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Performance of Interleukin-27 in Diagnosis of Neonatal Sepsis

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ABSTRACT

Background: Neonatal sepsis remains a major cause of mortality and morbidity in neonates, Traditional methods for diagnosis like blood culture has a low sensitivity and delayed results in neonates. Interleukin-27 (IL-27) is a heterodimeric cytokine produced by antigen presenting cells upon exposure to microbial products and inflammatory stimuli IL-27 regulates T cell function and has both pro- and anti-inflammatory effects. Ablation of IL-27 activityconfers a survivaladvantage in sepsis. Thus, it is biologically plausible that IL-27 can serve as a sepsis diagnostic biomarker.The aim of the present study was to evaluate the value of interleukin-27 in diagnosis of neonatal sepsis. **Patients and methods:**This study involved 50 neonates admitted to NICU at ZagazigUniversity Hospitals. Neonates were divided into two groups: Cases groupof 25 neonates with manifestations of neonatal sepsis&Control groupof 25 neonates. Full history and clinical examination were done.Laboratory investigationmainly Measurement of IL-27 were performed.**Results:** the mean age in septic group was 9.77±5.8 days and 4.24± 6.75days.There is non-significant difference between the studied groups regarding gender, age and birth weight.There is statistically non-significant difference between the studied groups regarding platelet count. There is statistically significant difference between them concerning CRP**.**There is statistically significant difference between the studied groups concerning IL-27**.**Regarding culture examination, patients had growth for E. coli. Klebseilla pneumonia, staph epididymis, staph hominis, staph aureus, streptpyogenes and acenitobacter in cultures.There is statistically significant negative correlation between IL-27 among the studied patients and both gestational age. **Conclusion:**Interleukin-27 is a better sepsis marker for predicting outcomes and guides the initiation of antibiotic therapy in neonates.

Keywords: Interleukin-27; Sepsis; Neonates

INTRODUCTION

Neonatal sepsis is still considered as a major laboratory and medical challenge due to non-specific clinical signs, lack of standard boundary limit values of sepsis markers and difficulty of differentiating it from non-infectious conditions such as respiratory distress syndrome **(1).**Identification of biomarkers is mandatory to enable fast and reliable diagnosis sepsis in its earliest stages **(2).**

The need for accurate biomarkers to aid in the timely and accurate diagnosis of neonatal sepsis thus remains as important as ever. The ideal biomarker should demonstrate a consistent and predictable pattern in both response to infection and treatment **(3).** There are no management guidelines addressing the need for sepsis evaluations in late preterm infants. The high proportion of infants evaluated with a blood culture and the small number of infection episodes suggests that the yield from

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sepsis evaluations in the majority of late preterm infants is low. Among very premature infants sepsis evaluations and early onset sepsis rates are higher (90% and 1-2%, respectively)**(4).**Therefore, this study aimed to evaluate the value of interleukin-27 in diagnosis of neonatal sepsis

PATIENTS AND METHODS

This study involved 50 neonates admitted to NICU at Zagazig University Hospitals. Neonates were divided into two groups: Cases group (A) included 25 neonates with manifestations of neonatal sepsis.Control group (B) included 25 neonates. They were presented with other manifestations as jaundice than neonatal sepsis and selected from our NICU.Their infection was excluded by complete blood count, C- reactive protein and blood cultures.An informed consent was taken from parents or guardian of each eligible neonate before his /her enrollement.

Inclusion & Exclusion criteria:

Neonates were considered at risk for sepsis based on the presence of one the prolonged rupture of membranes,endotracheal intubation, mechanical ventilation,umbilical catheterization or total parenteral nutrition Clinical signs as respiratory distress or apnea, tachycardia, or bradycardia. While, neonates with intracranial hemorrhage and subdural hematoma, supraventricular, hypoplastic left heartsyndrome and hypovolemic shock were excluded.

Full history, clinical examination and laboratory investigationwere done.

Measurement of IL-27 in plasma concentrations

IL-27 (EMD Millipore Corporation, Billerica, MA) and procalcitoninm(Bio-Rad, Hercules, CA) protein concentrations were measured in duplicated plasma samples using a magnetic bead multiplex platform and a Luminex 100/200 System (Luminex Corporation, Austin, TX), according to the manufacturers' specifications **(5)**.

Statistical analysis:

Data analyzed using Microsoft Excel software and Statistical Package for the Social Sciences (SPSS version 20.0) software. Data qualitative represent as number and percentage , quantitative continues group represent by mean ± SD. Differences between quantitative independent multiple by ANOVA or Kruskal Wallis,. P value was set at <0.05 for significant results &<0.001 for high significant result.

RESULTS

In the current study, the mean age in septic group was 9.77±5.8 days and 4.24± 6.75days.There is non-significant difference between the studied groups regarding gender, age and birth weight**(Table 1)**.There is statistically non-significant difference between the studied groups regarding platelet count**(Figure 1).**

There is statistically significant difference between them concerning CRP**(Figure 2).**There is statistically significant difference between the studied groups concerning IL-27**(Figure 3).**

Regarding culture examination, patients had growth for E. coli. Klebseilla pneumonia, staph epididymis, staph hominis, staph aureus, streptpyogenes and acenitobacter in cultures shown in **(Table 2)**.There is statistically significant negative

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correlation between IL-27 among the studied patients and both gestational age **(Figure 3).**

Table (1) Comparison between the studied groups regarding demographic data:

Parameters	Study groups		
	Sepsis group N=25(%)	Control group N=25 (%)	p
Gender (%): Female Male	44 56	62 38	0.217
Age (day): Mean ± SD	9.77 ± 5.8	4. 24 ± 6. 75	0.334
Birth weight (kg): Mean ± SD	2.25 ± 1.07	2.80 ± 0.73	0.402

t Independent sample t test χ^2 Chi square test Z Mann Whitney test

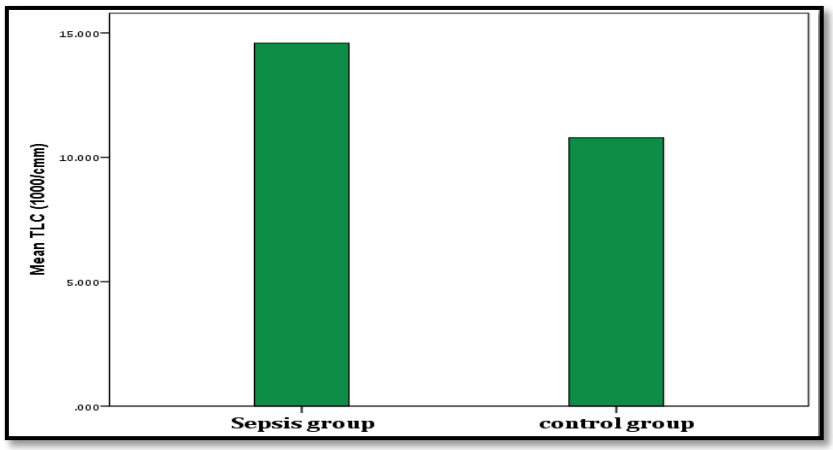

Figure (1) Simple bar chart showing comparison between the studied groups regarding TLC level

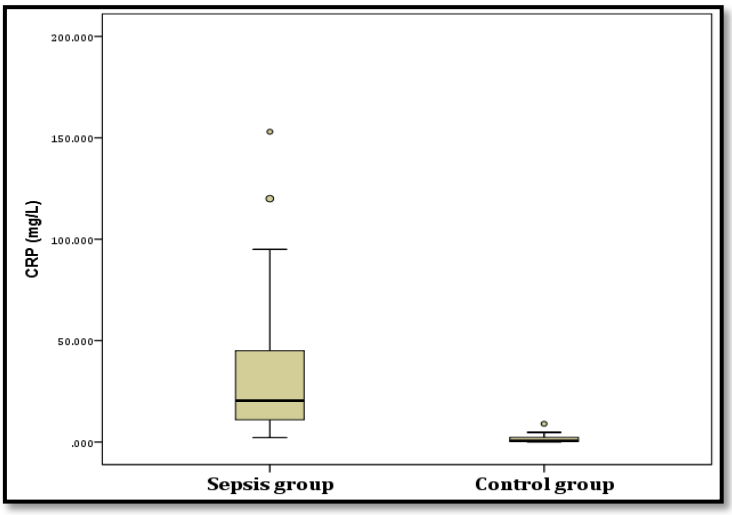

Figure (2) Boxplot showing comparison between the studied group regarding CRP level

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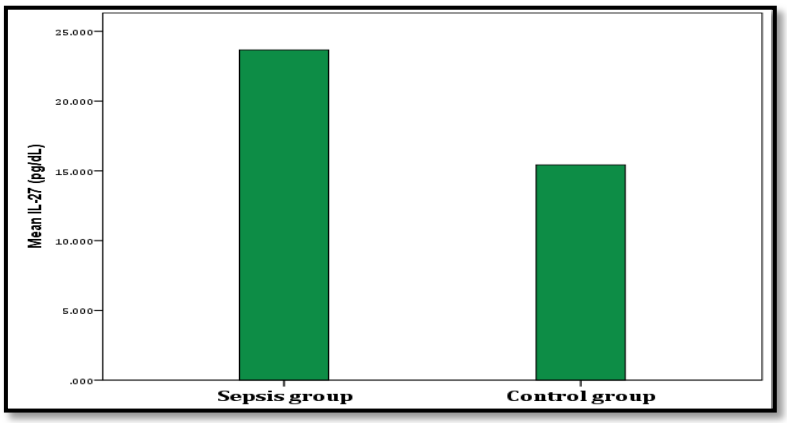

Figure (3) Simple bar chart showing comparison between the studied group regarding IL-27 level

Table (2) Comparison between the studied groups regarding result of culture examination:

Culture	Study groups
	Sepsis group
	N=25 (%)
Actinobacter	7
E.coli	35
Klebsiella pneumonia	10
staph epidermidis	5
Staph hominis	7.5
Staph aureus	15
Strept pyogenes	3

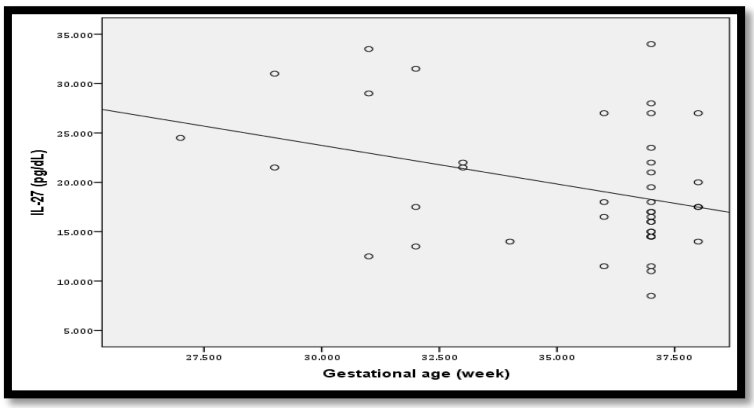

Figure (3) Scatter dot graph showing significant negative correlation between IL-27 and gestational age

DISCUSSION

Neonatal sepsis refers to an infection involving the bloodstream in newborn infants less than 28 days old. It remains a leading cause of morbidity and mortality among neonates, especially in middle and lower-income countries **(6).**Rapid and precise diagnosis of neonatal sepsis is a pivotal process, as it augments the effectiveness of medical treatment leading to a proper outcome. An accurate ruling out of sepsis is also critical as it allows avoidance of neonatal exposure to broad-

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spectrum antibiotics and reduces the risk of emergence of antibiotic resistant bacterial strains (**7).**In addition to blood culture, polymerase chain reaction (PCR) amplification of highly conserved DNA sequences found in all bacteria would permit rapid and sensitive detection of bacteria in blood specimens. But its results do not depend on the bacterial viability and so it may still be positive even after antibiotic treatment **(8).**

Suspected neonates are subjected to broad-spectrum antibiotic treatment empirically until sepsis can be excluded; this antibiotic overuse favors the development of resistance **(9)**. So, improving the accuracy of the diagnostic tests may decrease the indiscriminative use of antibiotics in cases without sepsis **(10).**

In this study we investigated 50 neonates admitted to NICU at Zagazig University Hospitals. Neonates were divided into two groups: Cases group (A) of 25 neonates with manifestations of neonatal sepsis & Control group (B) of 25 neonates. This study aimed to evaluate the value of interleukin-27 in diagnosis of neonatal sepsis.

Our study revealed non-significant difference between the studied groups regarding gender, age and birth weight**.Fahm et al. (11)** enrolled 84 neonates and classified them into two groups. Early onset neonatal sepsis group involved 47 neonates (29 males and 18 females) with a mean age (27.04 ± 3.3 hours) and a control group that involved 37 neonates (22 males and 15 females) with a mean age (33.44 ± 4.0 hours). The mean of gestational age in weeks for the sepsis group was (35.66 ± 2.63) and for the control group was (36.30 ± 1.93).

Our study concur with **Jainet al. (12)** studied 106 neonates with suspected sepsis, the most common clinical presentation was the respiratory distress and letharginess.

In our study,there is statistically non-significant difference between the studied groups regarding platelet count. This is against results of **Murrayet al. (13)** reported that one of the major causes of thrombocytopenia in neonates is sepsis and thrombocytopenia may rapidly become very severe with the lowest platelet count reached within 24–48 hours after onset of infection. Also against results of **Ahmadet al. (14)** found out that 24.7% of thir septic neonates had thrombocytopenia . Median platelet count of cases died was significantly lower compared with the platelet counts of those cases who were discharged.

Similar results with**Horniket al. (15)** showed that low white blood cell counts, low absolute neutrophil counts, and high immature-to-total neutrophil ratios were associated with increasing odds of infection (highest odds ratios: 5.38, 6.84, and 7.97, respectively). Specificity and negative predictive values were high (73.7–99.9% and >99.8%). However, sensitivities were low (0.3–54.5%) for all complete blood cell count indices analyzed.

The current study showed neonates had growth for E. coli. Klebseilla pneumonia, staph epididymis, staph hominis, staph aureus, streptpyogenes and acenitobacter**.Rashwanet al. (16)** found out that Klebsiellapneumoniae and Staphylococcus aureus were the most common Gram-negative and Gram-positive

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isolates, respectively. **Al-Zahraniet al. (9)** in Saudi Arabia found that Gram-negative organisms (Klebsiella and E. coli) were the most common, followed by GBS.

Our results agree with the study of **Fahm et al. (11)**revealed blood culture test of the early onset neonatal sepsis group revealed *Klebsiellapneumoniae*as the major detected organisms followed by methicillin resistant *Staphylococcus aureus*(MRSA); while *Escherichia coli* (*E. coli*) and coagulase negative *Staphylococcus* (CoNS) were detected in equal numbers, and both *Candida* and *Enterococcus* were the minor detected organisms: Klebsiellapneumoniae, MRSA, E.Coli, CoNS, Candida, and Enterococcus prevailed in cultures of 44.68%,21.28%,14.89%,14.89%,2.13% and 2.13% of their studied patients respectively.

Although Lancefield group B streptococcus (*Streptococcus agalactiae*) represent the major pathogen responsible for early onset sepsis **(17)**.The current study showed E-Coli was the most frequent isolated organism from blood culture in neonatal sepsis group, this difference may be attributed to intrapartum administration of ampicillin.

Our results are in agreement with **Hanna et al. (18)** suggest that IL-27 has a greater predictive value in patients with positive bloodstream infections compared with infections from other body compartments.

Moreover**Abo-Elmaged et al. (2015)**reported elevated IL-27 is correlated well with bacterial sepsis among neonatal patients with bloodstream infections and may provide additional diagnostic value along with other available biomarkers.Therefore, IL-27 levels in circulation may predict susceptibility to infection and related outcomes.

CONCLUSION

Interleukin-27 is a better sepsis marker for predicting outcomes and guides the initiation of antibiotic therapy in neonates.

No Conflict of interest.

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