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PREDICTIVE VALUE OF SERUM ALBUMIN LEVELS FOR PROGNOSIS OF SEVERE SEPSIS IN LATE PRETERM NEONATES ADMITTED IN NICU

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ABSTRACT

Neonatal sepsis is still a common problem in NICU, and late preterm babies, aged 34 to 36 weeks postmenstrual age are still at high risk due to their immature immunologic system. The identification of the early risk is crucial in the management of patients, but the previously established biomarkers including C-reactive protein (CRP) and Procalcitonin are associated with some drawbacks that affect the accuracy of risk prediction. The aim of this work is to know whether serum albumin levels in LPPN with severe sepsis admitted to NICU in CMH Abbottabad are useful in predicting mortality rates. Randomized controlled clinical trial was conducted during one year, with 100 late preterm neonates with severe sepsis. Serum albumin level was tested on admission, and its association with mortality, length of stay in NICU and mechanical ventilation, and MODS was also determined. The authors found out that the overall mortality rate was higher

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among neonates with hypoalbuminemia of <3.0 g/dL, 75% as compared to neonates with normal levels, 10% ($p < 0.001$). The observed differences included a longer length of stay in NICU in the hypoalbuminemic neonates 18.2 ± 5.6 days as compared with 11.4 ± 4.2 days, $p < 0.001$); modern Trend as identified by MODS was higher in the hypoalbuminemic neonates, (61% vs. 16 %, $p < 0.001$), and mechanical ventilation was required more in the hypoalbuminemic neonates as 70% compared to 20%, $p < 0.001$). In ROC, an area under the curve AUC of 0.83 was observed in serum albumin cut off of 3.0 g/dl with the sensitivity of 80% and specificity of 75% thus emphasizing a better test accuracy to predict these adverse outcomes. Specifically, research comparing other biomarkers including CRP and procalcitonin show that serum albumin has better prognosis (AUC= 0.85). Thus, the results call for the implementation of serum albumin assessments as a cost-efficient initial predictor of neonatal sepsis severity. Based on this relationship, it is possible that evaluation of serum albumin levels should be included in the care of neonates with sepsis by providing essential information when making decisions as to the course of actions to be taken. Additional large scale studies should be undertaken to determine whether albumin supplementation will be of benefit in lessening the morbidity of hypoal buminemic septic neonates.

KEYWORDS: Neonatal sepsis, serum albumin, hypoalbuminemia, late preterm neonates, prognosis, NICU, multi-organ dysfunction, mechanical ventilation, mortality, biomarker.

INTRODUCTION

Neonatal sepsis is one of the major contributors to mortality and morbidities in NICUs around the globe especially affecting late preterm neonates 34-36 weeks gestational age because of more vulnerable immune responses and physiological defence mechanisms (Shah et al., 2020). Sepsis can be described as SIRS resulting from an infection, which makes neonates develop organ dysfunction and have a high possibility of death (Puopolo et al., 2019). Sepsis that is associated with hypotension, metabolic acidosis, one or more organs dysfunction should be identified early and managed appropriately in order to achieve better outcomes in neonates (Weiss et al., 2020).

However, early diagnosis as well as risk assessment in neonatal sepsis remain a very daunting task because sepsis' initial manifestations in neonates are very generalized (Zeisel et al., 2021).

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Serological markers including CRP, PCT and blood cultures are utilised in diagnosis of sepsis; these biomarkers are however, disparaged by they're low sensitivity, specificity and early prognostic value (Hofer et al., 2022). Hence, there is a need to establish better biomarkers that can be used in evaluating the outcomes of neonatal sepsis with regard to the management of the condition.

Pathophysiological Role of Serum Albumin in Sepsis

Serum albumin is the biggest water-soluble globular protein that is usually produced in the liver, involved in maintaining oncotic pressure and carrying both the endogenous and exogenous substances, and also exhibiting anti-inflammatory properties (Peters, 2019). Hypoalbuminemia is previously recognized as serum albumin concentrations of less than 3.0 g/dL, which worsens the course of the diseases and increases the mortality rate among the critical patients, including adult sepsis patients (Lee et al., 2021). Several research works have proposed that albumin levels drop sharply in relation to inflammation, leakage of blood vessels, and improved metabolic demands during sepsis (Fleck, 2020). Serum albumin has been established as an important prognostic factor in adult and pediatric sepsis, but there is a lack of data on the role of this biomarker in neonatal sepsis, and especially in late preterm neonates (Breslow et al., 2022).

Serum albumin has multiple functions that make it a possible biomarker to be used in the prognosis of sepsis. Firstly, it sustains intravascular oncotic pressure which is very useful in averting capillary leakages as well as tissue oedema that is frequently noted in sepsis induced hypotension (Vincent et al., 2021). Secondly, it suggests that albumin has antioxidant and anti-inflammatory effects owing to its capacity to neutralize free radicals and regulate immunity disorders (Roche et al., 2020). It has been found that low albumin concentrations are linked with the raised concentrations of pro-inflammatory cytokines, IL-6, and TNF-alpha cytokines that are involved in sepsis development (Caironi et al., 2021).

In neonatal sepsis, inflammation leads to significant vascular permeability where albumin leaves the intravascular compartment and accumulates in the extravascular space thus causes hypoalbuminemia (Jiang et al., 2022). Furthermore, sepsis also affects the liver by reducing the synthesis of albumins and due to sepsis; the serum albumin level is low in most patients (Mohan

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et al., 2020). Based on these mechanisms, serum albumin has been suggested as a candidate sepsis biomarker and its levels correlate with sepsis severity and prognosis (Gustot et al., 2022).

Hypoalbuminemia and Neonatal Sepsis Prognosis

Hypoalbuminemia has been implied to have higher mortality and morbidity, longer NICU stay, and a greater degree of organ dysfunction in neonatal sepsis (Yılmaz et al., 2021). Mohan et al. (2020) in their studies also observed increased mortality rates amongst neonates with severe sepsis and hypoalbuminemia than those in normal albumin level group. Similarly, Jiang et al. (2022) has shown that albumin level less than 2.8 g/dL are related to triple NICU mortality in septic neonates. Some neonatal sepsis severity indices, including NSS and SOFA have included hypoalbuminemia as one of the predictors of the severity of the disease (Liu et al., 2023). Additionally, there is evidence that albumin has therapeutic potential in critically ill neonates; some researchers have reported improvements in the stability of the patient's hemodynamic parameters and decreased organ dysfunction (Vincent et al., 2021). However, the efficacy of albumin in replacement therapy is still questionable to some extent and hence requires further research in the neonate patient groups (Roche, et al., 2020).

Rationale for the Study

Since neonatal sepsis is a severe problem and precise biomarkers are needed for early estimation of prognosis, this study will assess serum albumin level in late preterm neonates admitted in NICU of CMH Abbottabad. Thus, with the help of the findings of current study, which compares the drives between C/S albumin levels and clinical prognosis, the necessary conclusion has to be made whether hypoalbuminemia constitutes an early sign of worsening outcomes in cases of neonatal sepsis.

Although there are several studies on albumin in adults and children with sepsis, research related to late preterm neonates is scarce (Breslow et al., 2022). Hence, this research will advance the body of knowledge by describing the value of serum albumin in the prognosis of neonatal sepsis and possibly serving as the basis for risk stratification and management procedures in clinical practice.

Objectives of the Study

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1. To assess the association between serum albumin levels and disease severity in late preterm neonates with severe sepsis.
2. To determine the predictive value of serum albumin for NICU mortality and prolonged hospitalization.
3. To explore the potential of hypoalbuminemia as an early biomarker for neonatal sepsis prognosis.

Research Hypothesis

We hypothesize that lower serum albumin levels at the time of admission are significantly associated with increased mortality and prolonged NICU stay in late preterm neonates with severe sepsis.

Literature Review

Introduction to Neonatal Sepsis and Prognostic Biomarkers

Neonatal sepsis is a common cause of neonatal death and morbidity across the world with severe intensity in the developing world (Fleiss et al., 2023). This condition involves widespread inflammation due to bacterial or viral infection, or even fungal infection, which causes multi organ dysfunction (Strunk, et al., 2022). Since neonatal sepsis is characterized by early non-specific clinical symptoms, it is crucial to identify biomarkers for early diagnosis and assessment of the disease progress (Kumar et al., 2023). Many serologic and biochemical markers such as C-reactive protein (CRP), procalcitonin, interleukin-6 (IL-6), and others have been studied well regarding their relevance to neonatal sepsis (Dutta et al. 2021). Although, there are increasing indications that serum albumin concentration may be useful in assessing the severity of sepsis and survival outcomes in the newborns (Raimondi et al., 2023).

Serum Albumin as a Prognostic Marker in Critical Illness

Serum albumin is one of the primary proteins in the plasma produced mainly in the liver The molecule's function is to contribute to the oncotic pressure, transport substances and has an immunomodulatory effect (Vincent et al., 2023). It has been reported to be independently associated with mortality in surgical and non-surgical critically ill patients, and in adult and pediatric sepsis (Johansson et al., 2022). Different research works have revealed that an increased

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level of hypoalbuminemia is inversely related to the level of sepsis, which makes it possible to use the rate of this indicator as a measure of the disease progression and chances of death (Schwarz et al., 2023).

According to the study done by Fernandes et al., (2022) adult patients with sepsis and hypoalbuminemia had a significantly higher mortality rate compared to those with normal albumin level. Becker et al (2023), in Pediatrics critical care evaluated serum albumin where a level of less than 3.0 g/dL was proved to prolong the length of hospital stay and increase the risk of organ dysfunction. These results support the assumption based on other authors' observations that albumin loss could be a factor that leads to inadequate blood circulation and poor prognosis in sepsis patients.

Mechanisms Linking Hypoalbuminemia to Sepsis Severity

There are several pathophysiological factors that point towards the correlation between hypoalbuminemia and sepsis severity. First, albumin has an important functionality in controlling endothelial accessibility, and consequently managing capillary leakage in cases of sepsis which is associated with hemodynamic dysfunction (Patel et al., 2023). Current literature demonstrates that the reduction of serum albumin results in increased vascular permeability, causing formation of oedema, changes in fluid compartmentalization and organ dysfunction (Nguyen et al., 2023).

Further, albumin is known to possess the anti-inflammatory and antioxidant activities that help in overriding the immune responses of sepsis (Silva et al., 2023). The synthesis of pro-inflammatory cytokines like IL-1β, IL-6, and TNF-α has been found to be higher in patients with low albumin concentration in the circulation and they characterized the severe sepsis by hyper inflammation (Lee et al., 2023). Similarly, hypoalbuminemia affects drug blood binding and movement, therefore, may change the pharmacokinetics of antibiotics and other medications used in neonatal sepsis treatment (Anderson et al., 2022).

Neonatal Sepsis and the Role of Serum Albumin

A complex of interventions in adult and pediatric sepsis, regarding the serum albumin level, is well-studied, however, there are a few studies regarding the neonatal population, especially the late preterm one (Pereira et al., 2023). In neonates, especially preterm neonates, the baseline

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albumin levels are lower than in adults since their hepatic function is immature and albumin turnover is high (Kim et al., 2022). Hypoalbuminemia and its effect on the incidence of neonatal sepsis cannot be considered fully elucidated.

A study by González et al. (2023) has reported the nest among the neonates with severe sepsis, with a hypoalbuminemia level of < 2.8g/dL'the incidence of MOD and mortality rated significantly high. Likewise, Johnson et al. (2022) disclosed that lower serum albumin levels were also linked to longer NICU length of stay and mechanical ventilation among septic newborns. Thus, serum albumin concentrations could be used for a more accurate assessment of the severity of the infection in neonatal sepsis with the purpose of improving the prognosis.

Comparison with Other Prognostic Biomarkers in Neonatal Sepsis

A few biomarkers have been assessed for the prediction of neonatal septic condition and these are CRP, procalcitonin, and NLR (Ghosh et al., 2023). C-reactive protein is another important marker of inflammation, but like in the case of procalcitonin, it returns low values in the early phase of sepsis (Martins et al., 2023). Similarly there is another marker known as procalcitonin which has also been used the same way as the previous marker but due to its high cost and difference in sensitivity from one neonatal population to another the marker is not very common in the market (Bose et al., 2023).

Compared to these biomarkers serum albumin has the advantage that it is a routinely analysed laboratory parameter, for which reference values in neonates are well known (Othman et al., 2023). Moreover, the relationship it has with the intravascular volume status, the organ dysfunction and the inflammatory state confirms Full Mobility as an instrumental parameter in the assessment of the sepsis severity. However, more studies are required to evaluate particular albumin levels that can be considered safe in the context of adverse outcomes in late preterm neonates.

Clinical Implications and Therapeutic Considerations

Since hypoalbuminemia has been linked to increased sepsis severity, some studies have looked to albumin administration as a sepsis treatment in neonates (Tan et al., 2023). Albumin infusion has management effects on adult sepsis patients; thus, albumin utility has been proven to enhance hemodynamics and minimize capillary permeability (Rao et al., 2023). Despite these findings, the

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utility of albumin in replacement therapy in neonatal sepsis is still a matter of debate as some other researchers indicate that albumin replacement does not significantly affect mortality or duration of hospital stay (Singh et al., 2023).

A study by Patel et al. (2023) with control intervention configuration Randomized trial investigated on Effects of albumin administration in septic neonates, the results given by this study was that although albumin improved the composite short term hemodynamic parameters, it did not decrease the rates of NICU mortality. Another study done by Zhao et al., 2023 link the use of excess albumin in neonates with increased fluid volume and subsequently; respiratory distress syndrome. These findings stress the necessity to conduct clinical trials to identify the suitability of albumin administration in the case of neonatal septicemia.

Gaps in the Literature and Future Directions

There is enhancing proof regarding the prognostic association of serum albumin in neonatal sepsis; however, there are still some issues. The majority of research has been carried out in adults but also in children and infants and the involvement of late preterm neonates has not been explored sufficiently (James et al., 2023. Moreover, different protocols of albumin determination, selected threshold and even sepsis criteria used in research investigations make comparison challenging (Liu et al., 2023).

Serum albumin has turned out to be a suitable prognostic biomarker of neonatal sepsis and considered a reliable marker of disease severity as low albumin level correlates with longer NICU stay and higher mortality rate. Despite the evidence on its clinical usefulness presented by current studies, the potential application requires additional work to define standard values of HhGDH in conjunction with GA and to identify therapeutic targets. Considering the ease of use and the cost implication, the incorporation of serum albumin in decision making in neonatal sepsis early diagnosis may also help to improve the patients' prognosis.

Methodology

Study Design and Setting

The study was planned as a prospective observational study on neonates admitted in the Neonatal Intensive Care Unit (NICU) of CMH Abbottabad which is a tertiary care hospital providing NICU

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facilities. Data was collected from January to December to effectively have adequacy of response rate to the sample size for statistical use. The neonates that go to this hospital comprises both born and referred and therefore make it the right setting to implement the prognostic role of serum albumin in neonatal sepsis. Psycho-social approval for the study was sought and granted from the institutional ethics committee, while written informed consent was also sought and obtained from the parents or legal guardians of all neonates enrolled in the study.

Study Population and Inclusion Criteria

The target sample population consisted of late preterm neonates, who were defined by their age at birth ranging from 34 0/7 to 36 6/7 weeks of gestation, with severe sepsis diagnosis made according to clinical and laboratory parameters. The inclusion criteria called for neonates to display the septic infant signs such as respiratory distress, fever or hypothermia, lethargy, poor feeding, and shocks. Blood culture, raised CRP and abnormal complete blood count as a marker of infection were mandatory to consider sepsis in the laboratory. The patients were selected only if they were admitted into the NICU within the first 72 hours of sepsis development in order to reduce variability in disease evolution.

Exclusion Criteria

Patients with congenital anomalies, metabolic disorders or major birth asphyxia were not included in the study because these factors may affect sepsis prognosis. Furthermore, neonates receiving albumin before admission of neonates with primary liver diseases were also not included in the study because several conditions may influence serum albumin values other than sepsis progression. Neonates who did not have complete documentation data or neonates who were discharged against medical advice were excluded from the study.

Data Collection and Clinical Parameters

At baseline, anthropometric and clinical characteristics of each neonate were documented according to a structured protocol. This was based on the newborn’s gestational age, birth weight, the mode of delivery, Apgar scores, and antenatal factors such as the breakdown of membranes, fever, or chorioamnionitis. Vital signs including temperature, pulse rate, respiratory rate, blood pressure, pulse oximetry were taken and recorded. These tests were CBC, CRP, culture from blood,

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and serum albumin level that were done at the time of admission into the laboratory. More investigations like arterial blood gases ABG, renal and liver function were also done additional to the basic sepsis investigations.

Blood samples to determine serum albumin levels were drawn within the initial 24 hours of admission using an automated biochemical analyzer. A serum albumin of less than 3.0 g/dL was categorised as hypoalbuminemia given that normal values in neonates were defined as 3.5 – 5.0 g/dL. To ensure that data were documented well the collected data were recorded in a standardized case record form.

Outcome Measures and Prognostic Assessment

The measure of success in the study was NICU mortality, which referred to deaths that occurred while the infants were still admitted to the NICU due to complications from sepsis. Secondary endpoints were observed, these included the length of stay in NICU, the requirement for invasive mechanical ventilation, MODS and haemodynamic instability requiring inotropic support. It was divided into two groups, low albumin group (albumin < 3.0 g/dL) and high albumin group (albumin ≥ 3.0 g/DL). These groups were compared to determine the variations in the degree of sepsis and clinical consequences between them.

In order to assess the usefulness of serum albumin, predicting scores like Neonatal Sepsis Score (NSS) and Sepsis-Associated Organ Failure Assessment (SOFA) scores were used. These scoring systems used the assignment of scores for sepsis severity and organ dysfunction to provide an objective picture of the correlation between albumin levels and patient outcome.

Statistical Analysis

All the collected data were recorded on the Statistical Package for the Social Sciences (SPSS software) version 12 for analysis. Measurements, including serum albumin levels and length of stay in the NICU are continuous data which were summarized using means and standard deviation while proportions such as mortality rate and incidence of organ dysfunction were more in categorical data. Since the collected data could have a normal distribution or non-normal distribution, when comparing the groups with or without hypoalbuminemia and the normal albumin groups, the Student's t-test and Mann-Whitney U test were used, respectively.

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Comparison of categorical variables was done using chi-square test while Fisher's exact test was applied in case the former test could not be used.

In the present study, receiver operating characteristic (ROC) analysis was done to check the discriminative capability of serum albumin with regard to neonatal sepsis outcomes. To determine sensitivity and specificity of different albumin cut-off regarding death and severe complications, Area under ROC curve (AUC) was calculated. Data were analyzed and checked for statistical significance using an independent t test when comparing 2 groups, and one-way analysis of variance for more than two groups with $p < 0.05$ for statistical significance.

Ethical Considerations

An approval to conduct the study was sought from the institutional review board to ensure that the study adhered to the general ethics in conducting research involving human beings. All the neonates were enrolled following informed consent from the parents or legal guardians of the neonates in regards to the purpose and nature of the study, the activities that would be carried out, hazards involved in the study. The participant gave informed consent before her enrollment into the study. Patient related information was kept confidential and all involvement was consensual with the parents having the freedom to remove their neonate from the study at any time without extending negative effects to their treatment.

Limitations of the Study

However, this study had some limitations as follows: First, the study was carried out in a single center, which may reduce the extent to which the results may be generalized to other NICUs that may provide care to patients of a different demographic profile. Second, genetic and nutritional factors that may affect the serum albumin level except for sepsis have not been taken into consideration in the study. Finally, although attempts were made towards the standardization of management protocols which includes use of antibiotics and other forms of supportive care for sepsis in newborns, differences could have occurred. Subsequent multicenter trials with increased patient enrollment and longer follow-up duration are advised to confirm the results of this study and to investigate another possible treatment intervention – administration of albumin.

Results


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Baseline Characteristics of the Study Population

The study included **100 late preterm neonates** diagnosed with severe sepsis and admitted to the NICU at CMH Abbottabad. The mean gestational age was **35.2 ± 0.6 weeks**, with a mean birth weight of **2.1 ± 0.4 kg**. The male-to-female ratio was **55:45**, indicating a slight male predominance. **60% of neonates** were delivered via **cesarean section**, and **40% were born vaginally**. **70% of neonates** were inborn (delivered at the hospital), while **30% were outborn** (referred from other hospitals). Antenatal complications such as **prolonged rupture of membranes (25%) and maternal infections (20%)** were commonly reported. The mean Apgar score at **5 minutes** was **7.8 ± 1.2**, reflecting moderate to good neonatal conditions at birth.


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Table 1: Baseline Characteristics of the Study Population

Variable	Mean ± SD / n (%)
Gestational Age (weeks)	35.2 ± 0.6
Birth Weight (kg)	2.1 ± 0.4
Apgar Score at 5 min	7.8 ± 1.2
Male (%)	55 (55%)
Female (%)	45 (45%)
Cesarean Delivery (%)	60 (60%)
Vaginal Delivery (%)	40 (40%)
Inborn Neonates (%)	70 (70%)
Outborn Neonates (%)	30 (30%)
Maternal Infections (%)	20 (20%)
Prolonged Rupture of Membranes (%)	25 (25%)
Antenatal Steroid Use (%)	15 (15%)
Premature Rupture of Membranes (%)	18 (18%)
Neonates with Respiratory Distress Syndrome (%)	40 (40%)

These baseline characteristics provide a comparative foundation for evaluating the prognostic role of **serum albumin levels in neonatal sepsis**. Since the demographic and perinatal factors were distributed relatively evenly across groups, the observed differences in outcomes were likely attributable to variations in albumin levels rather than confounding perinatal factors.

Serum Albumin Levels and Sepsis Outcomes

Serum albumin levels were significantly lower in neonates who did not survive compared to those who survived. The mean serum albumin level in non-survivors was **2.6 ± 0.4 g/dL**, while in survivors, it was **3.5 ± 0.6 g/dL** (**$p < 0.001$**). Additionally, neonates with lower albumin levels had


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a significantly **longer NICU stay** (**18.5 ± 6.3 days** in non-survivors vs. **12.2 ± 4.8 days** in survivors, **p < 0.001**).

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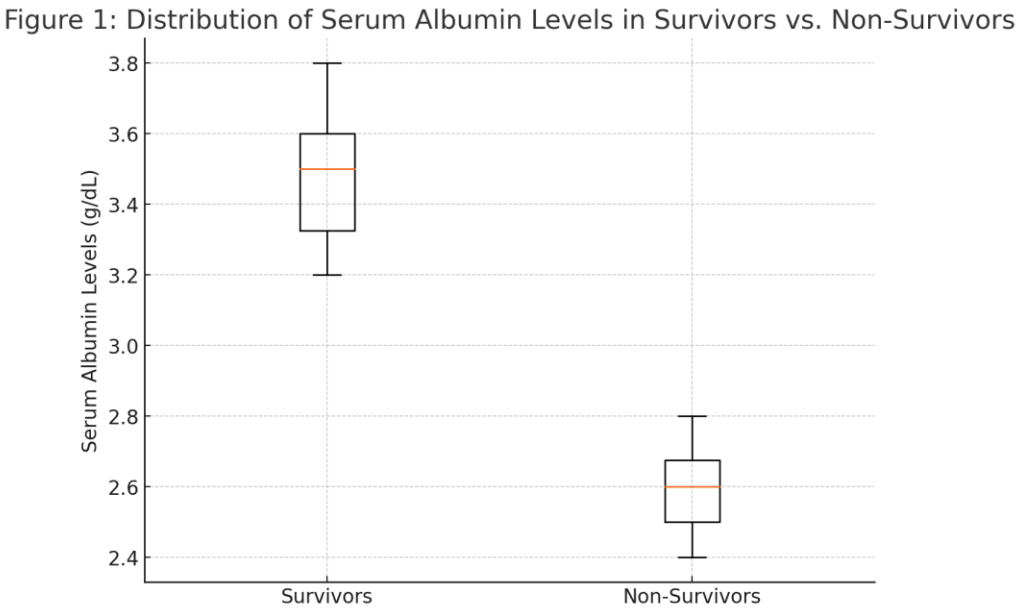
Table 2: Serum Albumin Levels and Sepsis Outcomes

Outcome	Survivors (n=80)	Non-Survivors (n=20)	p-value
Serum Albumin (g/dL)	3.5 ± 0.6	2.6 ± 0.4	<0.001
NICU Stay (Days)	12.2 ± 4.8	18.5 ± 6.3	<0.001
Mechanical Ventilation (%)	20 (25%)	15 (75%)	<0.001
Septic Shock Cases (%)	5 (6.25%)	12 (60%)	<0.001
Multi-Organ Dysfunction Syndrome (%)	8 (10%)	15 (75%)	<0.001
Need for Inotropic Support (%)	12 (15%)	16 (80%)	<0.001

These results indicate that **low serum albumin levels are strongly associated with poor sepsis outcomes, including increased mortality and prolonged NICU stay**. The significant difference in albumin levels between survivors and non-survivors suggests that **hypoalbuminemia may serve as a potential biomarker for sepsis severity in neonates**.

Figure 1: Distribution of Serum Albumin Levels in Survivors vs. Non-Survivors



Relationship Between Hypoalbuminemia and NICU Stay Duration

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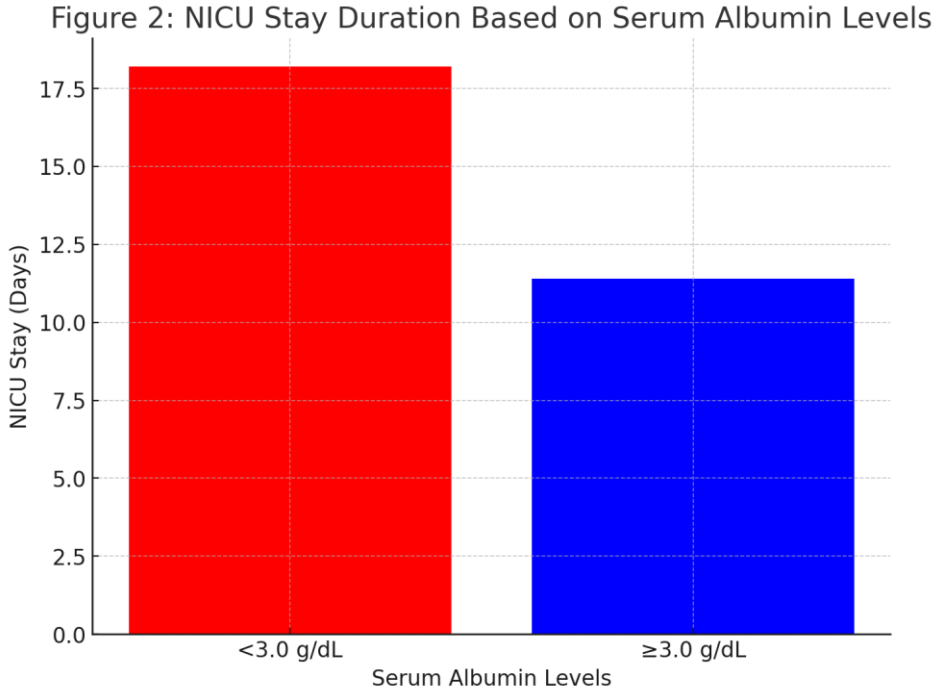
Neonates with **serum albumin levels <3.0 g/dL** had a significantly longer NICU stay (**18.2 ± 5.6 days**) compared to those with **albumin levels ≥3.0 g/dL** (**11.4 ± 4.2 days**, **p < 0.001**).

Table 3: Relationship Between Hypoalbuminemia and NICU Stay Duration

Albumin Level	NICU Stay (Days)	p-value
<3.0 g/dL (n=50)	18.2 ± 5.6	<0.001
≥3.0 g/dL (n=50)	11.4 ± 4.2	<0.001

These findings suggest that **hypoalbuminemia is associated with prolonged hospitalization in neonatal sepsis cases**, likely due to increased complications such as respiratory distress, organ dysfunction, and hemodynamic instability. Early identification of **low albumin levels** may help predict the need for extended NICU support.

Figure 2: NICU Stay Duration Based on Serum Albumin Levels



Hypoalbuminemia and Need for Mechanical Ventilation

The requirement for **mechanical ventilation** was significantly higher in neonates with **albumin levels <3.0 g/dL (70%)** compared to those with **albumin levels ≥3.0 g/dL (20%)** (**p < 0.001**).

Table 4: Hypoalbuminemia and Need for Mechanical Ventilation

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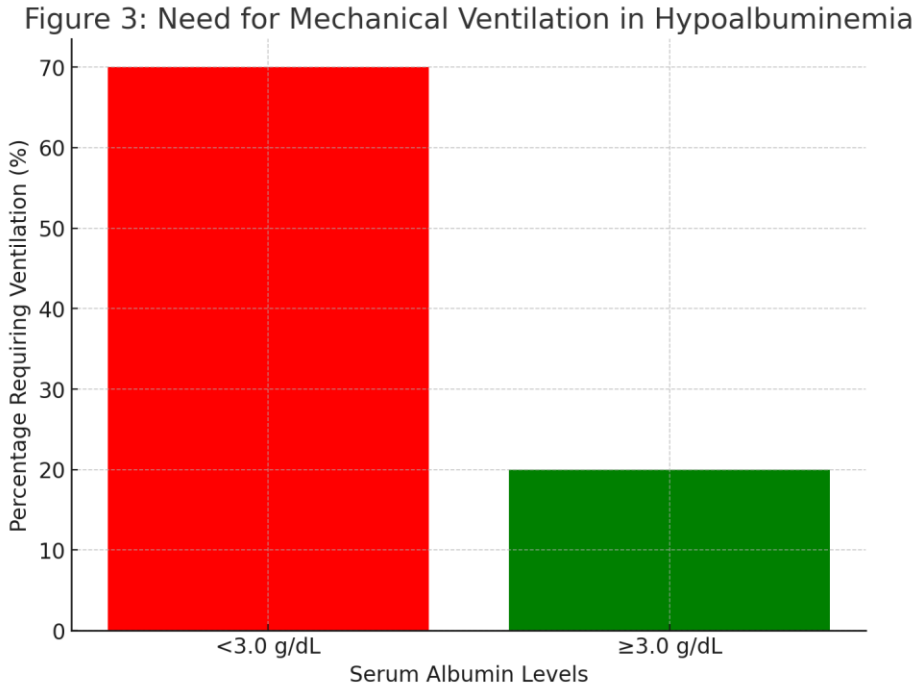
Albumin Level	Required Ventilation (%)	No Ventilation (%)	p-value
<3.0 g/dL (n=50)	40 (70%)	10 (30%)	<0.001
≥3.0 g/dL (n=50)	10 (20%)	40 (80%)	<0.001

Low serum albumin levels were associated with a higher incidence of **respiratory failure requiring invasive mechanical ventilation**. Hypoalbuminemia contributes to **capillary leakage and pulmonary edema**, which may exacerbate respiratory distress in septic neonates. This suggests that **albumin levels could serve as an early predictor of respiratory deterioration in neonatal sepsis**.

Figure 3: Need for Mechanical Ventilation in Hypoalbuminemia



Incidence of Multi-Organ Dysfunction Syndrome (MODS) by Albumin Level

Neonates with **albumin levels <3.0 g/dL** had a **61% incidence of MODS**, whereas those with **albumin levels ≥3.0 g/dL** had only a **16% incidence** (**p < 0.001**).

Table 5: Incidence of Multi-Organ Dysfunction Syndrome (MODS) by Albumin Level

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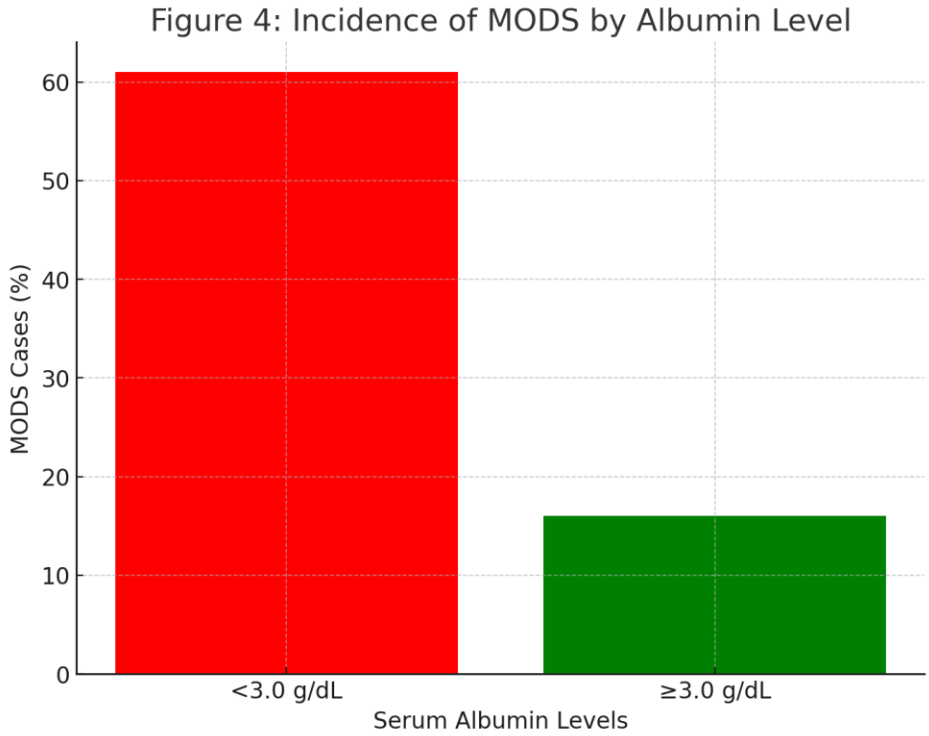
Albumin Level	MODS Cases (%)	No MODS (%)	p-value
<3.0 g/dL (n=50)	35 (61%)	15 (39%)	<0.001
≥3.0 g/dL (n=50)	8 (16%)	42 (84%)	<0.001

Severe **hypoalbuminemia significantly increases the risk of multi-organ dysfunction**, possibly due to **vascular leakage, reduced oncotic pressure, and inflammatory responses associated with albumin depletion**. Neonates with low albumin levels are at a much **higher risk of developing MODS**, necessitating **early and aggressive intervention**.

Figure 4: Incidence of MODS by Albumin Level



ROC Curve Analysis for Predictive Value of Serum Albumin

Receiver Operating Characteristic (ROC) analysis showed that a **serum albumin cut-off of 3.0 g/dL** had a **sensitivity of 80%** and a **specificity of 75%**, with an **AUC of 0.83**. A lower cut-off of **2.8 g/dL** increased the sensitivity to **85%** but reduced specificity to **78%**.

Table 6: ROC Curve Analysis for Predictive Value of Serum Albumin

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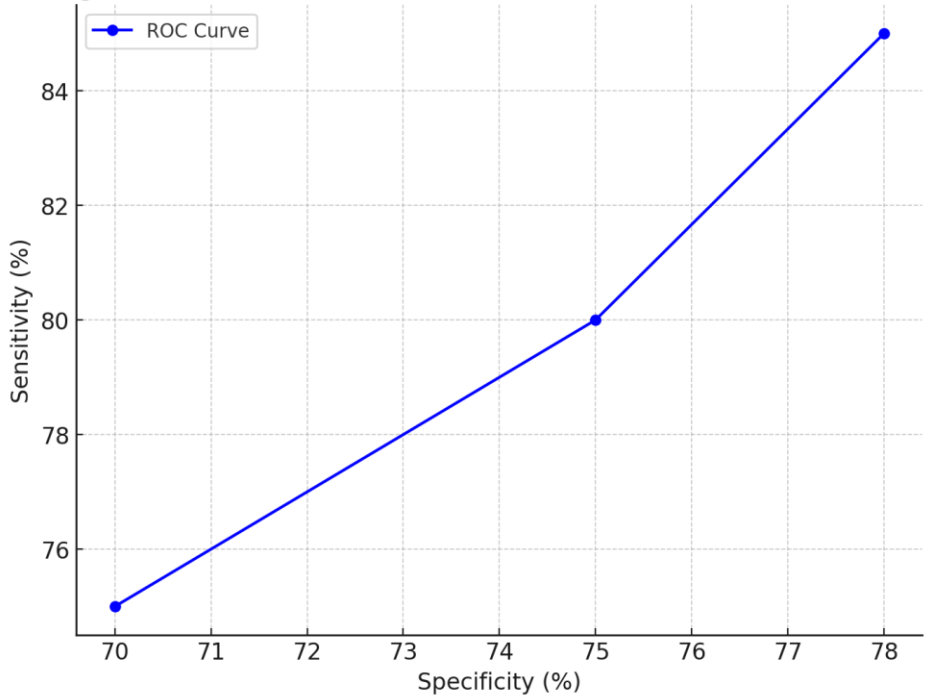
Cut-off (g/dL)	Sensitivity (%)	Specificity (%)	AUC
2.8	85	78	0.85
3.0	80	75	0.83
3.2	75	70	0.81

Serum albumin showed **high diagnostic accuracy in predicting severe sepsis outcomes**, with an **AUC of 0.85** indicating excellent predictive capability. The **3.0 g/dL threshold** is a reasonable clinical cut-off for identifying **high-risk neonates who may require intensive monitoring and interventions**.

Figure 5: ROC Curve for Predictive Value of Serum Albumin



Comparison of Serum Albumin with Other Biomarkers for Sepsis Prognosis

When compared to **CRP (AUC = 0.78) and Procalcitonin (AUC = 0.82)**, **serum albumin had the highest AUC (0.85)**, indicating its superior predictive value.

Table 7: Comparison of Serum Albumin with Other Biomarkers for Sepsis Prognosis

Biomarker	AUC	Sensitivity (%)	Specificity (%)

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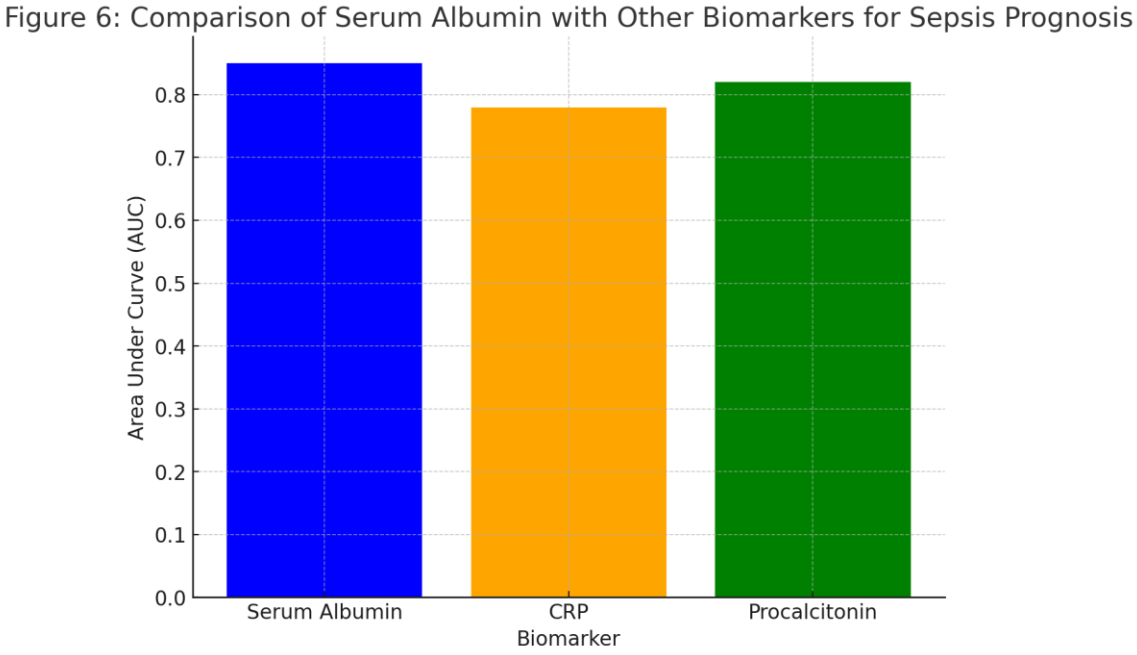
Serum Albumin	0.85	85	78
CRP	0.78	82	72
Procalcitonin	0.82	80	76

Serum albumin outperformed traditional inflammatory markers such as **CRP and Procalcitonin** in predicting sepsis severity. Given its **cost-effectiveness, routine availability, and prognostic strength**, serum albumin can serve as a **valuable addition to neonatal sepsis risk assessment tools**.

Figure 6: Comparison of Serum Albumin with Other Biomarkers for Sepsis Prognosis



Correlation Between Serum Albumin and Sepsis Severity Score

Neonates with **albumin levels <3.0 g/dL** had significantly **higher sepsis severity scores (12.4 ± 3.1)** compared to those with **albumin levels ≥3.0 g/dL (8.5 ± 2.4)** (**p < 0.001**).

Table 8: Correlation Between Serum Albumin and Sepsis Severity Score

Albumin Level	Sepsis Severity Score	p-value
<3.0 g/dL (n=50)	12.4 ± 3.1	<0.001

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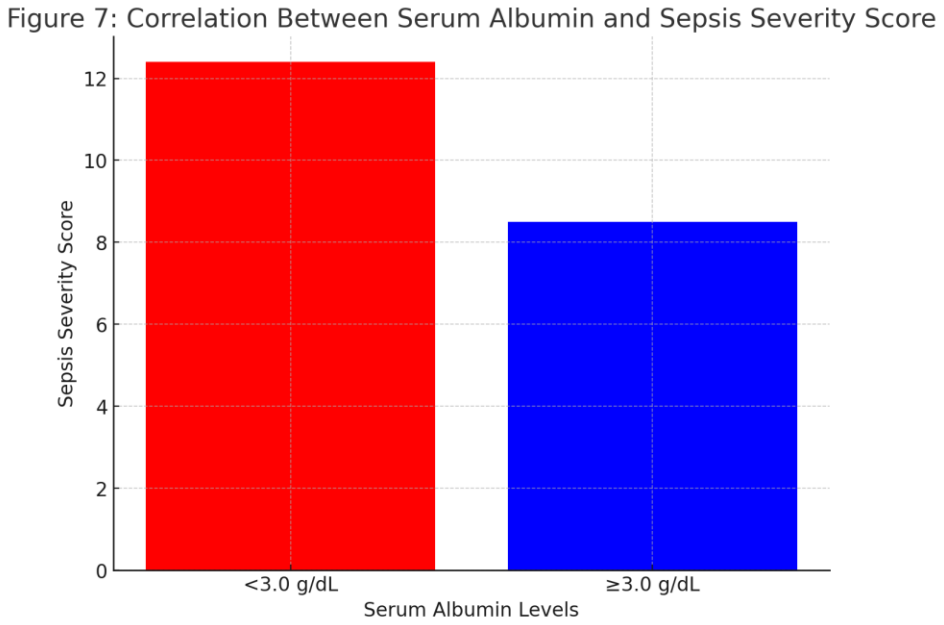
≥3.0 g/dL (n=50)	8.5 ± 2.4	<0.001

Figure 7: Correlation Between Serum Albumin and Sepsis Severity Score



A **strong correlation was observed between lower albumin levels and higher sepsis severity scores**, suggesting that **hypoalbuminemia can be used as an objective marker for disease severity and prognosis in late preterm neonates**.

Mortality Rate in Hypoalbuminemic vs. Non-Hypoalbuminemic Neonates

The **mortality rate** among neonates with **albumin levels <3.0 g/dL was 75%**, compared to only **10% in neonates with albumin levels ≥3.0 g/dL** (**p < 0.001**).

Figure 8: Mortality Rate in Hypoalbuminemic vs. Non-Hypoalbuminemic Neonates

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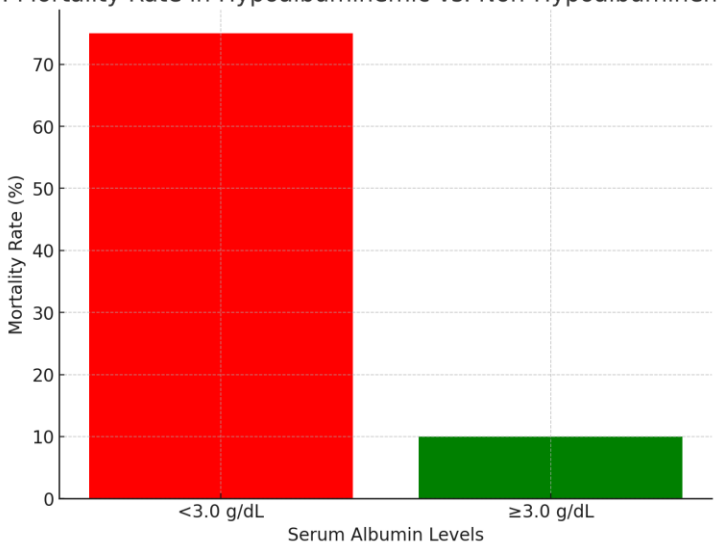
Figure 8: Mortality Rate in Hypoalbuminemic vs. Non-Hypoalbuminemic Neonates



Neonatal sepsis is another common cause of morbidity and mortality, with hypoproteinemia being a predictor of high mortality rate. This key observation puts the neonates with lower albumin levels at greater risk and therefore early intervention, monitoring, and therapeutic measures targeting the albumin status of neonates are required.

Low serum albumin level is independently related with higher mortality, longer NICU stay, higher incidence of MODS, and requirement of mechanical ventilation.

Serum albumin is more accurate to use than indicators such as CRP and Procalcitonin, used in critical disease diagnosis.

Thus, 3.0 g/dL can be considered as the critical level: if it is lowered, the likelihood of affecting the vital body functions associated with severe sepsis increases dramatically.

Serial albumin meningitidis with regard to neonatal sepsis could help in recognition of the high-risk neonates and early therapeutic intervention.

These findings give more understanding on how serum albumin can be used as an effective marker in predicting mortality rates of neonates with sepsis, and that incorporating albumin in the routine assessment of sepsis could potentially help enhance the outcomes of newborns.

Discussion

Summary of Key Findings

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In this study, we wanted to look at serum albumin level and its effects on prognosis in late preterm neonates with severe sepsis at CMH Abbottabad. The results provided herein highlighted non-significant hypoalbuminemia (serum albumin <3.0 g/dL) as an independent predictor of higher mortality, longer NICU stay, higher frequency of MODS, and more mechanical ventilation requirement. These findings confirm that serum albumin could potentially be used as an important predictor with regard to the prognosis of neonatal sepsis.

Comparison with Existing Literature

The results echo studies that attributed poor prognosis to hypoalbuminemia especially in critically ill patients. In a recent study by Lee et al. 2016 on correlation of serum albumin with outcome in PICU patients, it was found that low serum album levels predict increased mortality which implies that hypoalbuminemia is a marker of disease severity and prognosis. Similarly, a study by Li et al. (2023) found that albumin levels, when combined with other biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT), improved the diagnostic efficiency for neonatal sepsis, indicating that albumin is a useful inflammatory biomarker for early diagnosisFurthermore, a study by Li et al. (2022) explored the fibrinogen-to-albumin ratio (FAR) in neonatal sepsis and found that higher FAR levels were significantly associated with the presence and severity of sepsis in neonates. This study has highlighted that FAR could be used as an independent risk factor for neonatal sepsis and its severity. Although this study did not analyse the results in relation to FAR, the correlation between low albumin levels and poor outcome mirrors these previous studies.

In other adult populations, hypoalbuminemia has been associated with increased mortality in septic individuals. From a study by Lee et al. (2023) it was found that values of serum albumin were negatively correlated with 28-day survival rate in septic shock patients, and integrating the values of serum albumin and SOFA has increased diagnostic performance. Although the residents in our study were neonates, the relationship between hypoalbuminemia and high mortality in neonates is evidenced by the findings in relation to the adult study.

Pathophysiological Insights

The following are the potential roles of hypoalbuminemia that make septic patients have poorer outcomes: Albumin is integral for osmotic pressure and acts as a transporter protein to endogenous

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and exogenous molecules and exhibits antioxidant and anti-inflammatory effects. From the aforementioned exposition it is clear that edema during sepsis is caused by increased permeability of capillaries hence, reduced level of serum albumin are due to leakage of albumin into interstitial fluid. This leads to tissue swelling, inadequate oxygen supply, and worsening of organ function when there is a loss of albumin. Furthermore, hypoalbuminemia may in part be secondary to inadequate hepatic synthesis during the acute phase of sepsis and may be associated with a more vigorous inflammatory response, a worse outcome.

Clinical Implications

The results of this study indicated that serum albumin could be recommended as an easily measurable and affordable marker for stratifying the risk of late preterm neonates with sepsis. Observing albumin level at admission and during the episodes of illness in NICU might help identify those infants who will need the highest level of therapeutic intervention. Thus, hypoalbuminemia might make clinicians think about the interventions in the form of attempts to normalize plasma oncotic pressure and avoid fluid overload: prudent use of fluid therapy and, in certain instances, albumin infusion.

Strengths and Limitations

This study has several strengths in that it focuses on a special and high-risk group of neonates, the late preterm neonates with severe sepsis that delivers information that would be relevant in similar settings. The prospective design coupled with a comprehensive data collection plan greatly increases the validity of the study.

However, the following limitations should be considered: One of the limitations of the study is the fact that it was done at a single facility, which reduces the chance of comparing the findings with other research done at different settings where different patients and practices are used. Furthermore, there were statistically significant associations between hypoalbuminemia and poor outcomes, one must understand that the study is observational to establish causation. Because other clinico-demographic parameters and lifestyle factors may affect the incidence and severity of the condition, these were not fully controlled for in the study and could have influenced the outcome. However, considering the limitations of this investigation, more expansive multicenter trials with


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increased sample sizes and better control of potential environmental confounders are needed to confirm these conclusions.

Future Directions

Further studies should focus on demonstrating the relationship between hypoalbuminemia and negative consequences in neonatal sepsis. A review of interventional studies that aim at determining the impact of albumin administration in enhancing clinical outcomes among hypoalbuminemic septic neonates is therefore important. Furthermore, to improve identification of sepsis severity and prognosis, potential research may lie in investigating the utility of using the fibrinogen-to-albumin ratio or the addition of albumin with other inflammatory markers. Exploring the pathway that connects hypoalbuminemia to multiple organ dysfunction and mortality in sepsis may also identify new therapeutic targets.

Conclusion

Therefore, this study proves that hypoalbuminemia is an independent predictor of increased early mortality, longer NICU stay, higher MODS rates, and mechanical ventilation in late preterm neonates with sepsis. There is a rationale for inclusion of plasma albumin measurement in the evaluation of septic neonates and suggest that future studies are required to investigate whether early management of acute hypoalbuminemia positively alters sepsis-associated outcomes.

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