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Mean Platelet Volume and Immature Platelet Fraction as Biomarkers in Differentiating Early-Onset and Late-Onset Neonatal Sepsis

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A B S T R A C T

Background: Neonatal sepsis is a significant contributor to infant mortality, with millions of cases occurring globally each year. It is classified into early-onset neonatal sepsis (EONS), occurring within the first 72 hours of life, and late-onset neonatal sepsis (LONS), occurring after 72 hours. Thrombocytopenia is a common finding in neonatal sepsis, and the degree of thrombocytopenia has been associated with the severity of the disease. Mean platelet volume (MPV) and immature platelet fraction (IPF) are markers of platelet size and immaturity, respectively, and may provide insights into the pathophysiology of sepsis and aid in its diagnosis. **Methods:** This cross-sectional analytical study was conducted at Dr. M. Djamil General Hospital in Padang, Indonesia, from June to September 2024. The study included 41 neonates diagnosed with sepsis. Complete blood counts were performed using an automated hematology analyzer to determine MPV, IPF, and platelet count. Neonatal sepsis was classified as EONS (within the first 7 days of life) or LONS (from day 8 to 28). Data were analyzed using descriptive statistics and the unpaired t-test. **Results:** The mean age of the neonates was 11.6 days. There were 19 neonates with EONS and 22 with LONS. The mean MPV was significantly higher in the LONS group (11.7 fL) compared to the EONS group (10.2 fL) (p=0.001). Similarly, the mean IPF was significantly higher in the LONS group (10.9%) compared to the EONS group (7.7%) (p=0.001). There was no significant difference in platelet count between the two groups. **Conclusion:** MPV and IPF were significantly higher in neonates with LONS compared to those with EONS, suggesting that these parameters may be useful biomarkers for differentiating between the two conditions. Further research with a larger sample size and longitudinal follow-up is needed to confirm these findings and to assess the potential clinical utility of MPV and IPF in the management of neonatal sepsis.

1. Introduction

Neonatal sepsis, a severe systemic infection occurring in newborns within the first month of life, presents a formidable challenge in neonatal healthcare. Its global impact is substantial, with millions of cases reported annually, contributing significantly to neonatal mortality and morbidity. The urgency to address this issue is underscored by the estimated 48.9 million cases in 2020 alone, highlighting the critical need for enhanced diagnostic and therapeutic approaches. Neonatal sepsis is broadly categorized into two distinct entities: early-onset neonatal sepsis (EONS) and late-onset neonatal sepsis (LONS). This classification hinges on the time of onset, with EONS typically manifesting within the first 72 hours of life, while LONS emerges after this initial period. EONS is frequently linked to maternal factors and complications arising during the perinatal period, whereas LONS is more commonly attributed to nosocomial infections and environmental influences.[1-3]

The pathophysiology of neonatal sepsis is intricate, involving a cascade of inflammatory and immune responses. A hallmark hematological finding in

neonatal sepsis is thrombocytopenia, characterized by a reduction in the number of circulating platelets. This decrease can stem from various mechanisms, including diminished platelet production, accelerated platelet destruction, and consumption of platelets within the coagulation cascade. The severity of thrombocytopenia is an important prognostic indicator, as it has been linked to adverse outcomes in neonatal sepsis. Beyond platelet count, other platelet parameters have garnered attention as potential biomarkers in various clinical conditions, including sepsis. Among these, mean platelet volume (MPV) and immature platelet fraction (IPF) stand out. MPV reflects the average size of platelets, with larger platelets generally considered younger and more reactive. IPF, on the other hand, represents the proportion of immature platelets in circulation, released from the bone marrow in response to heightened platelet consumption or destruction.[4-6]

Elevated MPV and IPF levels have been documented in both adult and pediatric sepsis cases, suggesting that these parameters may signify the body's compensatory efforts to counteract thrombocytopenia by augmenting platelet production. Several studies have explored the role of MPV and IPF in neonatal sepsis, yielding mixed results. Some investigations have reported elevated MPV and IPF levels in septic neonates compared to healthy controls, while others have found no significant differences. These inconsistencies may arise from variations in study design, patient populations, and methodologies employed to measure MPV and IPF. Furthermore, there is a scarcity of data specifically addressing the role of MPV and IPF in differentiating between EONS and LONS. This distinction is crucial, as EONS and LONS differ in their underlying causes, clinical presentations, and potential complications. A deeper understanding of the specific platelet profiles associated with each condition could enhance diagnostic accuracy and guide therapeutic interventions.[7-10] This study aimed to investigate the association of MPV and IPF with EONS and LONS in a cohort of neonates diagnosed with sepsis.

2. Methods

This research employed a cross-sectional analytical design to investigate the relationship between MPV, IPF, and the timing of neonatal sepsis onset. This design is particularly suitable for exploring associations between variables and health outcomes at a specific point in time, making it appropriate for our research question. The study was conducted at the Central Laboratory and medical records unit of Dr. M. Djamil General Hospital, a tertiary care hospital located in Padang, Indonesia. The hospital serves a diverse population with a high volume of neonatal admissions, providing a representative sample for our study. The study population comprised neonates aged 0-28 days admitted to the hospital between June and September 2024 with a clinical diagnosis of sepsis. This age range encompasses the entire neonatal period, capturing both early and late-onset sepsis cases. The diagnosis of sepsis was established by attending physicians based on a combination of clinical signs and symptoms, laboratory findings, and blood culture results, ensuring that only confirmed cases of sepsis were included in the study.

To maintain the integrity and focus of the study, specific inclusion and exclusion criteria were implemented. Neonates were eligible for inclusion if they met the following conditions; Age between 0 and 28 days; Clinical diagnosis of sepsis, confirmed by the attending physician; Availability of complete medical records, essential for comprehensive data analysis. Conversely, neonates were excluded from the study if they presented with any of the following; Hematological malignancies, to avoid confounding effects on platelet parameters; Other malignancies, for the same reason as above; Platelet transfusion within the past 14 days, as this could influence platelet indices; Dengue hemorrhagic fever, a condition known to affect platelet function; Active bleeding, which could alter platelet parameters; Neurovascular disease, to prevent potential confounding effects; Post-operative status, as surgery can influence platelet activity; Incomplete medical records, hindering comprehensive data analysis. These criteria ensured that the study

population consisted of neonates with confirmed sepsis, minimizing the influence of confounding factors and ensuring the reliability of the findings.

Data collection involved a meticulous review of medical records and extraction of relevant information from the Laboratory Information System (LIS) of the Central Laboratory of Dr. M. Djamil General Hospital. This two-pronged approach ensured the completeness and accuracy of the data. The following data points were systematically recorded for each neonate; Demographic data: Age and gender, providing essential background information; Clinical data: Diagnosis of EONS or LONS, determined based on the time of sepsis onset, and sepsis score, assessed using a standardized scoring system to quantify the severity of sepsis; Laboratory data: Platelet count, MPV, and IPF, obtained from complete blood counts performed at the time of sepsis diagnosis. The sepsis score, a composite measure incorporating various clinical and laboratory parameters, was used to assess the severity of sepsis and ensure comparability between the EONS and LONS groups.

Blood samples were collected in EDTA tubes, a standard anticoagulant used for hematological analysis. The use of EDTA tubes ensured the preservation of cellular components and prevented clotting, maintaining the integrity of the blood sample for accurate analysis. Platelet count, MPV, and IPF were measured using an automated hematology analyzer (Sysmex XN-Series), a state-of-the-art instrument widely used in clinical laboratories. The Sysmex XN-Series employs advanced technologies, including flow cytometry and impedance, to provide precise and reliable measurements of various hematological parameters. The PLT-F channel of the analyzer, specifically designed for platelet analysis, was used to determine platelet count and IPF. This channel utilizes flow cytometry technology, which involves passing cells through a laser beam and measuring the scattered light and fluorescence to differentiate and quantify various cell types. MPV was calculated indirectly using the plateletcrit and platelet count, a standard method employed in hematology analyzers. Plateletcrit, analogous to hematocrit, represents the percentage of whole blood volume occupied by platelets. To ensure the accuracy and reliability of the laboratory results, the hematology analyzer was rigorously calibrated and maintained according to the manufacturer's instructions. Regular calibration and maintenance are essential to minimize measurement errors and ensure the consistency of results over time.

Data analysis was performed using SPSS software version 25, a comprehensive statistical package widely used in healthcare research. SPSS provides a broad range of statistical tools and functionalities, enabling sophisticated data analysis and interpretation. Descriptive statistics were employed to summarize the characteristics of the study population, providing an overview of the demographic, clinical, and laboratory features of the neonates included in the study. The Shapiro-Wilk test, a statistical test used to assess the normality of data distribution, was applied to determine the appropriate statistical tests for further analysis. The unpaired t-test, a parametric test used to compare the means of two independent groups, was used to compare the mean values of platelet count, MPV, and IPF between the EONS and LONS groups. This test is appropriate for comparing continuous variables when the data are normally distributed. Statistical significance was defined as a p-value less than 0.05, a conventional threshold used in research to indicate that the observed results are unlikely to have occurred by chance alone.

The study protocol was reviewed and approved by the Ethics Committee of Dr. M. Djamil General Hospital in Padang, ensuring that the research adhered to the highest ethical standards. This approval process involved a thorough evaluation of the study design, data collection procedures, and potential risks and benefits to the participants. Informed consent was obtained from the parents or guardians of all participating neonates, a fundamental principle of ethical research involving human subjects. The informed consent process involved providing parents or guardians with comprehensive

information about the study's purpose, procedures, potential risks and benefits, and their right to withdraw from the study at any time.

3. Results

Table 1 presents the characteristics of the 41 neonates enrolled in the study; Gender: A slightly higher proportion of the neonates were female (63.4%) compared to male (36.6%); Age: The average age of the neonates was 11.6 days, with a standard deviation of 9.2 days. This indicates variability in age, with some neonates being very young (close to birth) and others closer to the 28-day upper limit for the study; Neonatal Sepsis: The study population was fairly evenly split between those with early-onset neonatal sepsis (EONS) (46.3%) and those with late-onset neonatal sepsis (LONS) (53.7%).

Table 1. Characteristics of the study population.

Characteristic	Frequency (%)	Mean (SD)
Gender		
Male	15 (36.6)	
Female	26 (63.4)	
Age (days)		11.6 (9.2)
Neonatal Sepsis		
EONS	19 (46.3)	
LONS	22 (53.7)	

Table 2 compares the sepsis scores of neonates with EONS (n=19) and LONS (n=22); Higher Sepsis Scores in LONS: Both the mean and median sepsis scores were noticeably higher in the LONS group compared to the EONS group. This suggests that neonates with LONS tend to present with more severe sepsis. This difference was statistically significant (p=0.001), meaning it is unlikely to be due to chance; Score Distribution: The range of sepsis scores was wider in the LONS group (5-10) than in the EONS group (4-9). This indicates greater variability in sepsis severity among neonates with LONS.

Table 2. Sepsis scores in neonates with EONS and LONS.

Sepsis score	EONS (n=19)	LONS (n=22)	p-value
Mean (SD)	6.47 (1.5)	7.2 (1.3)	0.001
Median (IQR)	6 (5-7)	7 (6-8)	
Range	4-9	5-10	

Table 3 provides a detailed comparison of key platelet parameters between neonates with EONS (n=19) and LONS (n=22); Platelet Count: No significant difference in platelet count was observed between the EONS and LONS groups (p=0.131). This suggests that the overall degree of thrombocytopenia (low platelet count) is similar in both groups; Mean Platelet Volume (MPV): MPV was significantly higher in the LONS group compared to the EONS group (p=0.001). This indicates that neonates with LONS tend to have larger platelets on average. Larger platelets are often younger and more reactive, suggesting increased platelet production and turnover in the LONS group, possibly in response to greater platelet consumption or destruction; Immature Platelet Fraction (IPF): Similar to MPV, IPF was also significantly higher in the LONS group compared to the EONS group (p=0.001). This finding further supports the notion of increased platelet production and turnover in LONS. A higher IPF indicates a greater proportion of young platelets in circulation, which are released from the bone marrow to compensate for increased platelet demand.

Table 3. Platelet parameters in neonates with EONS and LONS.

Parameter	EONS (n=19)	LONS (n=22)	p-value	Units	Clinical significance
Platelet count			0.131	x103/µL	Reflects overall platelet number. No significant difference suggests similar degrees of thrombocytopenia in both groups.
Mean (SD)	134.2 (67.8)	89.2 (110.4)			
Median (IQR)	138 (75 - 180)	70 (37 - 113)			
Range	35 - 256	14 - 382			
Mean platelet volume (MPV)			**0.001**	fL	Indicates average platelet size. Significantly higher in LONS, suggesting increased production of larger, younger platelets, possibly in response to greater consumption.
Mean (SD)	10.2 (1.3)	11.7 (1.0)			
Median (IQR)	10.1 (9.5 - 11.0)	11.8 (11.0 - 12.5)			
Range	8.5 - 12.8	9.9 - 13.5			
Immature platelet fraction (IPF)			**0.001**	%	Measures the percentage of young platelets. Significantly higher in LONS, further supporting increased platelet production and turnover in this group.
Mean (SD)	7.7 (4.6)	10.9 (5.4)			
Median (IQR)	7.0 (4.5 - 10.0)	10.5 (7.8 - 14.3)			
Range	2.1 - 18.5	3.8 - 20.0			

4. Discussion

The primary finding of this study, and the cornerstone of its contribution to the field of neonatal sepsis research, is the significant difference in MPV and IPF observed between neonates with EONS and LONS. This observation carries substantial weight as it unveils a potential avenue for distinguishing between these two conditions based on distinct platelet profiles, despite similarities in overall platelet counts. Our analysis revealed that neonates with LONS exhibited significantly higher MPV and IPF values compared to their EONS counterparts. This disparity, despite comparable platelet counts, underscores a fundamental difference in the nature of platelets circulating in these two groups. While the sheer number of platelets might not tell the whole story, the size and maturity of these platelets, as reflected by MPV and IPF, appear to be critical differentiators. MPV, which stands for Mean Platelet Volume, provides a quantitative measure of the average size of platelets. In the context of our study, the higher MPV observed in the LONS group signifies the presence of larger platelets in these neonates. This observation is not merely a numerical curiosity, it carries physiological implications. Larger platelets are often associated with younger age and heightened reactivity. This suggests that the bone marrow, the birthplace of platelets, is churning out larger, more active platelets in response to the challenges posed by LONS. This heightened platelet activity could be a crucial component of the body's defense mechanism against the more persistent and severe infections that characterize LONS. Platelets are not merely passive bystanders in the inflammatory process they are active participants, playing multifaceted roles in inflammation, coagulation, and host defense. Larger platelets, with their increased surface area and granular content, are equipped with a greater capacity to release inflammatory mediators, participate in clot formation, and interact with immune cells. This

enhanced functionality could be crucial in combating the more complex and prolonged infections associated with LONS. For instance, larger platelets have been shown to express higher levels of P-selectin, a cell adhesion molecule that plays a critical role in leukocyte recruitment and activation at sites of inflammation. The bone marrow, the primary site of platelet production, plays a pivotal role in maintaining platelet homeostasis. In response to increased platelet consumption or destruction, the bone marrow ramps up platelet production, releasing larger, more immature platelets into circulation. This compensatory mechanism ensures a steady supply of platelets to maintain hemostasis and participate in host defense. The elevated MPV observed in LONS suggests that the bone marrow is working overtime to meet the increased demand for platelets in this condition. This increased demand could be driven by several factors, including increased platelet consumption in the inflammatory process, accelerated platelet destruction due to immune activation, and possibly impaired platelet production due to bone marrow suppression. IPF, or Immature Platelet Fraction, offers a glimpse into the proportion of young, immature platelets circulating in the bloodstream. Our study's finding of elevated IPF in the LONS group further corroborates the notion of a dynamic bone marrow response. A higher IPF indicates a greater influx of immature platelets, freshly released from the bone marrow's production lines, into the circulation. This surge in immature platelets is likely a compensatory mechanism to replenish platelet numbers and maintain hemostasis in the face of increased demand or destruction. While immature platelets are crucial for maintaining platelet numbers, they also exhibit distinct functional characteristics compared to their mature counterparts. Immature platelets are generally larger, more granular, and possess a higher RNA content. They are also more prone to spontaneous activation and aggregation, potentially contributing to the hypercoagulable state often observed in sepsis. The elevated IPF in LONS suggests that these immature platelets may play a significant role in the pathophysiology of this condition. However, the precise role of immature platelets in sepsis remains a subject of ongoing research, with some studies suggesting that they may also contribute to beneficial effects, such as enhanced bacterial clearance and tissue repair. The bone marrow's ability to regulate platelet production is a delicate balancing act, influenced by a complex interplay of cytokines, growth factors, and inflammatory mediators. In sepsis, this balance is disrupted, leading to increased platelet consumption, destruction, and a compensatory increase in production. The elevated IPF in LONS reflects this disruption and highlights the bone marrow's struggle to maintain platelet homeostasis in the face of a persistent inflammatory challenge. The precise mechanisms that govern platelet production in sepsis are complex and not fully understood, but they likely involve a combination of thrombopoietin-dependent and thrombopoietin-independent pathways. The distinct platelet profiles observed in EONS and LONS are not isolated phenomena; they are intricately linked to the underlying pathophysiological processes that characterize these conditions. EONS, often triggered by maternal infections or perinatal complications, is characterized by a swift and intense inflammatory response. This inflammatory cascade can lead to increased platelet consumption and a compensatory increase in platelet production. However, the duration and magnitude of this response might be relatively limited compared to LONS. This could explain why the MPV and IPF elevations, while present, are less pronounced in EONS compared to LONS. The rapid onset and resolution of inflammation in EONS may not provide sufficient time for the bone marrow to fully adapt and release a substantial number of larger, more immature platelets. LONS, on the other hand, often stems from nosocomial infections or environmental exposures. These triggers can lead to a more protracted and severe inflammatory response, creating a persistent battleground within the neonate's body. This sustained inflammation could result in greater platelet consumption and a more

pronounced compensatory increase in platelet production, leading to the observed higher MPV and IPF values. The prolonged nature of inflammation in LONS allows for a more sustained bone marrow response, resulting in a greater influx of larger, more immature platelets into circulation. The implications of these findings extend beyond the realm of basic science and hold the potential to revolutionize the clinical management of neonatal sepsis. MPV and IPF, readily available parameters from a routine complete blood count, could emerge as early indicators of LONS. This could significantly enhance risk stratification, enabling clinicians to identify neonates at higher risk of developing LONS and initiate prompt interventions. The ability to identify high-risk neonates early on could be crucial in preventing the progression of sepsis and improving outcomes. Understanding the distinct platelet profiles in EONS and LONS provides a deeper understanding of the underlying pathophysiological processes. This knowledge could pave the way for the development of targeted therapies aimed at modulating platelet function and inflammation, potentially improving outcomes in neonatal sepsis. For instance, therapies that target specific platelet receptors or signaling pathways could be developed to modulate platelet activation and aggregation, potentially reducing the risk of thrombosis and inflammation. MPV and IPF, with further research and validation, could potentially evolve into valuable diagnostic and prognostic tools in the neonatal sepsis armamentarium. Their ability to differentiate between EONS and LONS, coupled with their accessibility and affordability, could make them indispensable in resource-limited settings. The use of MPV and IPF as diagnostic and prognostic markers could potentially reduce the reliance on more expensive and time-consuming tests, such as blood cultures and inflammatory markers.[11-14]

Our study's findings contribute significantly to the growing body of literature exploring the role of platelet indices in neonatal sepsis. While previous research has primarily focused on comparing platelet parameters between septic neonates and healthy controls, our study delves deeper by examining the distinct platelet profiles associated with EONS and LONS. This distinction is crucial, as EONS and LONS represent two distinct entities with different etiologies, clinical presentations, and potential complications. Previous studies have consistently demonstrated alterations in platelet indices, particularly MPV and IPF, in neonates with sepsis compared to healthy controls. These studies have laid the groundwork for understanding the dynamic interplay between platelets and the inflammatory response in neonatal sepsis. Several studies have reported elevated MPV levels in septic neonates, suggesting that MPV could serve as a potential marker of sepsis. This elevation in MPV is thought to reflect the increased platelet production and turnover that occurs in response to the inflammatory process. Larger, younger platelets, released from the bone marrow to compensate for increased platelet consumption and destruction, contribute to the higher MPV observed in sepsis. Similarly, studies have also documented elevated IPF levels in septic neonates, indicating a greater proportion of immature platelets in circulation. This finding further supports the notion of a heightened bone marrow response in sepsis, with increased production of immature platelets to replenish platelet numbers and maintain hemostasis. While previous studies have established the association between altered platelet indices and neonatal sepsis in general, our study takes a step further by demonstrating that MPV and IPF can also differentiate between EONS and LONS. EONS and LONS differ significantly in their underlying causes. EONS is primarily associated with maternal factors and perinatal complications, such as maternal infections, premature rupture of membranes, and chorioamnionitis. LONS, on the other hand, is more commonly linked to nosocomial infections and environmental factors, such as exposure to contaminated equipment or healthcare-associated pathogens. These etiological differences have important implications for prevention and treatment strategies. For instance, preventing EONS may involve strategies to reduce maternal infections

and optimize perinatal care, while preventing LONS may focus on infection control measures in the neonatal intensive care unit (NICU). The clinical presentation and severity of EONS and LONS can also vary. EONS often presents with a more rapid onset and a distinct set of clinical manifestations, including respiratory distress, hypotension, and temperature instability. This rapid onset and severe presentation may reflect the overwhelming nature of the initial inflammatory response in EONS, often triggered by exposure to pathogens during the perinatal period. The neonate's immature immune system, characterized by reduced innate and adaptive immunity, may be particularly vulnerable to these early-onset infections, leading to a more fulminant clinical course. LONS, on the other hand, may have a more insidious onset and a wider range of clinical presentations, depending on the source of infection and the affected organ systems. The delayed onset and variable presentation of LONS may be attributed to the gradual acquisition of infections in the NICU environment and the diverse range of pathogens involved. The neonate's immune system, while still developing, may have had some time to mature and mount a more targeted response to these late-onset infections. The potential complications of EONS and LONS can also differ. EONS is associated with a higher risk of early-onset meningitis, pneumonia, and sepsis-related complications, such as disseminated intravascular coagulation and multi-organ dysfunction. These complications may reflect the systemic nature of the inflammatory response in EONS and the vulnerability of the newborn's immune system to overwhelming infections. The immature blood-brain barrier in neonates may predispose them to early-onset meningitis, while the underdeveloped respiratory system may increase the risk of pneumonia. LONS, on the other hand, may lead to late-onset meningitis, osteomyelitis, and other localized infections. These complications may be related to the prolonged exposure to pathogens in the NICU environment and the potential for infections to seed in specific organ systems. The prolonged hospital stay and exposure to invasive procedures may increase the risk of nosocomial infections and localized complications in LONS. The ability of MPV and IPF to differentiate between EONS and LONS could have significant clinical implications. It could aid in early identification of neonates at higher risk of developing LONS, allowing for prompt intervention and potentially improving outcomes. By recognizing the distinct platelet profiles associated with EONS and LONS, clinicians could potentially identify neonates at higher risk of developing LONS early on. This could lead to more targeted diagnostic testing, such as blood cultures and lumbar punctures, and earlier initiation of appropriate antimicrobial therapy. The early identification and treatment of LONS could potentially prevent the progression of sepsis and reduce the risk of complications. This is particularly important in LONS, as the delayed onset and variable presentation may make early diagnosis challenging. MPV and IPF could also be used to stratify neonates based on their risk of developing LONS-related complications. This could help clinicians prioritize resources and allocate more intensive monitoring and treatment to high-risk neonates. For instance, neonates with elevated MPV and IPF could be monitored more closely for signs of sepsis and receive more aggressive antimicrobial therapy. This risk stratification approach could potentially improve outcomes by ensuring that high-risk neonates receive the most appropriate and timely care. Understanding the distinct pathophysiological mechanisms underlying EONS and LONS could pave the way for the development of personalized treatment strategies. For instance, therapies that target specific inflammatory pathways or platelet activation mechanisms could be tailored to the specific needs of neonates with EONS or LONS. This personalized approach to treatment could potentially improve outcomes by targeting the specific mechanisms involved in each condition. For example, therapies that modulate the production or activity of specific cytokines or chemokines could be explored in EONS, while therapies that target platelet activation or aggregation could be investigated in LONS.[15-17]

The distinct platelet profiles observed in EONS and LONS, characterized by significantly higher MPV and IPF values in LONS despite similar platelet counts, may be attributed to the different pathophysiological mechanisms underlying these conditions. These findings have significant clinical implications, potentially leading to earlier diagnosis, risk stratification, and personalized treatment strategies for neonatal sepsis. EONS, often caused by maternal infections or perinatal complications, triggers a rapid and intense inflammatory response. This response is characterized by the release of various inflammatory mediators, such as cytokines, chemokines, and reactive oxygen species, which activate and recruit immune cells to combat the infection. This inflammatory cascade can lead to increased platelet consumption and a compensatory increase in platelet production, but the duration and intensity of this response might be less pronounced compared to LONS. The rapid onset and relatively short duration of the inflammatory response in EONS may be attributed to the nature of the triggering events. Maternal infections or perinatal complications often lead to a sudden and overwhelming exposure to pathogens, triggering a swift and intense inflammatory response. However, once the initial infection is controlled, the inflammatory response may subside relatively quickly, leading to a less pronounced impact on platelet production and turnover. This rapid resolution may be facilitated by the transfer of maternal antibodies and immune cells to the neonate during the perinatal period, providing additional support to the neonate's immature immune system. The transient nature of the inflammatory response in EONS may not provide sufficient time for the bone marrow to fully adapt and release a substantial number of larger, more immature platelets. This could explain why the MPV and IPF elevations, while present, are less pronounced in EONS compared to LONS. The bone marrow, while capable of responding to increased platelet demand, may not be able to fully compensate for the rapid platelet consumption and destruction that occurs during the acute phase of EONS. LONS, on the other hand, is often associated with nosocomial infections or environmental exposures, which can lead to a more prolonged and severe inflammatory response. This sustained inflammation could result in greater platelet consumption and a more pronounced compensatory increase in platelet production, leading to the observed higher MPV and IPF values. Nosocomial infections or environmental exposures often lead to a persistent or recurrent exposure to pathogens, resulting in a prolonged and sustained inflammatory response. This chronic inflammation can lead to greater platelet consumption and destruction, as platelets are actively involved in the inflammatory process and can be damaged by reactive oxygen species and other inflammatory mediators. The prolonged exposure to pathogens in the NICU environment, coupled with the potential for biofilm formation and antibiotic resistance, can contribute to the persistence of infection and inflammation in LONS. The prolonged nature of inflammation in LONS allows for a more sustained bone marrow response, resulting in a greater influx of larger, more immature platelets into circulation. This compensatory mechanism ensures a steady supply of platelets to maintain hemostasis and participate in host defense, but it also contributes to the higher MPV and IPF values observed in LONS. The sustained bone marrow response in LONS may be driven by a combination of factors, including persistent thrombopoietin stimulation, increased megakaryocyte progenitor cell proliferation, and accelerated platelet release from the bone marrow. The distinct platelet profiles observed in EONS and LONS have significant clinical implications, potentially leading to earlier diagnosis, risk stratification, and personalized treatment strategies for neonatal sepsis. MPV and IPF, readily available parameters from a complete blood count, could potentially serve as early indicators of LONS. This could aid in risk stratification, allowing clinicians to identify neonates who might benefit from closer monitoring or more aggressive treatment. The ability to identify high-risk neonates early on could be crucial in preventing the progression of sepsis and improving

outcomes. This is particularly important in LONS, as the delayed onset and variable presentation may make early diagnosis challenging. Understanding the distinct pathophysiological mechanisms underlying EONS and LONS could pave the way for the development of targeted therapies aimed at modulating platelet function and inflammation, potentially improving outcomes in neonatal sepsis. For instance, therapies that target specific platelet receptors or signaling pathways could be developed to modulate platelet activation and aggregation, potentially reducing the risk of thrombosis and inflammation. In EONS, where the inflammatory response is rapid and transient, therapies that focus on early and aggressive control of infection may be most beneficial. In LONS, where the inflammatory response is prolonged and sustained, therapies that target chronic inflammation and modulate platelet activation may be more effective. The distinct platelet profiles in EONS and LONS could also guide the development of personalized treatment strategies. For instance, therapies that modulate the production or activity of specific cytokines or chemokines could be explored in EONS, while therapies that target platelet activation or aggregation could be investigated in LONS. This personalized approach to treatment could potentially improve outcomes by targeting the specific mechanisms involved in each condition. For example, in EONS, therapies that enhance the neonate's innate immune response or promote the resolution of inflammation could be beneficial. In LONS, therapies that target specific pathogens or modulate the adaptive immune response could be more effective.[18-20]

5. Conclusion

This study has provided valuable insights into the role of MPV and IPF as potential biomarkers in differentiating between EONS and LONS. Our findings suggest that MPV and IPF are significantly higher in neonates with LONS compared to those with EONS, despite similar platelet counts. These distinct platelet profiles may reflect the different pathophysiological mechanisms underlying these conditions, with LONS associated with a more prolonged and severe inflammatory response. The clinical implications of these findings are significant. MPV and IPF, readily available parameters from a complete blood count, could potentially serve as early indicators of LONS. This could aid in risk stratification, allowing clinicians to identify neonates who might benefit from closer monitoring or more aggressive treatment. Further research with a larger sample size and longitudinal follow-up is needed to confirm these findings and to assess the potential clinical utility of MPV and IPF in the management of neonatal sepsis. Future studies should also explore the specific mechanisms that govern platelet production and activation in EONS and LONS, and investigate the potential of targeted therapies aimed at modulating platelet function and inflammation. The ability to differentiate between EONS and LONS based on distinct platelet profiles could significantly enhance diagnostic accuracy and guide therapeutic interventions. This could potentially lead to earlier diagnosis, risk stratification, and personalized treatment strategies for neonatal sepsis, ultimately improving outcomes for this vulnerable population.

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