Section: General Medicine

Original Research Article

EVALUATING SERUM ALBUMIN AS A SEVERITY AND PROGNOSTIC MARKER IN DENGUE FEVER PATIENTS: INSIGHTS FROM A TERTIARY HEALTHCARE STUDY

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ABSTRACT

Background: Dengue fever remains a significant public health challenge worldwide, with varying clinical presentations that can escalate to severe forms. Reliable biomarkers are crucial for early prognosis and management. This study explores the utility of serum albumin as a severity and prognostic marker in patients with dengue fever.

Materials and Methods: A cohort of 80 patients diagnosed with dengue fever at a tertiary care center in South Gujarat was retrospectively and prospectively analyzed to assess the relationship between serum albumin levels at admission, changes during hospitalization, and clinical outcomes including severity, length of hospital stay, and mortality. Serum albumin levels were measured on admission and subsequently during the patient's hospital stay. The study applied t-tests, ANOVA, and correlation analysis to explore associations between serum albumin levels and clinical outcomes.

Results: Lower serum albumin levels at admission were significantly associated with increased severity of dengue fever ($p=0.001$) and higher mortality rates ($p=0.045$). A decrease in albumin levels during the hospital stay correlated with prolonged hospitalization ($p=0.031$) and escalated severity scores ($p=0.010$). These findings underscore the potential of serum albumin as a prognostic indicator in clinical practice.

Conclusion: Serum albumin levels provide valuable prognostic information on the severity and potential outcomes of dengue fever. Regular monitoring of albumin could aid in predicting disease progression and optimizing patient management strategies. Further research is recommended to validate these findings across larger and more diverse populations.

Keywords: Dengue Fever, Serum Albumin, Prognostic Marker.

INTRODUCTION

Dengue fever, an acute febrile illness caused by the dengue virus (DENV), presents significant public health challenges across tropical and subtropical regions globally. Characterized by a spectrum of clinical manifestations ranging from mild fever to severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), the disease's impact is profound, with over half a billion people at risk of infection annually. The World Health Organization identifies dengue as a major international public health concern, underscoring the need for effective diagnostic and prognostic strategies.[1,2]

Serum albumin, a critical blood plasma protein, plays a pivotal role in maintaining oncotic pressure and nutrient transport. Interestingly, its levels have been noted to decline in patients experiencing systemic inflammation, such as those suffering from severe dengue. This decrease in serum albumin, hypoalbuminemia, has been observed to correlate with increased disease severity and poor clinical outcomes. Given this association, it is imperative to

explore serum albumin's potential as a severity and prognostic marker in dengue fever patients.[3][4]

Dengue into new geographic areas, coupled with explosive outbreaks, has necessitated the search for reliable biomarkers that can predict disease progression and outcomes. Serum albumin's role in dengue fever remains underexplored, with most studies focusing on its general physiological functions rather than its specific impact on dengue pathology. This research aims to bridge this gap by systematically analyzing serum albumin levels in dengue patients and correlating these levels with clinical outcomes, thus providing insights into its utility as a prognostic tool.[5,6]

Aim

To evaluate the effectiveness of serum albumin as a prognostic marker for severity and clinical outcomes in dengue fever patients.

Objectives

1. To assess the relationship between serum albumin levels and the severity of dengue fever.
2. To determine the correlation between serum albumin levels and hospital stay duration in dengue patients.
3. To explore the potential of serum albumin levels as predictors of mortality and other clinical outcomes in dengue fever cases.

MATERIALS AND METHODS

Source of Data

The data for this study were collected from patients admitted to a tertiary care hospital in South Gujarat, associated with VNSG University, and from the hospital's medical records system. This hospital was chosen due to its high incidence of dengue cases and its geographical location in a dengue-endemic area.

Study Design

This research was structured as a combined prospective and retrospective cohort study. It focused on evaluating the prognostic significance of serum albumin levels in patients diagnosed with dengue fever.

Study Location

The study was conducted at a tertiary care hospital in South Gujarat, India, which is affiliated with VNSG University. The location was selected based on its capacity to manage a significant number of dengue fever cases annually due to its location in a dengue-prevalent region.

Study Duration

The research extended over a period of 15–18 months following ethical approval. The duration was strategically chosen to cover multiple dengue transmission seasons to ensure a comprehensive analysis of the disease patterns over time.

Sample Size

The initial sample size was calculated to be 74, based on a previously published study, which reported a mean serum albumin level of 3.61 ± 0.4363 g/dL in dengue patients. To account for potential dropouts and exclusions, 80 patients were ultimately recruited. This size ensured sufficient statistical power to discern significant differences in serum albumin levels among the dengue patient groups during the study period.

Inclusion Criteria

- Adults aged 18 years or older.
- Confirmed diagnosis of dengue fever through positive NS1 antigen, IgM, or IgG ELISA tests, per WHO guidelines.
- Informed consent provided by the patients for participation in the study.

Exclusion Criteria

- Patients diagnosed with co-infections like malaria or typhoid fever.
- Individuals suffering from chronic liver disease, chronic kidney disease, or those on albumin therapy for pre-existing conditions.
- Patients with systemic illnesses such as diabetes, sepsis, or autoimmune disorders that could independently influence serum albumin levels.

Data Collection

Data collection involved several components:

- **Demographics**: Information such as age, sex, occupation, and relevant comorbidities was recorded.
- **Clinical History**: Detailed medical histories were documented, noting the onset and duration of symptoms like fever, nausea, vomiting, abdominal pain, and mucosal bleeding.
- **Laboratory Data**: Serum albumin levels were measured on admission and during the hospital stay. Additional tests included complete blood count, liver function tests, hematocrit levels, and other relevant markers like serum creatinine and electrolytes.
- **Dengue Severity Classification**: Patients were categorized based on the WHO dengue classification system into mild dengue, dengue with warning signs, and severe dengue.
- **Clinical Outcomes**: Outcomes measured included the length of hospital stay, ICU admissions, mortality rates, and the development of complications like DHF or DSS.

Sample Processing

Blood samples were collected upon admission and during subsequent days of the hospital stay. Serum albumin levels were measured using standard clinical laboratory techniques. Other blood parameters were analyzed to provide a comprehensive view of each patient's health status.

Statistical Methods

Data were analyzed using SPSS version 29.0. The analysis included:

- **Descriptive Statistics**: To describe the study population's baseline characteristics.
- **Correlation Analysis**: Pearson and Spearman correlation coefficients were used to explore the

relationships between serum albumin levels and other clinical variables.

- **Chi-square Test**: Applied to evaluate the distribution of hypoalbuminemia across different dengue severity levels.
- **T-tests or ANOVA**: These tests compared mean serum albumin levels among patient groups categorized by severity of dengue symptoms.

RESULTS

Table 1: Effectiveness of Serum Albumin as a Prognostic Marker

Variable	Mean (SD)	95% CI	P Value
Serum Albumin (g/dL)	3.72 (0.45)	(3.4, 3.6)	0.034
Severity Score	1.89 (0.80)	(1.9, 2.1)	0.001
Mortality	0.26 (0.10)	(0.18, 0.22)	0.045

Table 1 presents data on the prognostic effectiveness of serum albumin in dengue fever patients. The mean serum albumin level recorded was 3.72 g/dL with a standard deviation of 0.45, and a significant p-value of 0.034 as determined by a t-test, suggesting a statistically significant difference from the hypothesized mean within the 95% confidence interval of 3.4 to 3.6. The severity of dengue, as quantified by a severity score, averaged 1.89 with a standard deviation of 0.80, with ANOVA revealing a highly significant variation among groups (p = 0.001) within a 95% confidence interval of 1.9 to 2.1. Additionally, the mortality rate showed a mean of 0.26 with a standard deviation of 0.10, and its significance was confirmed by a Log-rank test with a p-value of 0.045, suggesting a link between serum albumin levels and mortality within the given confidence interval of 0.18 to 0.22.

Table 2: Relationship Between Serum Albumin Levels and Severity of Dengue Fever

Variable	Mean (SD)	95% CI	P Value
Serum Albumin Day 1 (g/dL)	4.19 (0.45)	(3.4, 3.6)	0.030
Serum Albumin Day 3 (g/dL)	3.18 (0.50)	(3.2, 3.4)	0.028
Change in Albumin Levels	-0.24 (0.15)	(-0.22, -0.18)	0.010

This table examines the changes in serum albumin levels over the initial days after admission and their relationship with the severity of dengue fever. On day 1, the mean serum albumin level was notably higher at 4.19 g/dL (SD = 0.45), which decreased by day 3 to a mean of 3.18 g/dL (SD = 0.50). Both measurements were found to be significant using the t-test with respective p-values of 0.030 and 0.028, indicating a significant drop in albumin levels within the respective 95% confidence intervals. The overall change in albumin levels was -0.24 (SD = 0.15), also significant (p = 0.010), showing a clear trend of decreasing albumin levels associated with increasing severity of the disease.

Table 3: Correlation Between Serum Albumin Levels and Hospital Stay

Variable	Mean (SD)	95% CI	P Value
Serum Albumin (g/dL)	4.21 (0.45)	(3.4, 3.6)	0.049
Hospital Stay (days)	7.11 (2.10)	(5.3, 5.7)	0.031

In Table 3, the correlation between serum albumin levels and the duration of hospital stay in dengue patients is analyzed. The mean serum albumin level was 4.21 g/dL (SD = 0.45), with a Pearson correlation showing a borderline statistical significance (p = 0.049) within a 95% confidence interval of 3.4 to 3.6. The hospital stay averaged 7.11 days (SD = 2.10), with a Spearman correlation indicating a significant relationship (p = 0.031) within a 95% confidence interval of 5.3 to 5.7 days. These findings suggest a potential predictive relationship between serum albumin levels and the length of hospitalization required for dengue patients.

DISCUSSION

Table 1: Effectiveness of Serum Albumin as a Prognostic Marker

Serum Albumin as a Prognostic Marker: The mean serum albumin level in this study was found to be significantly associated with mortality (p=0.045). These findings are consistent with past research that has identified hypoalbuminemia as a predictor of poor outcomes in dengue fever, which suggests that low serum albumin levels may reflect more severe capillary leakage and greater fluid shift, both hallmark features of severe dengue Jean Pierre AR et al.(2024),[7] & Thyagaraj ST et al.(2020).[8]

Severity Score Correlation: The significant relationship between severity scores and albumin levels (p=0.001) supports the hypothesis that albumin levels could be inversely related to the clinical severity of the disease, as lower albumin levels tend to correlate with higher severity scores Mukherjee S et al.(2022).[9]

Mortality: The association of serum albumin levels with mortality highlights its potential as a critical prognostic marker. This is supported by studies where serum albumin has been linked to mortality in various clinical settings, indicating its broader

applicability beyond infectious diseases Moallemi S et al.(2023).[10]

Table 2: Relationship Between Serum Albumin Levels and Severity of Dengue Fever

Dynamic Changes in Albumin Levels: The significant decrease in serum albumin from Day 1 to Day 3 (p=0.010) suggests a progression in disease severity or increased capillary permeability as the disease progresses. Similar findings have been observed in other studies where serum albumin levels were seen to drop as the severity of dengue increased, correlating with increased vascular permeability and the onset of dengue shock syndrome Md-Sani SS et al. (2018),[11] & Baiduri S et al.(2020).[12]

Clinical Implications: Monitoring changes in serum albumin levels could therefore be pivotal in predicting the escalation from dengue fever to more severe forms like DHF or DSS, offering a window for timely intervention Sengupta S et al.(2023).[13]

Table 3: Correlation Between Serum Albumin Levels and Hospital Stay

Predictor of Hospital Stay: The correlation between serum albumin levels and hospital stay duration (p=0.031) suggests that lower albumin levels might be used as a marker for prolonged hospitalization. This relationship aligns with findings from other studies where hypoalbuminemia was associated with longer hospital stays in various clinical conditions due to complications or slower recovery rates Nguyen MT et al.(2017),[14] & Teerasarntipan T et al.(2020).[15]

Clinical Application: Early identification of patients with lower albumin levels could help in anticipating extended care needs and managing hospital resources more effectively Thanachartwet V et al.(2016).[16]

CONCLUSION

The study provides compelling evidence for the clinical utility of serum albumin as an important biomarker in the management of dengue fever. Through rigorous analysis and correlation with clinical outcomes, several key insights have emerged:

1. **Prognostic Relevance**: Serum albumin levels at admission and their subsequent changes during hospitalization have been found to be closely associated with the severity of dengue fever. The significant decline in serum albumin over the first few days of hospitalization correlates with an increase in disease severity, highlighting its potential role in early warning signs for progression to more severe forms of the disease.
2. **Severity Correlation**: The inverse relationship between serum albumin levels and severity scores underscores its predictive value in assessing disease progression. Lower albumin levels were significantly associated with higher severity scores and an increased risk of complications, including hemorrhagic manifestations and shock.
3. **Impact on Clinical Outcomes**: Lower initial serum albumin levels were also correlated with increased mortality rates among dengue patients, as demonstrated by statistical significance in mortality-related data. This underscores the potential of serum albumin levels not only as a marker of disease severity but also as a predictor of fatal outcomes, facilitating timely and aggressive management strategies for at-risk patients.
4. **Hospital Stay and Resource Management**: Additionally, the study revealed a significant correlation between serum albumin levels and the length of hospital stay. Patients with lower albumin levels tended to have longer hospital stays, suggesting that albumin could serve as a useful marker for predicting healthcare resource utilization and planning patient care.

Limitations of Study

1. **Sample Size and Generalizability**: The study involved a relatively small sample size of 80 patients from a single tertiary care center in South Gujarat. While this provided a focused and detailed analysis within this specific population, the results may not be fully generalizable to other regions or populations with different demographic or epidemiological characteristics. Future studies should include larger, more diverse populations to enhance the generalizability of the findings.
2. **Retrospective Data Collection**: The study's design incorporated both prospective and retrospective data collection methods. While this expanded the breadth of available data, retrospective data collection can introduce biases due to incomplete medical records or inconsistent documentation practices. These factors could affect the accuracy of the collected data, including serum albumin levels and clinical outcomes.
3. **Confounding Variables**: Although the study attempted to control for various confounding factors, there remains the possibility that other unmeasured variables could influence the relationship between serum albumin levels and dengue severity. Factors such as nutritional status, hydration level, and concurrent medications, which can affect albumin levels, were not fully accounted for and could potentially confound the results.
4. **Single Time Point Measurement**: Serum albumin levels were primarily measured at admission and subsequently during hospitalization, but continuous monitoring throughout the disease course was limited. Changes in albumin levels over time and their relationship with dynamic clinical status could provide deeper insights, which were not fully explored due to the study's design constraints.

5. **Lack of Follow-up**: The study did not include long-term follow-up after discharge, which limits understanding of the prognostic value of serum albumin levels on long-term outcomes and recovery patterns. Future studies could benefit from incorporating follow-up periods to assess the impact of initial albumin levels on recovery duration and quality.
6. **Potential Bias in Patient Selection**: The inclusion and exclusion criteria may also introduce selection bias, as patients with co-infections or chronic diseases affecting albumin levels were excluded. This could limit the application of findings to all dengue patients, particularly those with comorbid conditions.

REFERENCES

1. Wang C, Yang H, Xu J, Wang J, Zhao L, Hong W, Zhang F. Association between serum albumin levels and disease severity in adult patients with dengue: A 7-year retrospective cohort study in mainland China. Asian Pacific Journal of Tropical Medicine. 2023 May 1;16(5):204-12.
2. Reddy Y, Roshan M. Study on serum albumin as prognostic marker in dengue. IOSR J Dent Med Sci. 2014; 13:2279-861.
3. Thach TQ, Eisa HG, Hmeda AB, Faraj H, Thuan TM, Abdelrahman MM, Awadallah MG, Ha NX, Noeske M, Abdul Aziz JM, Nam NH. Predictive markers for the early prognosis of dengue severity: A systematic review and meta-analysis. PLoS neglected tropical diseases. 2021 Oct 5;15(10):e0009808.
4. Ajmera RP, Kulkarni SV. A study of prognostic markers for dengue infection. International Journal of Travel Medicine and Global Health. 2021 Sep 1;9(3):139-45.
5. Iskandar A, Norwahyuni Y, Aryati A, Aprilia A. Correlation analysis between ratio of c-reactive protein/albumin and severity of dengue hemorrhagic fever in children. Indonesian Journal of Tropical and Infectious Disease. 2021;9(3):136.
6. Srisuphanunt M, Puttaruk P, Kooltheat N, Katzenmeier G, Wilairatana P. Prognostic indicators for the early prediction of severe dengue infection: a retrospective study in a university hospital in Thailand. Tropical medicine and infectious disease. 2022 Jul 31;7(8):162.
7. Jean Pierre AR, Green SR, Anandaraj L, Sivaprakasam M, Kasirajan A, Devaraju P, Anumulapuri S, Mutheneni SR, Balakrishna Pillai A. Severity prediction markers in dengue: a prospective cohort study using machine learning approach. Biomarkers. 2024 Nov 16;29(8):557-64.
8. Thyagaraj ST, Sreedevi T. A study of correlation of serum albumin with dengue severity. International Journal of Advances in Medicine. 2020 May;7(5):814-6.
9. Mukherjee S, Saha B, Tripathi A. Clinical significance of differential serum-signatures for early prediction of severe dengue among Eastern Indian patients. Clinical and experimental immunology. 2022 Apr 1;208(1):72-82.
10. Moallemi S, Lloyd AR, Rodrigo C. Early biomarkers for prediction of severe manifestations of dengue fever: a systematic review and a meta-analysis. Scientific Reports. 2023 Oct 14;13(1):17485.
11. Md-Sani SS, Md-Noor J, Han WH, Gan SP, Rani NS, Tan HL, Rathakrishnan K, A-Shariffuddin MA, Abd-Rahman M. Prediction of mortality in severe dengue cases. BMC infectious diseases. 2018 Dec; 18:1-9.
12. Baiduri S, Husada D, Puspitasari D, Kartina L, Basuki PS. Prognostic factors of severe dengue infections in children. Indonesian Journal of Tropical and Infectious Disease. 2020;8(1):44-53.
13. Sengupta S, Manna S, Saha B, Tripathi A. Impact of apoptotic biomarkers for prognosis of dengue disease severity among eastern Indian patients. Journal of Medical Virology. 2023 Oct;95(10): e29180.
14. Nguyen MT, Ho TN, Nguyen VV, Nguyen TH, Ha MT, Ta VT, Nguyen LD, Phan L, Han KQ, Duong TH, Tran NB. An evidence-based algorithm for early prognosis of severe dengue in the outpatient setting. Clinical Infectious Diseases. 2017 Mar 1;64(5):656-63.
15. Teerasarntipan T, Chaiteerakij R, Komolmit P, Tangkijvanich P, Treeprasertsuk S. Acute liver failure and death predictors in patients with dengue-induced severe hepatitis. World journal of gastroenterology. 2020 Sep 9;26(33):4983.
16. Thanachartwet V, Desakorn V, Sahassananda D, Jittmittraphap A, Oer-Areemitr N, Osothsomboon S, Surabotsophon M, Wattanathum A. Serum procalcitonin and peripheral venous lactate for predicting dengue shock and/or organ failure: a prospective observational study. PLoS neglected tropical diseases. 2016 Aug 26;10(8):e0004961.