

Deoxyribonuclease 1 as a Marker of Neonatal Sepsis and Its Comparison with CRP

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ABSTRACT

Background: Neonatal sepsis is a bacterial bloodstream infection that causes severe clinical symptoms and is often fatal or results in permanent, irreversible impairments. In order to prevent the development of serious and sometimes deadly consequences, it is imperative that babies suspected of having sepsis have timely diagnosis and treatment.

Objective: This work aimed to investigate DNase 1 level in neonates with neonatal sepsis and compare DNase 1 to CRP as markers of neonatal sepsis.

Patients and methods: This is a prospective case-control study that included 60 neonates admitted to the neonatal intensive care unit (NICU) in Menoufia University Hospital from January 2023 to February 2024.

Results: TLC, CRP, AST, and DNase1 were significantly higher among cases than controls. While PH, PCO₂, HCO₃, and albumin were significantly lower among cases than controls. As well as total serum bilirubin (TSB), direct serum bilirubin (DSB), and Na⁺ were significantly lower among cases. On the other hand, there was no significant difference among the studied groups regarding urine culture, ALT, creatinine, Urea, and K⁺ (P>0.05). In the current study, 11 cases had positive blood culture (36.7%), 5 of them had Methicillin-resistant Staphylococcus aureus (MRSA) (16.7%), 4 had klebsiella MDR (13.3%), one case had E. coli or Gram -ve bacilli (3.3%).

Conclusion: In conclusion, DNase1 was significantly higher among CS LBW and pneumonia+ LONS diagnoses than NVD, NBW, and another diagnosis. DNase1 was significantly higher among cases than controls. Both CRP and DNase1 can be used as predictor tools for neonatal sepsis, but DNase1 had more sensitivity and specificity (98.7%, 68%) at cutoff level 0.9926 ng/ml, as compared to CRP (96.2%, 70.3%) at cutoff level 2.40.

Keywords: CRP, DNase 1, Neonatal sepsis.

INTRODUCTION

Neonatal infection is characterized as a systemic inflammatory reaction that develops in the neonate because of a suspected or proven infection ⁽¹⁾.

Neonatal bacterial infections account for approximately a quarter of all neonatal deaths annually, or 680,000 infant deaths, according to estimates from the WHO for 195 countries ⁽²⁾. Rapid and accurate diagnosis of neonatal sepsis poses challenges in routine clinical practice due to a multitude of factors. Therefore, it is necessary to enhance the accuracy of diagnostic tests ⁽³⁾.

The clinical diagnosis of sepsis in neonates presents a challenge due to the obscurity of several sepsis-related symptoms, which may also manifest in conjunction with other noninfectious conditions. Early diagnosis and appropriate antibiotic administration should be the focal points of treatment, well in advance of blood culture results; emphasis should be placed on the suspicion index, which is calculated using clinic and laboratory parameters ⁽⁴⁾. There are two distinct types of neonatal sepsis, Premature onset neonatal sepsis is the initial condition, presenting itself within the first 72 hours after birth ⁽⁵⁾. Postnatal and typically arises from the assimilation of maternal microbiota. Case fatality is approximately 16%; however, mortality is 54% among preterm neonates born between 22 and 24 weeks of gestation ⁽⁶⁾.

The second condition is late onset neonatal sepsis, which manifests beyond 72 hours postnatally and is attributed to environmental microorganisms.

Late-onset neonatal sepsis risk factors include mechanical ventilators, vascular access catheters and other nosocomial interventions that are frequently utilized in intensive care for premature infants ⁽⁵⁾.

On the first day of life, the immune system is initially exposed to a wide variety of microbes and pathogens, neutrophils serve as the primary line of defense against them through the secretion of neutrophil extracellular traps (NETS), which comprise proteolytic enzymes like neutrophil elastase (NE), DNA filaments, and citrullinated histones. Immune response hemostasis is ensured by DNases' degradation of NETS ⁽⁷⁾. Specific elevated markers of NET formation are associated with sepsis and other inflammatory conditions ⁽⁸⁾.

Thus, our aim was to investigate DNase 1 level in neonates with neonatal sepsis and compare DNase 1 to CRP as indicators of neonatal sepsis.

PATIENTS AND METHODS

This prospective case-control study included 30 neonates diagnosed with sepsis who were admitted to the neonatal NICU, Menoufia University Hospital, and 30 age and gender matched controls. This study was conducted between January 2023 and December 2023.

Inclusion criteria: Both sexes of neonates, born by spontaneous vaginal delivery or cesarean section having clinical symptoms and signs that were indicative of an early-onset infection or pneumonia and necessitate an evaluation for suspected sepsis as well as antibiotic treatment.

Exclusion criteria: Patients with known immunodeficiencies in their siblings and those who were born with fatal congenital or chromosomal abnormalities.

The included 60 neonates were divided into two groups; **Group I (cases)** consisted of 30 neonates diagnosed with sepsis and positive CRP >6 mg/L, who were admitted to NICU. Clinical sepsis was defined according to the following categories of clinical signs derived from sepsis score and CRP +ve result, and **Group II (control)**, consisting of 30 healthy volunteers matched sex and age.

The following was conducted on every neonate: Detailed history included name, age, sex, mode of delivery, and residence. Antenatal and perinatal data collection: Gestational age (GA) using new Ballard score (9). Birth weight (BW): were classified. Clinical or culture-proven chorioamnionitis (based on delivering an obstetrician's diagnosis). Maternal intrapartum antibiotic exposure (including the rationale for use, type, and duration of exposure prior to delivery categorized as < or ≥4 hours). Administration of antenatal glucocorticoids and timing of the final dose prior to delivery. Placental histology, e.g., placenta previa and accreta. Metabolic changes During enrollment, comorbidities were gathered, including streptococcus agalactiae (GBS) colonization and the incidences of premature rupture of membranes (PROM) in their mothers Apgar score NSe at 1 & 5 min as well as methods and duration of resuscitation.

Complete clinical examination: focusing on vital signs and general examination, including blood pressure, temperature, heart rate, and respiratory rate. Systemic examination included chest, abdominal, cardiac, and neurological examination with particular emphasis on clinical sepsis scores focusing on Lethargy, poor suckling, respiratory distress, apnea, altered muscle tone, bradycardia, cyanosis, poor perfusion, food intolerance, thermoregulatory disorders including hypothermia or fever and metabolic acidosis).

Investigations included complete blood count (CBC), C-reactive protein (CRP), serum electrolytes: Ca⁺⁺, Na⁺, K⁺, Kidney function tests (creatinine and urea), Liver function tests (AST and ALT), Venous blood gases (pH, PCO₂, HCO₃, BE), random blood sugar and deoxyribonuclease1 (DNASE1).

Blood culture: using Bactec device.

Ethical approval:

This work was approved by the Ethical Committee of Faculty of Medicine, Menoufia University. Before starting the study, each participant's parent provided signed informed consent. This investigation was conducted according to the code of the world medical association (Declaration of Helsinki) for studies including humans.

Statistical analysis

Results were tabulated and statistically analyzed using a SPSS V. 25.0 program. Data description was in the form of frequency and proportion for qualitative data and mean (±) SD for quantitative data. The mean is the sum of all observations by the number of observations. Standard deviation measures the degree of scattering of individual varieties around their means. Chi-squared (χ²), Standard student-t test (t), Mann-Whitney test (U), One way ANOVA (F), Kruskal Wallis test (K), Pearson correlation, The ROC curves. A P value below 0.05 was considered to indicate statistical significance.

RESULTS

Age, gender, GA, and mode of delivery did not differ significantly among the groups under investigation (P>0.05). While BW, APGAR score 1 MIN, and APGAR score 5 MIN were significantly lower among cases (2.81±0.64, 5.87±0.78, 7.53±1.17) than controls (3.31±0.33, 7.47±0.51, 9.47±0.51) respectively (P<0.001). Also, significant differences existed between the groups under study regarding BW delivery (P<0.001), (**Table 1**).

Table (1): Demographic and clinical data among the studied groups (n=60).

| | Variable | Cases (n=30) | | Controls (n=30) | | X ² | P value |
|-----------------------------|----------|--------------|-------|-----------------|--------|----------------|---------|
| | | N | % | N | % | | |
| Age (days) | Mean± SD | 13.87±10.76 | | 4.10±1.54 | | t=4.923 | 0.057 |
| Sex | Male | 19 | 63.33 | 15 | 50.00 | 1.086 | 0.297 |
| | Female | 11 | 36.67 | 15 | 50.00 | | |
| GA (weeks) | Mean± SD | 37.67±2.01 | | 37.70±0.79 | | t=0.085 | 0.933 |
| Birth weight (Kg) | Mean± SD | 2.81±0.64 | | 3.31±0.33 | | t=3.795 | <0.001* |
| Mode of delivery | CS | 27 | 90.00 | 21 | 70.00 | FE= | 0.053 |
| | NVD | 3 | 10.00 | 9 | 30.00 | | |
| Birth weight classification | NBW | 18 | 60.00 | 30 | 100.00 | FE= | <0.001* |
| | LBW | 12 | 40.00 | 0 | 0.00 | | |
| APGAR score 1 min | Mean± SD | 5.87±0.78 | | 7.47±0.51 | | t=9.451 | <0.001* |
| APGAR score 5 min | Mean± SD | 7.53±1.17 | | 9.47±0.51 | | t=8.324 | <0.001* |

GA: gestational age, CS: cesarean section, NVD: Normal vaginal delivery, LBW: Low birth weight, NBW: Normal birth weight, t: independent t test, X²: Chi square test, FE: Fisher exact test, *Significant.

TLC, CRP, AST, and DNASE1 were significantly higher among cases than controls (P<0.001). Also, Ica and Mg²⁺ were significantly lower among cases than controls (P<0.001). While PH, PCO₂, HCO₃, and Alb were significantly lower among cases than controls (P<0.001). As well as, TSB, DSB, and Na were significantly lower among cases than controls (P<0.001). In this respect, Hb, PLT, and HCT were significantly lower among cases than controls (P<0.05). On the other hand, there was no significant differences among the studied groups regarding urine culture, ALT, creatinine, urea, and K⁺ (P>0.05), (**Table 2**).

Table (2): Laboratory investigations among the studied groups (n=60).

| Variable | Cases (n=30) | | Controls (n=30) | | t | P value |
|----------------------------|----------------------|---|-------------------|---|---------|---------|
| | N | % | N | % | | |
| | Mean± SD | | Mean± SD | | | |
| | Median (IQR) | | Median (IQR) | | | |
| Random blood sugar (mg/dl) | 150.20±35.83 | | -- | | --- | --- |
| TLC (x10 ⁹ /L) | 14.80 (2.30-23.80) | | 8.35 (4.50-11.20) | | U=93.0 | <0.001* |
| Hb (g/dl) | 8.87±2.11 | | 13.93±2.35 | | 7.564 | <0.001* |
| PLT (x10 ⁹ /L) | 125.00 (30.4-627) | | 252.00 (185-403) | | U=560.0 | <0.001* |
| HCT (%) | 30.79±7.93 | | 37.7±4.55 | | 9.052 | 0.029* |
| CRP (mg/ dl) | 64.50 (10.10-245.00) | | 4.25 (2.30-5.70) | | U=436 | <0.001* |
| PH | 7.24 (7.00-7.32) | | 7.40 (7.33-7.45) | | U=0.0 | 0.955 |
| PCO ₂ (mmHg) | 30.00 (25.00-34.00) | | 43.00 (35-54) | | U=211 | <0.001* |
| HCO ₃ (mmol/L) | 12(9.00-15.00) | | 21.00 (18-25) | | U=447 | <0.001* |
| ALT (U/L) | 28.50 (12.00-203.00) | | 28.50 (21-39) | | U=0.00 | 0.965 |
| AST (U/L) | 72.00 (15.00-379.00) | | 46.00 (38-55) | | U=225.0 | 0.001* |
| Alb (g/dl) | 3.25 (1.10-4.50) | | 3.85 (3.50-4.60) | | U=129.0 | <0.001* |
| TSB (mg/dl) | 5.68±1.34 | | 17.86±1.33 | | 18.04 | <0.001* |
| DSB (mg/dl) | 0.83±0.20 | | 3.13±0.68 | | 10.12 | <0.001* |
| Creatinine (mg/dl) | 0.48±0.11 | | 0.43±0.10 | | 0.80 | 0.424 |
| Urea (mg/dl) | 33.41±8.11 | | 31.70±7.81 | | 0.56 | 0.573 |
| Na ⁺ (mmol/L) | 135.65±4.57 | | 140.3±3.22 | | 4.55 | <0.001* |
| K ⁺ (mmol/L) | 4.43±0.69 | | 4.17±0.47 | | 1.67 | 0.099 |
| Ica (mg/dl) | 0.711±0.15 | | 1.04±0.05 | | 2.34 | 0.023* |
| Mg ⁺⁺ (g/L) | 0.96±0.21 | | 1.27±0.31 | | 6.26 | <0.001* |
| DNASE1 (ng/ml) | | | | | U= | |
| Median (IQR) | 2.89 (0.95-43.94) | | 0.38 (0.23-0.48) | | 523.9 | <0.001* |

Median and IQR: non-parametric test.

TLC: Total Leukocyte Count, **Hb:** hemoglobin, **PLT:** platelet count, **HCT:** hematocrit test, **CRP:** C-reactive protein, **PCO₂:** partial pressure of carbon dioxide, **HCO₃:** bicarbonate, **ALT:** alanine transaminase, **AST:** aspartate aminotransferase, **Alb:** Albumin, **TSB:** Total Serum Bilirubin, **DSB:** Direct Serum Bilirubin, **Na:** Sodium, **K:** Potassium, **DNASE:** deoxyribonuclease, *: significant, **DNASE:** Deoxyribonuclease, **X²:** Chi square test, *: significant, U: Mann Whitney u test, t: independent test.

Regarding the blood culture, 11 cases had positive results (36.7%), 5 of them had MRSA (16.7%), 4 had klebsiella MDR (13.3%), one case had ECOLI or Gram -ve bacilli (3.3%) (**Table 3**).

Table (3): Blood culture among the studied groups (n=60).

| Variable | Cases (n=30) | | Controls (n=30) | | X ² | P value |
|----------------------|--------------|------|-----------------|-------|----------------|---------|
| | N | % | N | % | | |
| Blood culture | | | | | | |
| NG | 19 | 63.3 | 30 | 100.0 | | |
| MRSA | 5 | 16.7 | 0 | 0.0 | 13.46 | 0.009* |
| Klebsiella MDR | 4 | 13.3 | 0 | 0.0 | | |
| ECOLI | 1 | 3.3 | 0 | 0.0 | | |
| Gram -ve bacilli | 1 | 3.3 | 0 | 0.0 | | |

NG: no growth, **MRSA:** Methicillin-Resistant Staphylococcus aureus, **MDR:** multidrug resistance, **X²:** Chi square test, *: significant.

Regarding the outcome of the study, a significant difference was noted between the examined groups (P=0.005). Among cases, 23 (76.67%) were discharged and 7 (23.33%) were died. Moreover, hospital stays significantly longer among cases group (14.50±6.62) than controls (2.97±0.89), (P<0.001) (**Table 4**).

Table (4): Outcome among the studied groups (n=60).

| Variable | Cases (n=30) | | Controls (n=30) | | t | P value |
|------------------------------|--------------|-------|-----------------|--------|-------|-------------------|
| | N | % | N | % | | |
| Outcome | | | | | | |
| Discharge | 23 | 76.67 | 30 | 100.00 | FE= | 0.005* |
| Died | 7 | 23.33 | 0 | 0.00 | 7.925 | |
| Hospital stays (days) | | | | | | |
| Mean± SD | 14.50±6.62 | | 2.97±0.89 | | 9.455 | <0.001* |

FE: Fisher exact test, t: independent test, *: significant

DISCUSSION

Approximately one-third of the four million neonatal deaths that are attributed to infections occur annually on a global scale. Bacterial meningitis and sepsis remain major causes of neonatal mortality, particularly among preterm newborn infants. It is critical to provide prompt diagnosis and treatment for newborns suspected of having sepsis to avoid the development of critical and potentially fatal complications. Diagnosis of suspected neonatal sepsis is challenging in comparison to the clear and effective treatment alternatives. Diagnosing sepsis in premature infants presents challenges owing to the limited availability of dependable diagnostic tests and the indistinct clinical manifestations ⁽¹⁰⁾.

Regarding age, gender, GA, or mode of delivery, there was no statistically significant difference among the groups that were examined. While BW, APGAR score 5 MIN and APGAR score 1 MIN were significantly lower among cases than controls. Also, regarding birth term delivery, the groups under investigation showed a significant difference. In line with our study, **Ragab et al.** ⁽¹¹⁾ did not observe any statistically significant difference in gender or mode of delivery among the groups under investigation, whereas the neonatal sepsis group exhibited a significant decrease in both BW and GA compared to the control group. There was no significant association observed between the mode of delivery and an elevated sepsis incidence. This also aligns with the results reported by **Mustafa et al.** ⁽¹²⁾ who discovered no relation between neonatal sepsis and mode of delivery.

This disagrees with **Aguilar and Maramba-Lazarte** ⁽¹³⁾, who found more than half of neonates who developed septicemia 58 (56%) were delivered via cesarean section and 45 (44%) were delivered by vaginal delivery. However, infants delivered vaginally had a higher incidence of early-onset sepsis than those delivered via cesarean section, according to **Hornik et al.** ⁽¹⁴⁾. This could potentially be explained by the increased likelihood of vaginal flora contamination during labor among those who deliver vaginally.

Ragab et al. ⁽¹¹⁾ documented a significant association between decreased GA and BW with an elevated incidence of sepsis. This aligns with the findings of **Du et al.** ⁽¹⁵⁾, neonates with suspected sepsis had significantly lower GA and BW than those with no sepsis. This disagrees with **Dzwonek et al.** ⁽¹⁶⁾ who found not statistically significant between preterm case

and control groups regarding GA and BW. This may be due to different inclusion criteria and sample size of patients included in this study. Additionally, premature birth and APGAR scores below 7 at 5 minutes were associated with early onset neonatal sepsis and neonatal sepsis overall, according to **Rafi et al.** ⁽¹⁷⁾. **Gebremedhin et al.** ⁽¹⁸⁾ similarly observed that patients exhibited a significantly lowered APGAR score in comparison to the control group. Unlike our study, **Abd Elbeshery et al.** ⁽¹⁹⁾ found no statistically significant difference among the groups under investigation regarding demographic data, concerning the APGAR score at 1 minute and 5 minutes.

Our study showed that TLC, CRP, AST and DNASE1 were significantly higher among cases than controls while Hb, PLT, HCT, PH, PCO2, HCO3 and Alb were significantly lower among cases than controls. As well as, TSB, DSB and Na were significantly lower among cases than controls. Conversely, urine culture, ALT, creatinine, Urea, and K showed no statistically significant differences observed among the groups under investigation. Consistent with our study, **Wahab Mohamed and Saeed** ⁽²⁰⁾ discovered that the septic group exhibited a significantly higher TLC than the control group. **Abd Elbeshery et al.** ⁽¹⁹⁾ showed that confirmed NS had significantly higher TLC and I/T ratio values than suspected NS and controls, whereas HB and PLT values decreased significantly.

Furthermore, **Ragab et al.** ⁽¹¹⁾ reported that the neonatal sepsis group had significantly decreased hemoglobin levels and platelet counts. These agree with **Yapakçı et al.** ⁽²¹⁾, who found hemoglobin levels were lower in the septic group than in the control group. Moreover, **Mondal et al.** ⁽²²⁾ discovered that platelet count was lower in both proven and probable sepsis cases than in control cases. Additionally, **Hofer et al.** ⁽²³⁾ reported that despite the emergence of novel biomarkers, CRP remains one of the most extensively researched and widely employed laboratory assays utilized in the diagnosis of neonatal sepsis at present. In accordance with the research conducted by **Chirico and Loda** ⁽²⁴⁾, a significant rise in CRP occurs 10–12 hours after the initiation of an infection. Several conditions result in elevated CRP levels.

Also, **Ragab et al.** ⁽¹¹⁾, Cases exhibited a significantly elevated serum CRP compared to controls. This finding is consistent with the results reported by **Hisamuddin et al.** ⁽²⁵⁾, which indicated that 29.25% of observable neonatal sepsis cases were confirmed via

blood culture, while 70.75% did not exhibit such sepsis on blood culture. In the diagnosis of acute neonatal sepsis, CRP exhibited a specificity of 53.49% and a sensitivity of 76.92%, whereas it demonstrated a negative predictive value of 48.94% and a positive predictive value of 80%. Due to the fact that CRP is one of the acute-phase reactants generated by the liver in reaction to microbial invasion or trauma, it exhibited a diagnostic accuracy of 70.07% in identifying neonatal sepsis.

Moreover, **Abd Elbeshery et al.** ⁽¹⁹⁾ discovered that CRP levels in NS (confirmed & suspected) were significantly higher than in controls. Consistent with our discovery, **Abd Elbeshery et al.** ⁽¹⁹⁾ discovered that CRP levels in the NS (confirmed & suspected) were significantly elevated compared to the control group, with a cutoff value of 22 mg/l, a moderate specificity (80%), and a high sensitivity (94%). Although high cutoff values are debated, the diagnostic accuracy of CRP remains largely variable.

According to a study by **Hisamuddin et al.** ⁽²⁵⁾, the CRP has a specificity of 53.49% and a sensitivity of 76.92% when used to diagnose acute NS, with an NPV of 48.94% and PPV of 80%. **Pradhan et al.** ⁽²⁶⁾ reported that the diagnostic accuracy of CRP was 70.07 % overall in the diagnosis of NS. CRP estimation was found to play a role in the diagnosis of NS, but its specificity is insufficient to constitute a dependable sole indicator. In 2016, CRP sensitivity for sepsis was determined to be 84.3% at a cutoff of 50 mg/l, with a specificity of 46.1% and AUC of 0.683 (CI = 0.529–0.836). The diagnostic accuracy remained unchanged even when combined with additional sepsis parameters.

However, **Póvoa et al.** ⁽²⁷⁾ stated that the specificity of CRP is 75% and the sensitivity is 98.5%. In addition, **Pradhan et al.** ⁽²⁶⁾ revealed that these variations could potentially be attributed to patient-related factors, various etiology of NS, individual responses to sepsis or genetic variation, and the accuracy of diagnostic kits. Notably, increased plasma concentrations of DNase1 were observed in both the EONS and LONS groups, according to **Lenz et al.** ⁽²⁸⁾. **Cheng et al.** ⁽²⁹⁾ stated that further research is required to evaluate these impressions due to the possibility of alternative pathophysiological explanations. CfDNA and its dipeptide DNase I participate in several immunological processes, including necrosis. Additionally, it would be intriguing to investigate the relationship between DNase1 enzyme activity and DNase1 concentration to discover the regulation of proteins in preterm infants under septic conditions.

Our study showed that 11 cases had positive blood culture (36.7%), 5 of them had MRSA (16.7%), 4 had klebsiella MDR (13.3%), one case had ECOLI or Gram -ve bacilli (3.3%). The findings of a study conducted by **Ragab et al.** ⁽¹¹⁾ indicated that 64 (69.7%) cases had positive culture results and 28 (30.4%) cases had negative culture results. These results align with the conclusions stated by **Hisamuddin et al.** ⁽²⁵⁾, who stated

that 30% of sepsis cases had culture-proven sepsis, in addition, **El-Mashad et al.** ⁽³⁰⁾ stated that culture-proven sepsis was present in 52.5 % of all sepsis cases.

Furthermore, pathogenic organism identification in neonates with sepsis syndrome is a challenging endeavor, according to **Edmond and Zaidi** ⁽³¹⁾. A small sample size is frequently obtained from newborns, and the administration of antepartum or intrapartum antibiotics to mothers may reduce the bacterial load in neonates. Sterile venipuncture in infants may present significant technical challenges, which can result in extremely high contamination rates. The function of coagulase-negative Staphylococci (e.g., Staphylococci epidermidis), which are both pathogenic and part of the normal skin flora in preterm infants and those with indwelling blood vessel catheters, may also be misunderstood.

Contrary to the findings of our research, **Ragab et al.** ⁽¹¹⁾ documented that Klebsiella pneumoniae was the prevailing microorganism detected in positive blood cultures (26.1%), followed by Pseudomonas (13.0%), and the least common organisms were methicillin-resistant Staphylococcus aureus (10.9%), Candida albicans (8.7%), Escherichia coli (6.5%), and Staphylococcus aureus (4.3%). Consistent with the results reported by **Celik et al.** ⁽³²⁾, K. pneumonia was the prevailing microorganism in positive blood cultures. On the other hand, **Kayange et al.** ⁽³³⁾ found that most of the isolates were composed of gram-negative bacteria, whereas Klebsiella pneumoniae was the most frequently recovered isolates in their research. The prevalence of a pathogen responsible for septicemia within the unit may be attributed to the selective pressure exerted by antibiotics. This has been found to be true with neonatal septicemia due to *Klebsiella pneumoniae*.

Our study showed that, among cases, 23 (76.67%) were discharged and 7 (23.33%) had died. Consistent with our research, **Kayange et al.** ⁽³³⁾ discovered that neonatal sepsis had a 19% mortality rate, which is comparable to what **Singh et al.** ⁽³⁴⁾ observed in other East African studies; this can be attributed to hospitals providing comparable services and management approaches. Although the observed difference was not statistically significant, neonates who were presented with early-onset disease had a higher mortality rate.

CONCLUSION

In conclusion, DNASE1 was significantly higher among CS LBW and pneumonia+ LONS diagnoses than NVD, NBW, and other diagnoses. DNASE1 was significantly higher among cases than controls. Both CRP and DNASE1 can be used as predictor tools for neonatal sepsis, but DNASE1 had more sensitivity and specificity (98.7%, 68%) at cutoff level 0.9926 ng/ml, as compared to CRP (96.2%, 70.3%) at cutoff level 2.40mg/l.

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REFERENCES

1. **Alkan Ozdemir S, Ozer E, Ilhan O et al. (2018):** Diagnostic value of urine soluble triggering receptor expressed on myeloid cells (sTREM-1) for late-onset neonatal sepsis in infected preterm neonates. *J International Med Research.*, 46(4):1606-16.
2. **Liu L, Oza S, Hogan D et al. (2015):** Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. *Lancet*, 385(9966):430-40.
3. **Song Y, Chen Y, Dong X et al. (2019):** Diagnostic value of neutrophil CD64 combined with CRP for neonatal sepsis: A meta-analysis. *Americ J Emergency Med.*, 37:1571–1576.
4. **Arcagok B, Karabulut B (2019):** Platelet to lymphocyte ratio in neonates: a predictor of early onset neonatal sepsis. *Mediterranean J Hematolo and Infect Dis.*, 11(1): e2019055. doi: 10.4084/MJHID.2019.055.
5. **Procianoy R, Silveira R (2020):** The challenges of neonatal sepsis management. *Jornal de Pediatria.*, 96:80-86.
6. **Shane A, Sánchez P, Stoll B (2017):** Neonatal sepsis. *Lancet*, 390: 1770–1780.
7. **Mantovani A, Cassatella M, Costantini C et al. (2011):** Neutrophils in the activation and regulation of innate and adaptive immunity. *Nat Rev Immunol.*, 11:519–31.
8. **Shen X, Cao K, Jiang J et al. (2017):** Neutrophil dysregulation during sepsis: an overview and update. *Journal of Cellular and Molecular Medicine*, 21(9):1687-1697.
9. **Ballard J, Khoury J, Wedig K et al. (1991):** New Ballard Score, expanded to include extremely premature infants. *J Pediatr.*, 119(3):417-23.
10. **Aliefendioglu D, Gürsoy T, Çağlayan O (2014):** Can resistin be a new indicator of neonatal sepsis. *Pediatr Neonatol.*, 55:53–57.
11. **Ragab S, El-Sayed H, El-Deeb S (2022):** Salivary C-reactive protein, mean platelet volume, and neutrophil-lymphocyte ratio as diagnostic markers of neonatal sepsis. *Menoufia Medical Journal*, 35(4):1810-14.
12. **Mustafa S (2005):** Evaluation of C-reactive protein as early indicator of blood culture positivity in neonates. *Pak J Med Sci.*, 21: 96–73.
13. **Aguilar C, Maramba-Lazarte C (2011):** A cross-sectional analysis of neonatal bacteremia in the neonatal intensive care unit of the Philippine general hospital from July to December 2006. *PIDSP Journal*, 12: 17-27.
14. **Hornik C, Benjamin D, Becker K et al. (2012):** Use of the complete blood cell count in early-onset neonatal sepsis. *Pediatr Infect Dis J.*, 31:799-04.
15. **Du J, Li L, Dou Y et al. (2014):** Diagnostic utility of neutrophil CD64 as a marker for early-onset sepsis in preterm neonates. *PLoS One*, 9:e102647. doi: 10.1371/journal.pone.0102647.
16. **Dzwonek A, Neth O, Thiébaud R et al. (2008):** The role of mannose-binding lectin in susceptibility to infection in preterm neonates. *Pediatr Res.*, 63:680–685.
17. **Rafi A, Miah M, Wadood A et al. (2020):** Risk factors and etiology of neonatal sepsis after hospital delivery: A case-control study in a tertiary care hospital of Rajshahi, Bangladesh. *PLoS One*, 15(11): e0242275. doi: 10.1371/journal.pone.0242275
18. **Gebremedhin D, Berhe H, Gebrekirstos K (2016):** Risk factors for neonatal sepsis in public hospitals of Mekelle City, North Ethiopia, 2015: unmatched case control study. *PLoS One*, 11(5): e0154798. doi: 10.1371/journal.pone.0154798.
19. **Abd Elbeshery M, Husein S, Abed N (2022):** Genetic Expression of High Mobility Group Box 1 in Neonatal Sepsis. *Benha Medical Journal*, 39(3):971-85.
20. **Wahab Mohamed W, Saeed M (2012):** Mannose-binding lectin serum levels in neonatal sepsis and septic shock. *J Matern Fet Neonat Med.*, 25:411–414.
21. **Yapakçı E, Tarcan A, Çelik B et al. (2009):** Serum pro-hepcidin levels in term and preterm newborns with sepsis. *Pediatr Int.*, 51:289–292.
22. **Mondal S, Nag D, Bandyopadhyay R et al. (2012):** Neonatal sepsis: role of a battery of immunopharmacological tests in early diagnosis. *Int J Appl Basic Med Res.*, 2: 43-47.
23. **Hofer N, Zacharias E, Müller W et al. (2012):** An update on the use of C-reactive protein in early-onset neonatal sepsis: current insights and new tasks. *Neonatology*, 102:25–36.
24. **Chirico G, Loda C (2011):** Laboratory aid to the diagnosis and therapy of infection in the neonate. *Pediatr Rep.*, 3: 1. doi: 10.4081/pr.2011.e1.
25. **Hisamuddin E, Hisam A, Wahid S et al. (2015):** Validity of C-reactive protein (CRP) for diagnosis of neonatal sepsis. *Pak J Med Sci.*, 31:527-31.
26. **Pradhan S, Ghimire A, Bhattarai B et al. (2016):** The role of C-reactive protein as a diagnostic predictor of sepsis in a multidisciplinary intensive care unit of a tertiary care center in Nepal. *Indian J Crit Care Med.*, 20(7):417-420.
27. **Póvoa P, Almeida E, Moreira P et al. (1998):** C-reactive protein as an indicator of sepsis. *Intensive Care Med.*, 24(10): 1052–6.
28. **Lenz M, Maiberger T, Armbrust L et al. (2022):** cfDNA and DNases: New Biomarkers of Sepsis in Preterm Neonates—A Pilot Study. *Cells*, 11(2):192. doi: 10.3390/cells11020192.
29. **Cheng Z, Abrams S, Toh J et al. (2020):** The critical roles and mechanisms of immune cell death in sepsis. *Frontiers in Immunology*, 11:1918. doi: 10.3389/fimmu.2020.01918.
30. **El-Mashad G, El-Sayed H, Rizk M et al. (2017):** Mean platelet volume and serum uric acid in neonatal sepsis. *Menouf Med J.*, 30:581-87.
31. **Edmond K, Zaidi A (2010):** New approaches to preventing, diagnosing, and treating neonatal sepsis. *PLoS Med.*, 7:e1000213. doi: 10.1371/journal.pmed.1000213
32. **Celik I, Demirel G, Uras N et al. (2015):** The role of serum interleukin-6 and C-reactive protein levels for differentiating aetiology of neonatal sepsis. *Arch Argent Pediatr.*, 113:534–537.
33. **Kayange N, Kamugisha E, Mwizamholya D et al. (2010):** Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza- Tanzania. *BMC Pediatr.*, 10: 39. doi: 10.1186/1471-2431-10-39.
34. **Singh S, Dutta S, Narang A (2003):** Predictive clinical scores for diagnosis of late onset neonatal septicemia. *J Trop Pediatr.*, 49(4):235–9.