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ABSTRACT

EARLY DIAGNOSIS OF NEONATAL SEPSIS - NEWS AND PERSPECTIVES

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A B S T R A C T

Neonatal sepsis is a serious and frequently life-threatening disease that impacts newborns, especially those delivered prematurely (1). Although there have been improvements in neonatal care, sepsis continues to be a major cause of illness and death among newborns worldwide. Prompt and precise identification of neonatal sepsis is crucial to promptly begin suitable therapeutic interventions. Nevertheless, the symptoms of neonatal sepsis often lack specificity, which poses a challenge in promptly diagnosing the condition (2). The primary objective of this research theme is to identify biomarkers that are dependable and to develop novel diagnostic techniques that can improve the early detection and treatment of neonatal sepsis.

Although medicine is continuously evolving, sepsis and its treatment represent a permanent challenge for clinicians because over the years antibiotic-resistant microorganisms have been selected and are one of the main causes of mortality among vulnerable populations, especially premature newborns who have compromised immunity and lack special care measures that greatly increase the risk of sepsis (3).

The main difficulty in diagnosing neonatal sepsis stems from its non-specific clinical manifestations, which can be easily confused with other neonatal conditions like respiratory distress syndrome or metabolic disorders. Conventional diagnostic techniques, such as blood cultures and clinical evaluations, frequently lack accuracy and precision, resulting in delays in the identification and management of diseases. These delays

can lead to significant complications, extended hospital stays, and higher mortality rates.

The primary objectives of this research are to evaluate the efficacy of specific biomarkers in the early diagnosis of neonatal sepsis and to develop advanced analytical techniques that integrate these biomarkers for improved diagnostic accuracy. Specifically, this thesis aims to:

- Assess the reliability of ferritin, lactate dehydrogenase (LDH), and hemoglobin as biomarkers for neonatal sepsis.
- Investigate the potential of D-dimer levels as prognostic markers for the severity and outcomes of neonatal sepsis.
- Explore the integration of multimodal biosignals, including pulse oximetry, near-infrared spectroscopy (NIRS), and skin temperature monitoring, for early detection of sepsis.

This research is divided into two main parts:

1. **General Part:** This section provides a comprehensive overview of neonatal sepsis, including its definition, pathophysiology, historical context, clinical signs and symptoms, and current diagnostic and treatment methods. It sets the stage for the specific investigations conducted in the special part.
2. **Special Part:** This section is dedicated to the empirical studies aimed at achieving the research objectives. It includes detailed chapters on the evaluation of specific biomarkers and the integration of advanced diagnostic techniques.

The overarching hypothesis of this research is that the use of specific biomarkers and advanced analytical techniques can significantly improve the

early diagnosis and prediction of neonatal sepsis. This is based on the following specific hypotheses:

1. Elevated levels of ferritin and LDH are reliable indicators of neonatal sepsis.
2. High D-dimer levels correlate with increased severity and poor outcomes in neonatal sepsis.
3. The integration of multimodal biosignals improves the diagnostic accuracy for early detection of sepsis compared to traditional methods.

The first study assesses the evaluation of Ferritin, LDH, and Hemoglobin as Predictive Markers. Neonates with sepsis will have significantly elevated levels of ferritin and LDH compared to those without sepsis, while hemoglobin levels will not show substantial differences. A case-control study involving 86 neonates was conducted to measure the levels of ferritin, LDH, and hemoglobin. Statistical analyses, including logistic regression and receiver operating characteristic (ROC) curve analysis, were used to evaluate the predictive value of these biomarkers. The study found that ferritin and LDH levels were significantly higher in neonates with sepsis, with ferritin and LDH demonstrating excellent discriminatory power for diagnosing neonatal sepsis. Hemoglobin levels were not significantly associated with sepsis.

The second study evaluated the prognostic Value of D-dimer levels. Elevated D-dimer levels are indicative of severe sepsis and correlate with adverse clinical outcomes, including increased mortality rates and prolonged hospitalization. The study analyzed D-dimer levels in neonates diagnosed with sepsis and assessed the correlation with clinical outcomes using logistic regression models and ROC curve analysis. High D-dimer levels were significantly associated with severe sepsis and poor clinical outcomes, suggesting that D-dimer is a valuable prognostic marker for neonatal sepsis.

The third study evaluated the integration of multimodal biosignals. The integration of multimodal biosignals, including pulse oximetry, NIRS, and skin temperature monitoring, enhances the early detection of neonatal sepsis compared to traditional diagnostic methods. The study employed advanced analytical techniques to integrate and analyze data from multiple biosignals. Machine learning algorithms were used to develop predictive models, which were then validated against clinical outcomes. The integrated biosignal approach showed superior diagnostic accuracy for early sepsis detection compared to traditional methods, highlighting the potential of this innovative approach in clinical practice.

This research encompasses substantial individual contributions in the design and execution of empirical studies, gathering and analysis of data, and the creation of sophisticated diagnostic models. The researcher played a crucial role in combining various approaches from different fields, such as clinical, laboratory, and computational methods, to tackle the intricate problem of diagnosing early neonatal sepsis.

This thesis contributes to the field of neonatal care by showing that certain biomarkers, specifically ferritin, LDH, and D-dimer, when combined with the integration of multiple biosignals, can greatly enhance the early detection and prediction of neonatal sepsis. The results indicate that these novel diagnostic methods have the potential to result in earlier interventions, thereby decreasing the mortality and morbidity rates linked to neonatal sepsis. Future research should prioritise the validation of these biomarkers and diagnostic models in larger and more diverse populations. Additionally, efforts should be made to develop integrated diagnostic platforms that can be widely used in clinical settings.