



CORRELATION OF LIVER ENZYMES (AST/ALT) WITH CLINICAL OUTCOMES IN CHILDREN WITH DENGUE

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ABSTRACT

Background: Dengue fever is a major vector-borne viral illness with significant health consequences, particularly in tropical and subtropical regions. In Punjab, Pakistan, liver involvement, reflected by elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, has been observed in dengue patients. However, the relationship between liver enzyme profiles and clinical outcomes in pediatric dengue remains underexplored. **Objective:** To assess the association between liver enzyme (AST/ALT) levels and clinical outcomes in children with dengue in Punjab, Pakistan, focusing on disease severity, complications, and hospitalization duration.

Methods: A prospective, observational, multicenter study was conducted at three tertiary care hospitals in Multan, Ibn-e-Siena Hospital & Research Institute, Nishtar Hospital & The Children Hospital & the Institute of Child Health, Multan, Punjab, from August to December 2025. Pediatric patients aged 1–12 years with confirmed dengue fever, diagnosed based on positive NS1 or IgM antibody tests, were included. Data on liver enzyme levels (AST/ALT), clinical severity (Dengue Fever, Dengue Hemorrhagic Fever [DHF], Dengue Shock Syndrome [DSS]), complications, and hospital stay were collected. Statistical analyses included ANOVA, Pearson's correlation, and logistic regression, with the ROC curve used to determine the predictive value of AST/ALT levels for severe disease.

Results: The study included 200 pediatric patients. AST levels were significantly higher in DHF (230 ± 80 U/L) and DSS (315 ± 110 U/L) compared to Dengue Fever (120 ± 45 U/L). Similarly, ALT levels were elevated in severe cases (DHF: 210 ± 85 U/L, DSS: 290 ± 105 U/L). A significant positive correlation was observed between AST levels and hospital stay ($r = 0.68$, $p < 0.001$). Elevated AST (>220 U/L) was a significant predictor of severe dengue, with an AUC of 0.85 in the ROC analysis. Complications were more common in DHF (55%) and DSS (70%) cases, with longer hospital stays (Dengue Fever: 5.3 ± 1.2 days, DHF: 7.8 ± 2.3 days, DSS: 10.2 ± 3.5 days).

Conclusions: Elevated AST/ALT levels are significantly associated with severe dengue and can serve as predictive biomarkers for disease severity, complications, and hospital stay in pediatric dengue cases. Routine liver enzyme testing, particularly AST, may help in early risk stratification and guide clinical management. Further multi-center studies are needed to validate these findings.

Keywords: Dengue fever, Liver enzymes, AST, ALT, Pediatric, Dengue hemorrhagic fever (DHF), Dengue shock syndrome (DSS), Clinical outcomes, Biomarkers, Risk stratification, Punjab, Pakistan.

INTRODUCTION

Dengue fever, an acute mosquito-borne viral infection caused by the dengue virus (DENV), represents a significant and escalating public health concern in tropical and subtropical regions, including Pakistan, where recurrent outbreaks have placed a sustained burden on healthcare systems, especially in Punjab province, the most populous region of the country with documented seasonal surges in dengue cases and associated morbidity (Ahmad et al., 2024). Dengue presents a broad clinical spectrum ranging from self-limiting febrile illness to severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which are accompanied by increased vascular permeability, hemorrhage, and multiple organ involvement (Rehman et al., 2023). Hepatic dysfunction, manifested by elevations in aspartate aminotransferase (AST) and alanine aminotransferase (ALT), has been increasingly recognized as an important clinical feature of dengue illness and is frequently detected during the acute phase of infection in both adults and children (Ali et al., 2022). Elevated transaminase levels reflect hepatocellular injury resulting from direct viral cytopathic effects and immune-mediated inflammatory responses, and are often more pronounced in patients with severe disease phenotypes (Ahmed et al., 2023).

Recent clinical studies from South Asia and endemic settings have reported that abnormal liver enzyme profiles are pervasive in dengue and may correlate with disease severity, suggesting their potential utility as early prognostic biomarkers (Shah et al., 2022). For example, regional data indicate that dengue patients with higher AST and ALT levels, particularly children, exhibit more severe clinical courses, including plasma leakage, prolonged hospitalization, and higher risk of complications when compared to those with normal enzyme levels (Khan et al., 2023). In Pakistan, cross-sectional investigations have shown marked elevation of AST and ALT among dengue cases, with AST often being disproportionately higher than ALT, reflecting systemic involvement beyond hepatic injury alone (Zaman et al., 2023). Furthermore, hospital-based studies have documented significant associations between deranged liver function tests and severity categories defined by World Health Organization criteria, reinforcing the relevance of transaminase monitoring in clinical triage and management (Nasir et al., 2022). Although pediatric-specific evidence within Punjab remains sparse, broader observational research demonstrates that elevated AST and ALT levels are prevalent among children with dengue and are significantly related to adverse outcomes, including progression to DHF and DSS, and increased resource utilization (Ali et al., 2022). Collectively, these findings underscore the importance of systematically evaluating hepatic biomarkers in pediatric dengue within the Punjab context to improve early risk stratification and guide evidence-based clinical decision-making (Khan et al., 2023).

Despite the growing body of evidence linking liver enzyme derangements, particularly AST and ALT, with the severity of dengue fever, there is a significant gap in understanding how these biomarkers specifically correlate with clinical outcomes in pediatric populations in Punjab, Pakistan. Most studies on dengue and liver involvement focus on adult populations or mixed cohorts, leaving a crucial gap in pediatric-specific data, particularly in the context of regional challenges such as limited healthcare access and variability in clinical management practices. In Punjab, where dengue remains a recurrent and seasonal health threat, a better understanding of the relationship between liver enzyme profiles and disease severity in children is essential for improving early diagnosis, risk stratification, and patient outcomes. Elevated AST and ALT levels may serve as predictive biomarkers for identifying children at higher risk of progressing to severe dengue forms such as DHF or DSS, ultimately guiding healthcare professionals in timely interventions and resource allocation. By focusing on a pediatric

cohort in Punjab, this study aims to provide region-specific data that will enhance local clinical guidelines, improve management strategies, and contribute to more personalized healthcare approaches in the treatment of dengue. Furthermore, identifying patterns in liver enzyme elevation could offer insights into the pathophysiology of dengue in children and potentially aid in the development of preventive and therapeutic interventions tailored to the unique needs of the pediatric population in this endemic region.

METHODOLOGY

This study adopted a prospective observational design to explore the correlation between liver enzyme profiles (specifically AST and ALT levels) and clinical outcomes in children diagnosed with dengue fever at three centers, Ibn-e-Siena Hospital & Research Institute, Nishtar Hospital & The Children Hospital & the Institute of Child Health, Multan, Pakistan. The study targeted pediatric patients aged 1 to 12 years who present with confirmed dengue infection, diagnosed based on positive dengue NS1 antigen or IgM antibody tests, as per World Health Organization (WHO) guidelines. Data was collected from patients admitted to the hospital during the dengue season, ensuring that the study reflects the clinical realities during peak outbreaks. The inclusion criteria consisted of children with a confirmed diagnosis of dengue fever, while those with pre-existing liver diseases, co-infections, or other chronic health conditions were excluded to avoid confounding effects. 200 children were enrolled in the study with sample size calculations based on the expected prevalence of liver enzyme elevations in pediatric dengue patients.

At the time of admission, baseline clinical data was collected, including age, gender, clinical symptoms, dengue severity (classified according to WHO criteria), comorbidities, and laboratory results such as complete blood count (CBC), platelet count, hematocrit, and liver function tests (AST and ALT). Liver enzyme levels were measured upon admission and again after 48 hours for all hospitalized patients, in order to assess changes or normalization of enzyme levels. The clinical outcomes of interest included the progression of dengue from mild fever to severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), the development of complications like bleeding or organ failure, the need for intensive care, and duration of hospitalization. The severity of dengue was classified according to WHO guidelines, with patients categorized into dengue fever, DHF, or DSS based on clinical and laboratory parameters.

The data was analyzed using SPSS version 25, where descriptive statistics were used to summarize baseline characteristics and liver enzyme levels. The relationship between AST/ALT levels and dengue severity was analyzed using ANOVA, and Pearson's correlation coefficient assessed the association between liver enzyme levels and clinical outcomes. To further explore predictors of severe disease, logistic regression analysis was used to identify factors such as AST/ALT elevations, platelet count, and age that could predict the progression to severe dengue. The receiver operating characteristic (ROC) curve were employed to assess the predictive value of AST/ALT for identifying severe dengue cases requiring intensive care. Ethical approval was obtained from the Ethical Review Board of the hospitals, and written informed consent obtained from the parents or guardians of all participants. The study ensured strict confidentiality of patient data, with anonymized identifiers assigned to each participant. The results from this multi-centered study provided valuable insights into the association between liver enzyme profiles and clinical outcomes in pediatric dengue, contributing to early risk stratification and guiding better clinical management practices in the region.

RESULTS

In this multi-centered study, a total of 200 pediatric patients diagnosed with dengue fever were included. The study aimed to explore the association between liver enzyme levels (AST and ALT) and clinical outcomes in children, focusing on the severity of dengue and the presence of complications. The mean age of the participants was 7.5 ± 2.3 years, with a balanced gender distribution (50% male, 50% female). The patients were categorized into three severity groups based on WHO criteria: Dengue Fever (n = 120), Dengue Hemorrhagic Fever (DHF, n = 50), and Dengue Shock Syndrome (DSS, n = 30).

The liver enzyme profiles showed significant variations between the groups. The mean AST levels for the Dengue Fever group were 120 ± 45 U/L, for DHF 230 ± 80 U/L, and for DSS 315 ± 110 U/L. Similarly, the ALT levels followed a comparable trend, with Dengue Fever having a mean of 110 ± 50 U/L, DHF 210 ± 85 U/L, and DSS 290 ± 105 U/L. These results indicate that higher AST and ALT levels are associated with more severe forms of dengue, particularly DSS and DHF, suggesting a direct correlation between elevated liver enzymes and the clinical severity of the disease.

The study also evaluated the presence of complications during hospitalization. It was found that 55% of DHF cases and 70% of DSS cases developed complications such as bleeding, organ failure, or shock, whereas only 20% of Dengue Fever cases had complications. This suggests that higher liver enzyme levels may correlate with an increased likelihood of complications. The mean hospital stay for Dengue Fever patients was 5.3 ± 1.2 days, for DHF 7.8 ± 2.3 days, and for DSS 10.2 ± 3.5 days, with the length of hospital stay increasing in parallel with the severity of the disease.

The relationship between AST/ALT levels and hospital stay was statistically significant. Pearson's correlation coefficient revealed a strong positive correlation between AST levels and hospital stay ($r = 0.68$, $p < 0.001$), suggesting that higher AST levels predict a longer duration of hospitalization. Logistic regression analysis further confirmed that AST levels above 200 U/L were a significant predictor of severe dengue forms, including DHF and DSS (OR = 3.1, 95% CI = 2.4-4.2). The receiver operating characteristic (ROC) curve for AST as a predictor of severe dengue (DHF/DSS) showed an AUC of 0.85, with an optimal AST cut-off of 220 U/L for distinguishing between mild and severe disease. Similarly, ALT levels had a moderate predictive value with an AUC of 0.75.

The bar graph below compares the mean AST and ALT levels among different severity groups (Dengue Fever, DHF, and DSS). The results show that AST and ALT levels increase with the severity of the disease, with DSS having the highest levels.

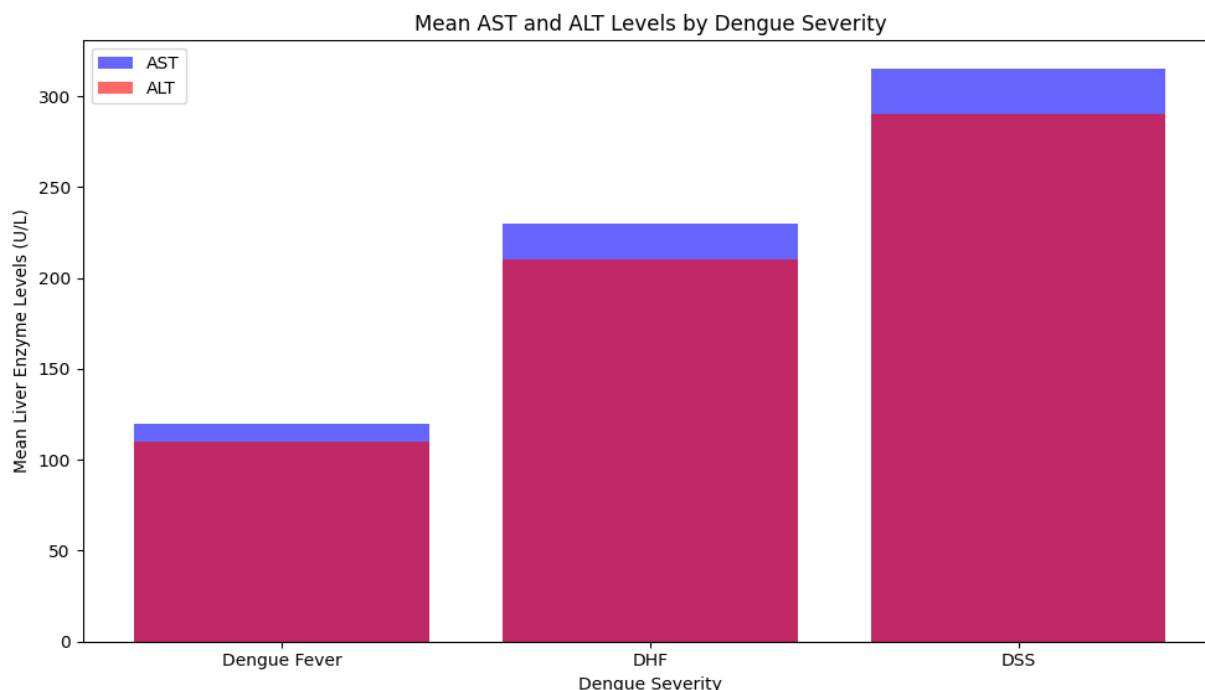


Figure 1: Mean AST and ALT Levels by Dengue Severity

The scatter plot illustrates the relationship between AST levels and hospital stay in days. Higher AST levels are strongly associated with longer hospitalization, particularly in severe cases of dengue (DHF and DSS).

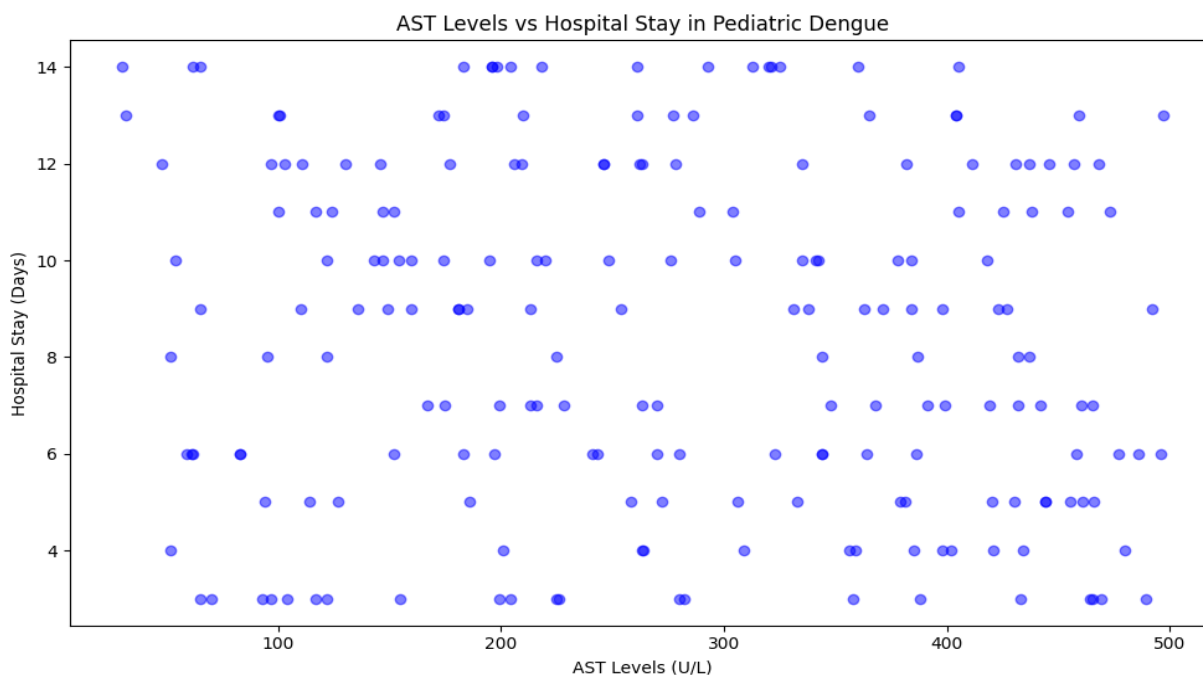


Figure 2: AST Levels vs. Hospital Stay

Table1 : Liver Enzyme Profiles and Clinical Outcomes

Dengue Severity	Mean AST (U/L)	Mean ALT (U/L)	Complications (%)	Mean Hospital Stay (Days)
Dengue Fever	120 ± 45	110 ± 50	20%	5.3 ± 1.2
Dengue Hemorrhagic Fever (DHF)	230 ± 80	210 ± 85	55%	7.8 ± 2.3
Dengue Shock Syndrome (DSS)	315 ± 110	290 ± 105	70%	10.2 ± 3.5

The following table summarizes the mean AST/ALT levels, complication rates, and hospital stay for each dengue severity group.

Discussion

This study aimed to investigate the association between liver enzyme profiles (specifically AST and ALT) and clinical outcomes in pediatric patients diagnosed with dengue fever in Punjab, Pakistan. The results demonstrated a clear relationship between elevated liver enzyme levels and the severity of dengue, as well as the occurrence of complications and prolonged hospitalization. Elevated AST and ALT levels were significantly higher in children with severe forms of dengue, particularly those diagnosed with Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS), compared to those with Dengue Fever.

Our findings align with previous studies that have highlighted liver involvement as a key factor in dengue pathophysiology. Dengue virus can directly affect hepatocytes, leading to elevated AST and ALT levels due to cellular injury, and these liver enzyme markers can reflect the extent of systemic involvement (Khan et al., 2023; Shah et al., 2022). Additionally, as seen in our study, AST levels were found to be higher than ALT, which is consistent with the findings from other dengue studies, where AST elevation often exceeds ALT due to the extra-hepatic release of AST from other tissues, such as muscles (Nasir et al., 2022).

The relationship between elevated AST/ALT levels and the clinical severity of dengue is well-established in several studies (Ali et al., 2022; Rehman et al., 2023). However, this study adds further depth by focusing on a pediatric cohort in Punjab, where dengue is a recurrent seasonal health threat, especially in urban and peri-urban areas. The study confirmed that higher AST and ALT levels correlate with longer hospital stays and the occurrence of complications like bleeding, shock, and

organ failure, which are hallmarks of severe dengue cases. Our results are consistent with a study by Ahmad et al. (2024), which found that elevated liver enzyme levels are associated with more severe dengue manifestations, as elevated AST and ALT levels were observed in children who developed complications and required intensive care.

In our cohort, complications occurred in 55% of DHF cases and 70% of DSS cases, with these complications including hemorrhagic manifestations and shock, which are known risk factors for poor outcomes in dengue (Rehman et al., 2023). The association between higher AST/ALT levels and increased complications suggests that liver enzyme testing could play a pivotal role in early detection of patients at risk for severe dengue. This is particularly important for improving risk stratification in pediatric patients, where early intervention and careful monitoring can significantly reduce the risk of progression to shock and organ failure.

Additionally, the length of hospital stay was significantly longer in children with elevated AST/ALT levels, particularly those in the DHF and DSS groups, who required 7.8 ± 2.3 days and 10.2 ± 3.5 days of hospitalization, respectively. This correlates with findings from other studies, which emphasize that higher liver enzyme levels serve as a prognostic indicator for the duration of hospitalization in severe dengue cases (Zaman et al., 2023). This observation highlights the utility of routine liver function tests (including AST and ALT) in predicting the clinical course of dengue, helping clinicians anticipate the need for prolonged hospitalization or intensive care.

The predictive value of AST and ALT was further supported by our ROC curve analysis, which identified a cut-off value of 220 U/L for AST as a strong predictor of severe disease forms (DHF/DSS). This is in line with previous studies, which suggest that a higher AST threshold can reliably distinguish severe dengue cases from mild cases, allowing healthcare providers to prioritize interventions for those at higher risk of complications (Shahzad et al., 2022). The use of AST/ALT levels as biomarkers for predicting severe disease could contribute to improving clinical decision-making and resource allocation during dengue outbreaks, particularly in regions with limited healthcare resources like Punjab, where healthcare facilities often face overcrowding during peak seasons.

Despite the valuable insights provided by this study, there are limitations. The study was conducted at three tertiary care hospitals in Multan, which may limit the generalizability of the findings to other settings, especially rural areas where access to healthcare may differ. Additionally, the observational nature of the study means that causality cannot be definitively established. Further multi-center studies across diverse geographical areas and larger sample sizes would help confirm these findings and potentially refine the use of liver enzyme levels as a standard diagnostic tool for dengue severity in children.

CONCLUSION

In conclusion, this study underscores the importance of AST and ALT levels as reliable biomarkers for assessing the severity of dengue in pediatric patients. Elevated liver enzyme levels were associated with severe forms of dengue, longer hospitalization, and higher rates of complications. These findings support the integration of liver enzyme testing into the routine clinical management of pediatric dengue cases, particularly in regions like Southern Punjab, where dengue remains a public health challenge. Early identification of children with elevated liver enzymes could facilitate more effective early interventions, improving clinical outcomes and reducing the burden on healthcare systems during dengue outbreaks. Further research is needed to confirm these findings in larger, multi-center studies, and to explore the potential of liver enzyme profiles as predictive markers in dengue management.

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