns were selected during follow up in our NICU, during the period from July 2018 to January 2019.

Cases of neonatal sepsis were selected for this study on the basis of standard risk factors, symptoms and signs of neonatal sepsis according to neonatal-specific SOFA .(3)

Neonates born by spontaneous vaginal delivery or cesarean section between gestational weeks 37 and 42, according to ultrasonographic investigations and the new Ballard Score, who were diag- nosed with suspected or proven sepsis, were included in the study. Delivery room data of all mothers and neonates (sex, BW, birth height [BH], birth head circumference [BHC], weeks of gestation [WG], Apgar scores at 1 and 5 minutes after birth, and mode of delivery) were recorded.

Exclusion criteria comprised multiple pregnancies, prematurity (< 37 completed gestational weeks), post-maturity (> 42 completed gestational weeks), small for gestational age (SGA) or large for gestational age (LGA) neonates by week of pregnancy, preeclampsia, gestational diabetes mellitus (GDM), chorioamnionitis, the mother used tobacco during pregnancy, congenital major anomalies, cyanotic congenital heart disease, and negative values of together with C-reactive protein (CRP), and procalcitonin were excluded from the study.

We hypothesized that NLR and PLR ratios in early- onset neonatal sepsis could be used as adjunct diagnostic methods. We calculated that a sample size of 40 in the study group and Another 40 neonates of matchable age and sex, apparently healthy were enrolled in the study as a control group. would allow us to detect differences between the 2 groups.
Clinical and Laboratory Evaluation

All sepsis workup was performed for the study group neonates at postnatal 24 hours of life. Proven neonatal sepsis is defined as a positive blood culture accompanied by systemic signs of infection (respiratory distress, apnea, cyanosis, abdominal distention, and so on) within the first 3 days of life. Suspected neonatal sepsis is defined from negative blood, urine, and CSF cultures, but significant clinical signs of infection and positive laboratory parameters (an immature to total neutrophil ratio [I/T ratio] > 0.2; total white blood cells [WBCs] of either < 5 × 10⁹/L or > 15 × 10⁹/L; thrombocytopenia [< 150,000/mm³]; CRP level > 1 mg/ dL; and procalcitonin level > 0.5 ng/mL). Meningitis was diagnosed from high leukocyte count (> 20/mm³), high protein concentration (> 150 mg/dL) in the CSF, and bacterial growth in the CSF culture.

Total blood count was that include hemoglobin, RBCS, red cell indices (MCV, MCH and MCHC), platelet count and white blood cell count (total and differential). It was determined by automated hematology analyzer, CELLTAC G (NIHON KOHDEN CORPORATION). Differential leucocytic count was confirmed by microscopic examination of Lishman stained blood film and I/T was calculated by the immature /total neutrophil ratio. The NLR was calculated by the neutrophil /lymphocyte ratio, and PLR by the platelets /lymphocyte ratio. ESR was determined by Westergren Method. CRP levels were measured by immunoturbidimetric method, and procalcitonin levels were measured by Electrochemiluminescence immunoassay “ECLIA” method (Roche cobas 6000; Roche Diagnostics GmbH, Mannheim, Germany).

The study protocol was approved by ethical committee, Faculty of Medicine, Minia University. A written consent was obtained from one of parents to agree to participate in the study.

Statistical Analysis

All statistical tests done by SPSS version 20 in the form of Descriptive data and Analytical statistics, Descriptive statistics were calculated for the data in the form of Mean and standard deviation for quantitative data. Mean ± SD and Frequency and distribution for qualitative data. In the statistical comparison between the different groups.

Results

This study was conducted with 60 term, appropriate for gestational age (AGA), singleton neonates, of them, 30 were diagnosed with neonatal EOS, and 30 were healthy controls. Comparison between studied patients with EOS and controls regarding the demographic characteristics in (Table 1), As shown in the table Studied patients with EOS had significant higher APGAR score at 1st minute and higher incidence of positive consanguinity (42.5%) compared to controls (17.5%), (p = 0.01). Maternal characteristics are shown in (Table 2 ),PROM was found to be a major maternal risk factor represented in 50% of cases, Mothers of patients had significant different causes of maternal illness such as (UTI, polyhydramnios, cardiac causes, abortion, abruption, HCV). The clinical characteristics of neonates with EOS are shown in(Table 3), Out of 40 Full-term neonates who were affected by early-onset sepsis, 29(72.5%) cases had respiratory distress, 8(20%) cases had cyanosis,3(7.5%) cases had Apnea. Refusal of feeding (ROF) was the most common complaint presented by cases 36 (90%) followed by vomiting 1(2.5%), feeding
intolerance 1 (2.5%). Out of 40 cases 22 (55%) had disturbed conscious level (DCL), 12 cases (30%) presented by seizures. Twenty-six cases (65%) presented with poor peripheral perfusion and shock. Out of 40 cases 29 (72.5%) cases were edematous, 11 (27.5%) cases had hepatomegaly. Markers in studied patients with EONS and control group are shown in (Table 4).

We found that Cases had significant higher leucocyte count compared to controls (p = 0.004). also Cases had significant lower platelet count and lymphocytes compared to controls, (p = 0.04). Also cases had significant increase in immature neutrophil count and I/T ratio compared to controls, (p = 0.0001).

Comparing NLR and PLR between cases and controls, cases had significant higher values of these ratios rather than controls indicating their valuable role in detection of early-onset neonatal sepsis (p = 0.0001).

Regarding CRP and Procalcitonin, cases had significant higher levels of CRP and Procalcitonin rather than controls (p = 0.0001).

We found that Out of 40 cases, the most common gram negative organism was isolated from blood culture causing neonatal sepsis was klebseilla (50%), followed by staph hemolyticus (17.5%), then coagve staph (7.5%), candida albicans (7.5%), MRSE (5%), enterococcus (5%), MRSA(2.5%), candida and klebseilla (2.5%). (table 5) .from our statistical study we found that At a cutoff value 0.1; NLR had sensitivity 67% and specificity 99% and at a cutoff value 7; PLR had sensitivity 70% and specificity 73% .Also at a cutoff value 4.7; CRP had sensitivity 80% and specificity 70% and at a cutoff value 85.5; Procalcitonin had sensitivity 82% and specificity 90%. Also NLR had PPV 98%, PLR had PPV 72% and thus suggest that NLR and PLR are strong positive diagnostic markers in detecting early onset neonatal sepsis, also their negative results NPV of NLR (75%), NPV of PLR (71%) are very good at reassuring that neonates don’t have neonatal sepsis (table 6).

**Discussion**

Neonatal sepsis is a significant global health problem associated with high mortality and poor long-term outcomes for survivors particularly in under-resourced settings (22).

In one Egyptian study, the total mortality rate for the proven neonatal sepsis was 51% and 42.9% for EOS and LOS, respectively. Coagulase negative staphylococci were predominant isolates in both EOS and LOS followed by Klebsiella pneumoniae. Also they noticed that most of the bacterial isolates had low sensitivity to the commonly used empiric antibiotics. However, 70.1% exhibited multidrug resistance. Best sensitivities among Gram-positive isolates were found against imipenem, ciprofloxacin, vancomycin, and amikacin. (23)

We aimed in our study to assess the Platelet to Lymphocyte ratio (PLR) and the Neutrophil to Lymphocyte ratio (NLR) and determine their value as diagnostic markers for detection of EOS in Full-term newborns.

During sepsis or tissue infection Neutrophils are activated, causing their numbers in circulation to rapidly rise (24). Neutrophils are the most abundant leukocyte circulating in the bloodstream, comprising well
over 50% of leukocytes, and these cells are particularly adept at phagocytosing and killing microbes (25).

Circulating platelet–neutrophil complexes occur in a diverse range of inflammatory disorders and sepsis). Activated platelets bind to neutrophils in the blood and mediate neutrophil recruitment to sites of injury and infection (26).

Though White blood cell count (WBC) is one of the routinely done diagnostic tests for sepsis work up, was believed to be reliable indicators of infection but now are known to be insensitive and nonspecific. Furthermore, a single leukocyte count obtained shortly after birth is not adequately sensitive for diagnosing neonatal sepsis (27).

We found that Cases had significant higher leucocyte count compared to controls indicating role of leukocytosis in diagnosis of neonatal sepsis (p = 0.004). also Cases had significant lower platelet count and lymphocytes compared to controls, this observation correlates relation of thrombocytopenia and neonatal morbidity as major consequences of neonatal sepsis (p = 0.04). Also cases had significant increase in immature neutrophil count and I/T ratio compared to controls, this indicates the importance of CBC with differential in detecting early-onset neonatal sepsis (p = 0.0001)

IN Our study, Comparing NLR and PLR between cases and controls, cases had significant higher values of these ratios rather than controls indicating their valuable role in detection of early-onset neonatal sepsis (p = 0.0001).

In our study CRP is important biomarker in the diagnosis of neonatal sepsis, that agreed with (Sorsa and Abebe, 2018) (27), (Hotoura et al., 2012) (28) who reported that CRP is a useful diagnostic test for the early stages of neonatal sepsis reaching a peak during the first 24–48 hours with better sensitivity and specificity. (Albrich and Harbarth, 2015) (29), (Gillfillan and Bhandari, 2017) (30), (Ng et al., 2004) (31) and (Franz et al., 2004) (32) stated that diagnostic accuracy of CRP clearly improves by the combination with other biomarkers such as interleukins or procalcitonin. Our study revealed the significance of Procalcitonin as alternative biomarker to CRP in diagnosis of EONS, that agreed with (Chiesa et al., 2015) (33).

Moreover our results are in contrary with (Çelik et al., 2016) (19) who reported that though, white blood cell (WBC) count, immature/total leukocyte ratio (IT ratio), absolute leukocyte count and acute phase reactants such as C-reactive protein (CRP), procalcitonin (PC) and interleukin-6 (IL-6) are the most frequently used parameters for the diagnosis of newborn sepsis, these inflammatory markers, however, may be affected by maternal and fetal non-infectious conditions, and their different half-lives may decrease their ability to provide a definitive diagnosis of sepsis.

Our results show higher incidence of klebseilla in blood culture and these results agreed with (Vergnano et al., 2005) (34) who stated that Gram negative organisms are mainly represented by Klebsiella, Escherichia coli, Pseudomonas, and Salmonella, Gram positive organisms: Staphylococcus aureus, coagulase negative staphylococci (CONS), Streptococcus pneumoniae, and Streptococcus pyogenes.
Isolated Neonatal surveillance in developed countries generally identifies GBS and E coli as the dominant EOS pathogens and CONS the dominant LOS pathogen followed by GBS and Staph aureus (Vergnano et al., 2005) (34). Our results shows that blood culture was significantly valuable in diagnosis of neonatal sepsis, this is consistent with (Walker et al., 2019)(35), (Arayici et al., 2019) (36) and (Wynn and J.L., 2016)(37) who stated that blood culture is the gold standard laboratory technique for diagnosis. (Weinbren et al., 2018) (38) found the same result that laboratory processing of blood cultures has remained static over the past 30 years, despite increasing antibiotic resistance and advances in analyser design.

On the other hand; even though blood culture is said to be the gold standard diagnostic test for sepsis, there are a number of limitations including; unavailability in the majority of developing country, associated technical problem and it takes more than three days to see at least the first preliminary result .As a result, the diagnosis of neonatal sepsis is based on clinical assessment and the management also rely on empirical treatment protocol which usually results in unnecessary hospital stay, increase irrational use of antibiotics and incur an unnecessary cost for the family (27).

From the results of our study we concluded that:

- NLR, PLR are reliable predictive markers in detecting early onset neonatal sepsis as PPV of NLR was 98%, PLR was 72%..
- Regarding to laboratory findings, Leucocytosis, thrombocytopenia, high CRP, high Procalcitonin and positive blood culture were associated with risk of neonatal sepsis.
- NLR and PLR shows higher specificity results compared to CRP and Procalcitonin.

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Tables

Table (1):
|                                | patients with EONS | Controls N= 40 | P value N= 40 |
|--------------------------------|-------------------|----------------|--------------|
| **Age (days)**                 |                   |                |              |
| Mean ± SD                      | 2.25 ± 0.9        | 2 ± 0.9        | 0.2          |
| Median                         | 3                 | 2              |              |
| **Weeks of gestation**         |                   |                |              |
| Mean ± SD                      | 36.8 ± 0.2        | 36.7 ± 0.7     | 0.7          |
| Median                         | 37                | 37             |              |
| **Birth weight**               |                   |                |              |
| Mean ± SD                      | 2.9 ± 0.2         | 3 ± 0.2        | 0.1          |
| Median                         | 2.9               | 3              |              |
| **Maternal age**               |                   |                |              |
| Mean ± SD                      | 25.8 ± 4          | 25.7 ± 4.1     | 0.9          |
| Median                         | 26.5              | 26             |              |
| **Apgar score(minutes)**       |                   |                |              |
| 1st : Mean ± SD                | 5.2 ± 0.8         | 12.2 ± 4.5     | 0.0001*      |
| Median                         | 5                 | 9              | 0.09         |
| 5th : Mean ± SD                | 8.9 ± 0.3         | 9.07 ± 0.3     |              |
| Median                         | 9                 | 9              |              |
| **Consanguinity**              |                   |                |              |
| positive                       | 17 (42.5%)        | 7 (17.5%)      | 0.01*        |
| negative                       | 23 (57.5%)        | 33 (82.5%)     |              |

P value calculated by Mann-Whitney test for all quantitative variables except for maternal age calculated by independent sample t-test and by chi-square test for qualitative variables (< 0.05 is considered significant).

Table (2):
| Patients with EONS (n = 40) |
|---------------------------|
| Maternal age              |
| Mean ± SD Range           |
| 25.8 ± 4.05               |
| Maternal illness          |
| UTI                       |
| 11 (27.5%)                |
| Polyhydramnios            |
| 2 (5%)                    |
| Cardiac                   |
| 2 (5%)                    |
| Abortion                  |
| 4 (10%)                   |
| Abruptio                  |
| 1 (2.5%)                  |
| HCV                       |
| 2 (5%)                    |
| PROM                      |
| Yes                       |
| 20 (50%)                  |
| No                        |
| 20 (50%)                  |
| Consanguinity             |
| Yes                       |
| 17 (42.5%)                |
| No                        |
| 23 (57.5%)                |

Table (3):

| Signs                                         | N (%)         |
|-----------------------------------------------|---------------|
| Respiratory                                   |               |
| RD                                            | 29 (72.5%)    |
| Cyanosis                                      | 8 (20%)       |
| Apnea                                         | 3 (7.5%)      |
| Feeding                                       |               |
| ROF                                           | 36 (90%)      |
| Fair                                          | 2 (5%)        |
| Vomiting                                      | 1 (2.5%)      |
| Intolerance                                   | 1 (2.5%)      |
| Neurological                                  |               |
| DCL                                           | 22 (55%)      |
| Seizures                                      | 12 (30%)      |
| Fair neurological                             | 6 (15%)       |
| Cardio-Circulatory (peripheral perfusion,      |               |
| shock)                                        | 26 (65%)      |
| Poor                                          | 14 (35%)      |
| Fair                                          |               |
| GIT                                           |               |
| Oedema                                        | 29 (72.5%)    |
| Hepatomegaly                                  | 11 (27.5%)    |
Table (4):

|                          | Cases                      | Controls                  | P value N=40 |
|--------------------------|----------------------------|---------------------------|--------------|
| WBCs                     |                            |                           |              |
| Mean ± SD                | 17 ± 9.3                   | 11.9 ± 4.7                | 0.004*       |
| Median                   | 15.5                       | 11.7                      |              |
| Interquartile range      | 10.2–22.4                  | 8–15.8                    |              |
| Platelets                |                            |                           |              |
| Mean ± SD                | 193 ± 84                   | 227.5 ± 78.4              | 0.04*        |
| Median                   | 174.5                      | 234                       |              |
| Interquartile range      | 136-257.5                  | 162.5-303.2               |              |
| Immature neutrophils     |                            |                           |              |
| Mean ± SD                | 13.6 ± 19                  | 2.8 ± 12.3                | 0.0001*      |
| Median                   | 8                         | 0                         |              |
| Interquartile range      | 0-20.3                     | 0–0                       |              |
| I/T                      |                            |                           |              |
| Mean ± SD                | 0.5–0.9                    | 0.05–0.2                  | 0.0001*      |
| Median                   | 0.1                       | 0                         |              |
| Interquartile range      | 0-0.5                      | 0–0                       |              |
| Lymphocytes              |                            |                           |              |
| Mean ± SD                | 23.2 ± 15                  | 37.9 ± 15.5               | 0.0001*      |
| Median                   | 18.5                      | 35.5                      |              |
| Interquartile range      | 12.2–34.7                  | 25-51.5                   |              |
| CRP                      |                            |                           |              |
| Mean ± SD                | 14-13.4                    | 8.1 ± 13.7                | 0.0001*      |
| Median                   | 7.7                       | 2.8                       |              |
| Interquartile range      | 4.9–17.9                   | 1.3–8.6                   |              |
| Procalcitonin            |                            |                           |              |
| Mean ± SD                | 139.1 ± 66.7               | 53.8 ± 26                 | 0.0001*      |
| Median                   | 126.5                      | 54.5                      |              |
| Interquartile range      | 97–157                     | 35.2–76                   |              |
| NLR                      |                            |                           |              |
| Mean ± SD                | 0.8 ± 1.1                  | 0.08 ± 0.3                | 0.0001*      |
| Median                   | 0.4                       | 0                         |              |
| Interquartile range      | 0-1.1                      | 0–0                       |              |
| PLR                      |                            |                           |              |
| Mean ± SD                | 15 ± 12.4                  | 5.9 ± 3.5                 | 0.0001*      |
| Median                   | 9.7                       | 5.5                       |              |
| Interquartile range      | 6.2–22                     | 3.09–7.5                  |              |

P value calculated by Mann-Whitney test except for WBCs calculated by independent sample t-test (< 0.05 is considered significant).

(WBCS = white blood cells, I/T = immature to total neutrophilic count, NLR = neutrophil to lymphocyte ratio, PLR = platelet to lymphocyte ratio)
Table (5):

| Blood culture      | N (%) |
|--------------------|-------|
| Klebsiella         | 20 (50%) |
| Candida albicans   | 3 (7.5%) |
| Candida-klebsiella | 1 (2.5%) |
| Staph hemolyticus  | 7 (17.5%) |
| Strept pneumonia   | 1 (2.5%) |
| MRSA               | 1 (2.5%) |
| MRSE               | 2 (5%) |
| enterococcus       | 2 (5%) |
| Coag –ve staph     | 3 (7.5%) |

(MRSA = Methicillin-resistant Staphylococcus aureus, MRSE = Methicillin-resistant Staphylococcus epidermidis, CoNS = coagulase-negative staphylococci)

Table (6):

| Cutoff value | AUC  | 95% CI   | Sensitivity | Specificity | PPV  | NPV  |
|--------------|------|----------|-------------|-------------|------|------|
| NLR          | 0.1  | 0.79     | 0.68–0.89   | 67%         | 99%  | 98%  | 75%  |
| PLR          | 7    | 0.78     | 0.68–0.88   | 70%         | 73%  | 72%  | 71%  |
| CRP          | 4.7  | 0.76     | 0.65–0.87   | 80%         | 70%  | 72%  | 77%  |
| Procalcitonin| 85.5 | 0.92     | 0.86–0.98   | 82%         | 90%  | 89%  | 83%  |

(NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, PPV: positive predictive value, NPV: negative predictive value, LR+: positive likelihood ratio, LR-: negative likelihood ratio.)