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(RESEARCH ARTICLE)

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The role of neonatal procalcitonin and pro-inflammatory cytokines at birth in prediction of sepsis in neonates

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Abstract

Background: Septicemia, characterized by the presence of bacteria in the blood, is a life-threatening condition, particularly in neonates due to their underdeveloped immune systems. Early detection and prompt treatment are crucial for improving recovery outcomes. While several biomarkers have been proposed for diagnosing neonatal sepsis, none have proven fully reliable. This study aimed to investigate the potential of procalcitonin, IL-1β, IL-6, and TNF-α levels at birth as predictors for neonatal septicemia.

Methods: The study enrolled 246 neonates, collecting umbilical cord serum samples during delivery to analyze the levels of these biomarkers using enzyme-linked immunosorbent assay (ELISA). Neonates were monitored for a month, with those who developed septicemia forming the experimental group and those who did not serving as controls.

Results: Using the one-way analysis of variance (ANOVA), serum procalcitonin levels at birth was statistically significantly ($p < 0.05$) higher among neonates who developed septicemia in week 1 and 2 compare to the non-septicemic neonates. IL-6 and TNF-α also showed a statistically significant increase in neonates who developed septicemia in week 1. IL-1β showed no significant increase/decrease between septicemic neonates and non-septicemic neonates. PCT and TNF-α showed a strong positive correlation with neonatal septicemia while multiple regression analysis using IL-1β, IL-6, TNF-α and birth weight returned a statistically significant value; an indication of the predictive potentials of these markers in neonatal septicemia.

Conclusion: The study established that PCT and proinflammatory cytokines at birth are valuable biomarkers for predicting neonatal septicemia and should be integrated into clinical practice for early detection

Keywords: Inflammatory cytokines; Septicemia; Neonates; Interleukin; Procalcitonin

1. Introduction

Neonatal sepsis is a systemic infection that affects infants within their first 28 days of life, posing a significant risk for morbidity and mortality among newborns [1]. Early-onset neonatal sepsis (EOS) is defined by its onset timing, with variability depending on the infant's context. For infants in neonatal intensive care units (NICUs), EOS is characterized by bacteremia occurring within 72 hours of birth, while in term infants, it is defined as occurring within the first 7 days [2]. In preterm infants, early-onset neonatal sepsis (EOS) is most consistently defined as occurring within the first 3 days of life and is typically caused by bacterial pathogens transmitted vertically from the mother before or during delivery [3].

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A recent meta-analysis estimated the global incidence of neonatal sepsis to be 2824 per 100,000 live births [4], significantly higher than estimates reported in 2018 at 2202 per 100,000 live births [5]. Global estimates are primarily based on data from high-income countries (HICs). However, morbidity and mortality following neonatal sepsis are highest in low- and middle-income countries (LMICs), where data is scarce [6]. One major factor responsible for higher morbidity and mortality incidence rate in LMICs is lack of proper diagnostic techniques and poorly equipped health care facilities.

Neonatal sepsis remains a leading cause of morbidity and mortality in newborns due to their underdeveloped immune systemic which is unable to mount sufficient immune response against infection arising from the bloodstream [7]. It can be caused by bacteria, viruses, fungi and parasites, however bacterial sepsis accounts for most of the reported cases [7]. White blood cells (WBCs) are commonly used as markers of inflammation, but they are not reliable for diagnosing septicemia on their own, as various factors can influence their normal levels [8].

Based on time of onset, neonatal sepsis is categorised into Early Onset Sepsis (EOS) occurring within 72 hours after birth and Late Onset Sepsis (LOS) occurring after 72 hours of birth [9]. The place of birth, whether the neonate is born within the hospital (ie "inborn"), or the neonate was admitted to hospital with signs of sepsis (ie "outborn"), are often used when analysing the epidemiology and risk factors of neonatal sepsis [10, 11]. Data from previous studies suggests that EOS causing pathogens is transmitted from mother to neonate before or during delivery [12]. Early-onset neonatal sepsis is typically caused by organisms that colonize the genitourinary tract of mothers, leading to contamination of the amniotic fluid, placenta, cervix, or vaginal canal. The pathogen can spread to the fetus when the amniotic membranes rupture or even before labor begins, causing an intra-amniotic infection [13]. Consequently, the infant may acquire the pathogen either in utero or during birth. Pregnancy procedures that disrupt the amniotic cavity, such as cervical cerclage and amniocentesis, can also increase the risk of intra-amniotic infection and subsequent neonatal sepsis [14]. During labor, maternal risk factors for neonatal sepsis include prolonged rupture of membranes, fever, vaginal colonization with group B streptococcus (GBS), and GBS bacteriuria [11]. Infant risk factors associated with early-onset sepsis include prematurity/low birth weight, congenital anomalies, complicated or instrument-assisted delivery, and low APGAR scores (≤6 at 5 minutes). The immature immune system of premature infants, characterized by low immunoglobulin levels due to decreased transplacental transfer of maternal IgG, further increases the risk of sepsis in preterm infants [15].

The gold standard method for diagnosing neonatal sepsis involves obtaining a complete white blood cell count with differential, a single blood culture, urine cultures, and a lumbar puncture for cell count and culture [16]. Additional markers, such as C-reactive protein (CRP) and procalcitonin (PCT), are commonly used to manage and monitor infections and are the most frequently studied acute-phase reactants in neonatal sepsis. Procalcitonin, a propeptide of calcitonin produced primarily by monocytes and hepatocytes, is significantly elevated during infections in neonates, children, and adults [17]. It has a half-life of approximately 24 hours in peripheral blood. Cytokines, including interleukin 1 (IL-1), interleukin 6 (IL-6), and tumor necrosis factor-alpha (TNF-α), have also been studied as measures for neonatal sepsis, although none are currently used in routine clinical practice.

Being that EON is mainly due to maternal complications before or during delivery, analysing the levels of these sepsis markers at birth could predict the potential of neonates developing septicemia within the first 28 days of life, hence this study was undertaken.

2. Material and methods

2.1. Location Area

The study was conducted in two (2) selected antenatal homes namely; General Hospital Obiaruku and Eku Baptist Government Hospital, Delta State, Nigeria. According to the Nigeria Population Commission (2007), Delta state occupy a 16,842 square kilometre (6,503 sq meters) area of land which is located between longitude $5^0.00$ and $6^0.45$`East and latitude $5^000$ and $6^0.30$` North of the equator. It is a densely populated area of an estimated population of 4,112.445 (2,069,309 males and 2,043,136 females).

2.2. Study design

Study was experimental in nature. Study sample comprise of average population of neonates [per year] in the selected antenatal home. Neonates were prospectively studied, grouped into two based on the presence or absence of sepsis. Umbilical cord serum sample was assessed at birth from participant neonates, and was analysed for PCT, IL-1, IL-6 and TNF levels. These neonates were monitored to ascertain those who will be diagnosed with septicemia within the first

30 days of life. Neonates who developed septicemia through a positive culture result within the first month of life served as the experimental group while neonates without any clinical sign of septicemia served as control. Study was conducted at the obstetric and pediatric unit of General Hospital Obiaruku and Eku Baptist Government Hospital in Delta state, Nigeria, using neonates at birth. A detailed history of their mothers was taken and recorded on proforma that was specially designed for the study. Mothers of participant neonates who had antibiotics therapy within the last month of gestation and those with known viral infections were excluded from the study.

2.3. Population of study

Study population targeted neonates in Eku Baptist Government Hospital and General Hospital, Obiaruku all in Delta state, Nigeria. All neonates delivered at the obstetric unit of these selected hospitals and met the inclusion criteria were recruited for participation in this study.

2.4. Sample size and sampling technique

Purposive sampling technique was used in this study. The sample size was calculated using the Kish formula; with a prevalence of 20% resulting in a sample size of 246 neonates [18].

$$n = (Z_{1-\alpha})\ 2\ (P\ (1-P)/D^2)$$

Where,

- $Z_{1-\alpha}$ = confidence level as z-score (95% = 1.96 from z-table)
- P = Prevalence (20%)
- D = Absolute value (5%)

2.5. Inclusion criteria

All neonates delivered at the obstetric unit of the selected hospitals and whose mothers gave informed consent were selected for participation in the study.

2.6. Exclusion criteria

Neonates of mothers who refused to provide informed consent were excluded from the study. Neonates of mothers who developed any clinical signs of sepsis in week 37, 38 and 39 of their pregnancy were also excluded from the study. Neonates of mothers who were on any form of antibiotic therapy that may interfere with result were also excluded from the study. Out born neonates admitted into the pediatric unit of selected hospitals were excluded from the study.

3. Ethical Considerations

Ethical clearance (REC/FBMS/DELSU/20/82) was obtained from the Research and Ethics committee of the College of Health Sciences, Faculty of Basic Medical Sciences, Delta State University, Abraka, Delta State, Nigeria. Also, the Hospitals Management Board (HMB) of the Delta state gave an approval (A. 551/Vol. III/36) before commencement of study; especially with the condition that participants' physicians were directly involved in data collection and monitoring post birth. Again, using a carefully structured consent forms, informed consent was obtained from mothers of all participant neonates, to seek their consensual permissions before commencing investigation. Only mothers who consented to cooperate (haven been briefed on the rules and nitty gritty of the study) were examined.

3.1. Consent form

Consent form for a Study on "Potential Utilisation of Neonatal and Maternal C-reactive Protein, Procalcitonin and Proinflammatory Cytokines as Biomarkers of Septicemia"

Please tick the appropriate boxes **(YES OR NO)*

Taking Part	**YES**	**NO**
I have read and understood the research information sheet data		
I have been given the opportunity to ask questions about the research		
I agree to take part in the research		

I understand that my blood sample and that of my newborn will be collected for this research		
I understand that my taking part is voluntary; I can withdraw from the study at any time and I do not have to give any reasons for why I no longer want to take part.		
Use of Provided information		
I understand my personal details will not be revealed to people outside this research		
I understand that my words may be quoted in publications, reports, web pages, and other research outputs		
I would like my real name used in the above		
Use of provided information beyond this project		
I agree for my provided data to be archived for future documentation, reference or other research purposes		
I understand that other genuine researchers will have access to my provided data only if they agree to preserve the confidentiality of the information as requested in this form.		
I understand that other genuine researchers may use my words publications, reports, web pages and other research outputs only if they agree to preserve the confidentiality of information as requested in this form.		
So, we can use the data obtained from your experimental tests legally		
I agree that copyright of any of my tests related to this research be assigned to and used by the Researcher		

_____ _____

Name of Participant (Date and Signature) **Mr. Kelvin Obakore Gbagbeke,** (**Researcher**)

3.2. Sample Collection and Assays

Umbilical cord sample was collected from the subjects for this study. This was done by clamping the umbilical cord and using a five millilitres (5ml) disposable syringe to obtained intravenous blood from the umbilical cord vein. The umbilical cord sample collected was transferred into an EDTA sample collection container. Cord samples were then centrifuged at 6000 rpm for 10 minutes. The supernatant was collected using a micro-pipette to carry out the assay. Hemolysed samples were not used as they are not suitable for ELISA assay!

Assay kits were purchased from Corban Medical Resources Nigeria Limited, Onitsha Anambra State, Nigeria. The measurement of cytokines in sera using Human ELISA kit (Elabscience, Houston, Texas, USA) was performed according to manufacturer's instructions at the Clinical Chemistry Laboratory of the Central Hospital Warri, Warri, Delta State, Nigeria as described in detail below.

PCT, IL-1β, IL-6 and TNF-α concentrations in blood/plasma was determined quantitatively in vitro. Components of the test kit include 96 well assay plate, standard, sample diluent, assay diluent A, assay diluent B, detection reagent A, detection reagent B, wash buffer (25 x concentrate), substrate, stop solution, plate sealer.

3.3. Test Principle

The kit includes a microtiter plate that has been pre-coated with an antibody specific to the target antigen. After that, a biotin-linked antibody preparation specific for the target antigen is applied to the relevant microtiter plate wells, and each microplate well is incubated with avidin coupled to Horseradish Peroxidase (HRP). Then, in each well, a TMB substrate solution is applied. The only wells that change colour are those that contain target antigen, biotin-conjugated antibody, and enzyme-conjugated Avidin. The colour change is detected spectrophotometrically at a wavelength of 450 nm ± 2 nm after the enzyme-substrate reaction is halted by adding a sulphuric acid solution. By comparing the optical density of the samples to the standard curve, the concentration of target antigen in the samples is determined.

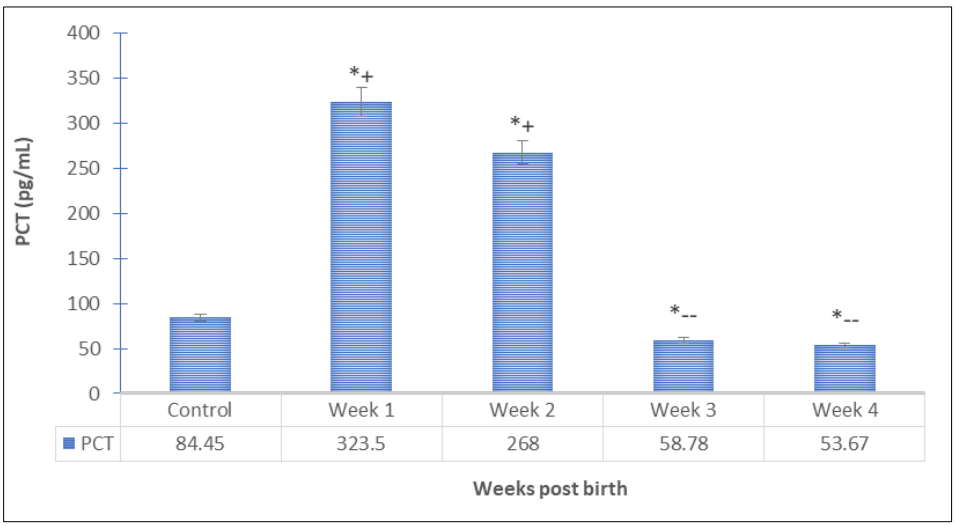
3.4. Assay procedure

- To the first two columns, Standard working solution was added: Each concentration of the solution is added in two wells, one on top of the other (100 uL for each well). The remaining wells was filled with the samples (100 uL for each well). The sealer that included with the kit was used to seal the plate. The wells were incubated for 90 minutes at 37°C.
- The liquid was removed from each well without washing it. To each well, 100 mL of Biotinylated Detection Ab working solution was added. The plate was sealed with the Plate Sealer. Everything was mixed together gently and incubated for 1 hour at 37°C.
- 350 uL of wash buffer was added to each well after aspirating or decanting the solution. After 1-2 minutes of soaking, the solution was aspirated from each well and wiped dry with clean absorbent paper. This step was repeated three times more. A microplate washer was used for this and other wash steps.
- Each well was filled with 100 liters of HRP Conjugate working solution. The plate was sealed with the Plate Sealer and incubated for 30 minutes at 37°C.
- The solution was removed from each well by aspirating or decanting it, then the wash process was repeated for five times as directed in step 3.
- Each well was filled with 90 litres of Substrate Reagent. A fresh coat of plate sealer was applied and incubated for around 15 minutes at 37°C. Light was kept away from the plate. Note: depending on the actual color change, the reaction time can be cut or extended, but not more than 30 minutes.
- To each well, 50 litres of Stop Solution was added.
- Using a microplate reader set to 450 nm, the optical density (OD value) of each well was determined at the same time.

3.5. Data and statistical analysis

Student's T-test and One Way Analysis of Variance (ANOVA) was used to compare differences in mean between and within groups. Pearson correlation coefficient was used to establish relationship between measured variables while multiple regression analysis was used for the predictive potential of variables. Confidence level for all statistical based calculations was set at p values < 0.05, while presenting results as mean ± SD.

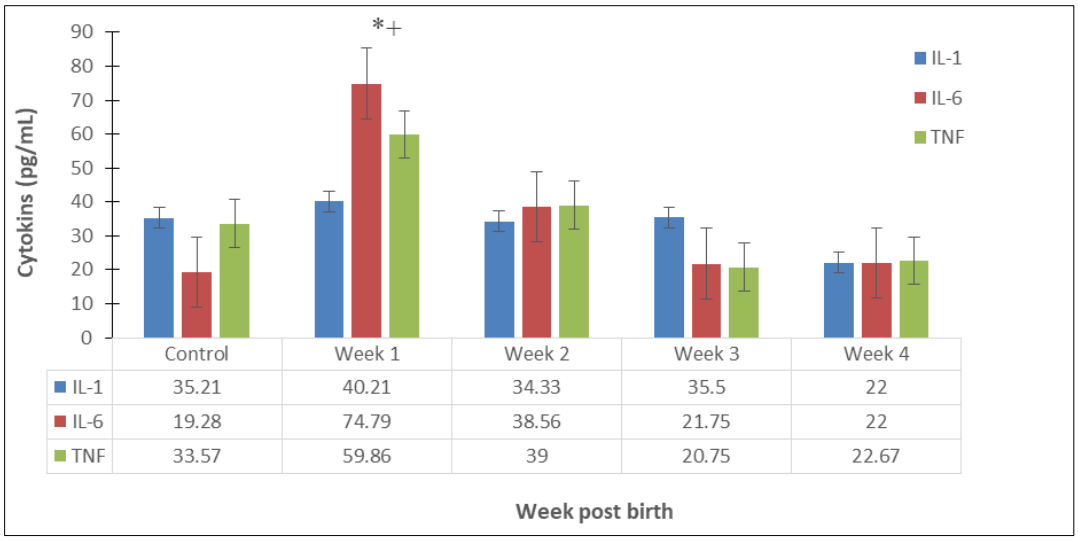
4. Results



*+ = significant increase ($p \leq 0.05$) compared to control; *-- = significant decrease ($p \leq 0.05$) compared to control.

Figure 1 Comparative changes in PCT level of neonates at birth grouped according to the week of septicemia diagnoses

Fig 1 show the comparative changes in PCT level of neonates at birth for control and experimental group based on time neonates were diagnosed with septicemia. The study showed that at birth, PCT level was significantly ($p \leq 0.05$) higher for neonates who develop septicemia in week 1 and 2 compared to those in control. Further comparison showed that neonates who developed sepsis in week 3 and 4 had a significantly lower levels of PCT at birth. This showed that PCT of neonates at birth can be used as a predictive marker of septicemia.



*+ = significant increase ($p \leq 0.05$) compared to control

Figure 2 Comparative changes in serum IL-1, IL-6 and TNF level of neonates at birth grouped according to the week of septicemia diagnoses

Figure 2 show comparative changes in neonatal serum IL-1, IL-6 and TNF at birth for neonates who were diagnosed with septicemia and those who were not septicemic (control) within the first month of life. The study shows that IL-6 and TNF level was significantly higher ($p \leq 0.05$) at birth among neonates who were diagnosed to have septicemia in the first week after birth. However, all other parameters analysed at birth showed no significant increase/decrease among neonates who were diagnosed to have septicemia in week 2, week 3 and week 4 compared to control.

Table 1 Comparative changes in neonatal PCT and Proinflammatory cytokines by gender

Parameters	Control		Experimental		t-Cal	t-test (p-val)	Remark
	Male	Female	Male	Female			
PCT (pg/mL)	81.67±5.40	87.04±11.00	269.15±72.03	255.76±58.22	0.252	0.8016	Insignificant
IL-1 (pg/mL)	34.50±0.41	35.83±0.79	38.75±5.23	35.88±4.69	0.430	0.6686	Insignificant
IL-6 (pg/mL)	18.32±0.77	20.12±1.38	52.33±12.66	51.06±12.75	0.353	0.7251	Insignificant
TNF (pg/mL)	35.95±2.63	31.48±1.70	46.58±10.20	43.39±7.71	0.618	0.5388	Insignificant

Above table compares changes in CRP, PCT and proinflammatory cytokines of new-born by gender. First, the table presents the average values of assayed parameters for normal (control) neonates and experimental (neonates who came back with sepsis). Next, student t-test then compares control males to experimental females and vice versa. The result was proven to be insignificant across boards ($p > 0.05$); indicative that neonatal gender caused no significant effect on PCT, IL-1, IL-6 and TNF levels at birth. Results are presented as Mean ± SEM.

Table 2 Multiple regression that predicts neonatal septicemia from serum CRP, PCT, Proinflammatory cytokines levels of neonates at birth, given neonatal birth weight.

Septicemia	Reg. Eqn.	SEM	t-stat	p-value	R^2	Remark
	$Y = b_0 + b_1x_1 + b_2x_2$					
Y	905.50 + -262.62 * PCT + (-1.33) * BW	0.005	0.143	0.2202	1.0102	Insignificant
Y	64.07 + (-11.15) * IL-1 + (-0.21) * BW	16.795	3.815	0.0007	0.9375	Significant
Y	149.04 + (-38.73) * IL-6 + (-0.51) * BW	43.029	3.46	0.0017	0.1597	Significant
Y	124.73 + (-31.81) * TNF + (-1.27) * BW	28.894	4.32	0.0002	0.2214	Significant

Y = Predicted neonatal serum variable (CRP, PCT, IL-1, IL-6 or TNF), b_0 = regression intercept (constant), b_1 = regression coefficient for predicted marker (constant), b_2 = regression coefficient for neonate's birth weight (constant), x_1 = known serum levels of assayed marker [CRP, PCT, IL-1, IL-6 or TNF], and x_2 = neonate's birth weight (Kg).

Table 3 Correlation between neonatal blood parameters at birth and neonatal sepsis presentation

Pearson	Markers			
	PCT	IL-1	IL-6	TNF
R	0.7131	0.4124	0.2225	0.6211
R squared	0.5107	0.3528	0.3722	0.5212
P value	0.0521	0.0332	0.0425	0.0122
Remark	SP	WP	WP	SP

Result of Pearson corelation coefficient (r) of above table shows a statistically significant ($p < 0.05$) strong positive (SP) correlation between umbilical cord PCT, TNF-α levels and presentation of neonatal sepsis post-birth. Here, neonates with high level of serum PCT and TNF-α at birth were more prone to developing septicemia after birth. IL-1β and IL-6 showed a weak positive (WP) correlation as against neonatal sepsis.

This aspect of the study focussed on the predictability of neonatal sepsis given neonatal birth weight, CRP, PCT, IL-1, IL-6 and TNF level at birth. Neonatal birth weight and IL-1, IL-6, TNF proved significant ($p \leq 0.05$) in predicting neonatal septicemia using the formular $Y = b_0 + b_1x_1 + b_2x_2$. However, neonatal PCT level and body weight at birth was not significant ($p > 0.05$) in septicemia prediction among sampled neonates.

5. Discussion

The study looked into the role of neonatal procalcitonin and pro-Inflammatory cytokines at birth in prediction of sepsis in neonates. Figure 1 of this study shows the comparative changes in umbilical cord procalcitonin (PCT) level between septicemic neonates and non-septicemic neonates. The figure proved that PCT was statistically significantly increased in septicemic neonates relative to control. In a special note, neonates who were diagnosed with septicemia in Week 1 and 2 showed a statistically significant ($p \leq 0.05$) increase in umbilical cord PCT levels than non-septicemic neonates at birth. Also, neonates who developed septicemia in week 3 and week 4 showed a significantly decreased level of PCT compared to control.

Several studies have linked higher PCT concentration to septicemia [19, 20]. PCT is currently known to be the standout marker for the diagnosis of bacterial infections as higher levels of serum PCT are found in patients with severe bacterial infections in comparison with patients with viral infections and other inflammatory conditions relative to viral infections and nonspecific inflammatory diseases [21]. In the absence of infection, PCT is produced by para-follicular cells (C cells) of the thyroid gland. However, in the presence of infection, it is produced by several cells of the body including the neuroendocrine cells of the lung and intestines [22]. This study observed a significant increased level of PCT at birth among neonates who developed septicemia in week 1 and 2 which indicates that PCT is sensitive even before the onset of known clinical symptoms of septicemia.

Figure 2 shows comparative changes in serum IL-1, IL-6 and TNF level of neonates at birth grouped according to the week of septicemia diagnoses after birth. Visibly from the figure is the increase in IL-6 and TNF-α level at birth seen in neonates who developed septicemia in week 1 compared control and other weeks. However, IL-1β level at birth remained unchanged in neonates who developed septicemia compared to the non-septicemic neonates. By this implication, IL-6 and TNF are useful markers in the diagnosis of early onset neonatal septicemia.

IL-6 is known for its short half-life, attributed to its binding with plasma proteins like α2-macroglobulin, early sequestration in the liver, or inhibition by other cytokines [23]. This cytokine is an especially early marker for neonatal sepsis, being released within 2 hours of the onset of bacteremia, peaking around 6 hours, and then declining over the subsequent 24 hours [24]. Notably, IL-6 levels can be significantly elevated up to 48 hours before clinical signs of sepsis appear. While some researchers have found the neonatal IL-6 response to be similar to that in adults, others have observed reduced IL-6 production in neonates [25] [26], directly contradicting the findings of this study. TNF-α is a potent pro-inflammatory cytokine crucial in immune responses, including inflammation, cell proliferation, differentiation, and apoptosis [27]. Bacterial lipopolysaccharide (LPS, endotoxin) is a primary stimulant for TNF-α

production by activated macrophages and T-lymphocytes [28]. Neonates who developed septicemia in the first week showed significantly high TNF-α levels at birth, highlighting the sensitivity of this cytokine to septicemia.

Neonatal gender showed no significant effect on the levels of PCT, IL-1β, IL-6 and TNF-α at birth as observed from table 1 of this study. Currently, there is little to no studies comparing the level of these markers in neonates at birth and gender. The study also reveals a relationship between neonatal IL-1β, IL-6, TNF-α levels and weight, with only PCT proving insignificant. This implies that for a given weight at birth, the regression equation $Y = b_0 + b_1x_1 + b2x2$ will evaluate to a value whose range can be used to extrapolate whether a gravida is prone to septicemia, upon comparison with a known range of normal serum IL-1β, IL-6 and TNF-α level. While no study has examined birth weight and serum IL-1β, IL-6, TNF-α level at birth, several studies have implicated low birth as a major contributing factor to development of both early and late onset neonatal sepsis [29, 30, 31]

6. Conclusion

The most crucial conclusion from this study is that sepsis is multifaceted and that it can affect serum PCT and proinflammatory cytokine levels of neonates with mild to severe symptoms that call for medical attention. According to the data analysis, PCT, IL-1β, IL-6, and TNF-α are particularly helpful markers for predicting neonatal sepsis. The use of these markers of septicemia in neonates at birth is likely to yield far efficient predictive potential as observed in this study. Findings from this study support the screening of PCT, IL-1β, IL-6 and TNF-α in neonates at the suspicion of septicemia in low to medium income communities where blood culture may not be readily available or while waiting for blood culture results.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare they have no conflicting interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study. In addition, ethical clearance (REC/FBMS/DELSU/20/82) was obtained from the Research and Ethics committee of the College of Health Sciences, Faculty of Basic Medical Sciences, Delta State University, Abraka, Delta State, Nigeria. Also, the Hospitals Management Board (HMB) of the Delta state gave an approval (A. 551/Vol. III/36) before commencement of study.

Data availability / Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available for reasons that authors have faced issues of raw data thefts in their previous articles and publications, just so for availing the public with raw data. Albeit, upon genuine and reasonable request from the corresponding author we will gladly oblige anyone with it. More so, as part of consent agreement between authors and participants, we do not have consent from our selected subjects to publish their raw data.

Authors Contributions

Kelvin Obakore Gbagbeke and Edith Ejenavwo: Collection, organisation and analysis of data.

Alexander Obidike Naiho: Interpretation and review of data as well proofreading of manuscript.

John Chukwuka Igweh: Developed and supervised study design ensuring that all research protocols are strictly adhered to.

References

[1] Edwards MS Baker, CJ. Sepsis in the newborn, In Gershon AA, Hotez PJ, Katz SL. (ed), Krugman's infectious diseases of children, 11th ed. Mosby, Philadelphia, PA. 2004; 545–561.

[2] Schuchat, A. Neonatal group B streptococcal disease—screening and prevention. N. Engl. J. Med. 2000; 343: 209–210.

[3] Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK, Smith PB, Manzoni P, Jacqz-Aigrain E, Kaguelidou F, Cohen-Wolkowiez M. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. Early Hum. Dev. 2012; 88: S69–S74.

[4] Fleischmann C, Reichert F, Cassini A, Horner R, Harder T. Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. Arch Dis Child. 2021; 1–8.

[5] Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. Lancet Respirat Med. 2018; 6(3):223–230.

[6] Popescu CR, Cavanagh MMM, Tembo B, Chiume M, Lufesi N. Neonatal sepsis in low-income countries: epidemiology, diagnosis and prevention. Expert Rev Anti Infect Ther, 2020; 1.

[7] Sands K, Carvalho MJ, Portal E. Characterization of antimicrobial-resistant Gram-negative bacteria that cause neonatal sepsis in seven low- and middle-income countries. Nat Microbiol. 2021; 6(4):512–523.

[8] Gbagbeke KO, Gaber EB, Ofili M, Odigie OM, Okonkwo BC, Ativie RN, Naiho AO, Igweh JC. Comparative appraisal of granulocytes, c-reactive proteins of cord blood and body weight changes between septicemic and non-septicemic neonates and their mothers. AMJ. 2022; 62(02): 931-943.

[9] Stoll BJ, Puopolo KM, Hansen NI, Sanchez, PJ, Bell EF, Carlo WA, Cotten CM. Early-onset neonatal sepsis 2015 to 2017, the rise of Escherichia coli, and the need for novel prevention strategies. JAMA Pediatr. 2020;174(7):1–12.

[10] Solomon S, Akeju O, Odumade OA. Prevalence and risk factors for antimicrobial resistance among newborns with gram-negative sepsis. PLoS One. 2021; 16:1–25.

[11] Dhir SK, Sundaram V, Gautam V. Microorganisms profile and antimicrobial resistance pattern in outborn neonates in Northern India: a hospital-based observational study. J Trop Pediatr. 2021; 67(3):1–9.

[12] Li W, Tapiainen T, Brinkac L. Vertical transmission of gut microbiome and antimicrobial resistance genes in infants exposed to antibiotics at birth. J Infect Dis. 2020; 1–11.

[13] Polin RA, St Geme JW. Neonatal sepsis. Adv. Pediatr. Infect. Dis. 1992; 7:25–61

[14] Gibbs RS, Duff P. Progress in pathogenesis and management of clinical intraamniotic infection. Am. J. Obstet. Gynecol. 1991; 164:1317–1326.

[15] Benitz W.E, Gould JB, Druzin ML. Risk factors for early-onset group B streptococcal sepsis: estimation of odds ratios by critical literature review. Pediatrics. 1999; 103: e77.

[16] Edwards MS (2013). Clinical features and diagnosis of sepsis in term and late preterm infants. In Basow DS. (ed), UpToDate. UpToDate, Waltham, MA: http://www.uptodate.com/contents/clinical-features-and-diagnosis-of-sepsis-in-term-and-late-preterm-infants?source=search_result&search=neonatal+sepsis&selectedTitle=1~58.

[17] Altunhan H, Annagur A, Ors R, Mehmetoglu I. Procalcitonin measurement at 24 hours of age may be helpful in the prompt diagnosis of early-onset neonatal sepsis. Int. J. Infect. Dis. 2011; 15: e854–e858.

[18] Kish L, Sampling organizations and groups of unequal sizes. American Sociological Review. 1965; 20, 564-572.

[19] Idakari CN, Efunshile AM, Akase IE, Osuagwu CS, Oshun P, Oduyebo OO. Evaluation of procalcitonin as a biomarker of bacterial sepsis in adult population in a tertiary healthcare facility in Lagos, Nigeria. African Journal of Clinical and Experimental Microbiology. 2022; 23 (2): 131-140

[20] Suranadi IW, Sinardja CD, Suryadi IA. Role of Procalcitonin in Predicting Mortality and Organ Dysfunction at Intensive Care Admission. Int J Gen Med. 2022; 12(15): 4917-4923.

[21] Schuetz P, Briel M, Christ-Crain M, Stolz D, Bouadma L, Wolff M, et al. Procalcitonin to guide initiation and duration of antibiotic treatment in acute respiratory infections: an individual patient data meta-analysis. Clin Infect Dis. 2012; 55(5):651–62.

[22] Cleland DA, Eranki AP. Procalcitonin. StatPearls. Treasure Island (FL): StatPearls Publishing. 2021.

[23] Messer J, Eyer D, Donato L, Gallati H, Matis J, Simeoni U. Evaluation of interleukin-6 and soluble receptors of tumor necrosis factor for early diagnosis of neonatal infection. J Pediatr. 1996; 129:574–80.

[24] Gilfillan M, Bhandari V. Biomarkers for the diagnosis of neonatal sepsis and necrotizing enterocolitis: clinical practice guidelines. Early Hum Dev. 2017; 105:25–33.

[25] Schibler KR, Liechty KW, White WL, Rothstein G, Christensen RD. Defective production of interleukin-6 by monocytes: a possible mechanism underlying several host defense deficiencies of neonates. Pediatr Res. 1992; 31:18–21.

[26] Doellner H, Arntzen KJ, Haereid PE, Aag S, Austgulen R. Interleukin-6 concentrations in neonates evaluated for sepsis. J Pediatr. 1998; 132:295–9.

[27] Baud V, Karin M. Signal transduction by tumor necrosis factor and its relatives. Trends Cell Biol. 2001; 9:372–7.

[28] Bradley JR. TNF-mediated inflammatory disease. J Pathol. 2008; 2:149–60.

[29] Schlapbach LJ, Aebischer M, Adams M, Natalucci G, Bonhoeffer J, Latzin P. Impact of Sepsis on neurodevelopmental outcome in a Swiss National Cohort of extremely premature infants. Pediatrics. 2011; 128(2): e348–57

[30] Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal Sepsis. Clin Microbiol Rev. 2014; 27(1):21–47.

[31] Ludvigsson JF, Lu D, Hammarström L, Cnattingius S, Fang F. Small for gestational age and risk of childhood mortality: A Swedish population study. PLoS Med. 2018; 15(12): e1002717.