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Original Research Article

Study on Utility of Serum LDH, Creatinine Kinase, Albumin, APPT and Aminotransferases as Predictive Markers of Severe Dengue in Adults

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Abstract:

Background: This study aims to develop predictive markers for early detection and management of dengue, a significant arthropod-borne viral disease, to overcome challenges in distinguishing between severe and mild forms of the disease.

Aim: The study investigates the correlation between biochemical markers like serum LDH, Creatinine kinase, Albumin, aPTT, and aminotransferases and their use as predictive indicators of severe dengue in adults.

Methodology: The research is conducted on patients admitted to the Government Erode Medical College Hospital, Perundurai, throughout a one-year period (December 2023 to October 2024). This research was executed. As a prospective clinical research, written informed permission will be obtained prior to the investigation, after the provision of comprehensive information to the participants about the study. Patients with dengue fever will be evaluated for biochemical indicators including serum LDH, creatinine kinase, albumin, aPTT, SGOT, SGPT, and serum albumin by laboratory studies and clinical manifestations.

Results: Biomarkers like Lactate Dehydrogenase, Creatine Kinase, aPTT and aminotransferases are elevated and albumin is reduced in severe dengue.

Conclusion: Serum LDH, Creatine kinase, serum albumin, aimnotransferases, and aPTT should be evaluated during admission and early illness in patients with fever with thrombocytopenia to identify and treat severe cases of dengue fever, reducing mortality rates.

Keywords: Dengue, Aedes aegypti, biochemical markers, LDH, Creatinine kinase, Aptt, aimnotransferases, severe dengue.

Introduction

Dengue Fever, a significant public health threat in Tamil Nadu, has significantly impacted the healthcare system over the past decade due to its unpredictable clinical evolution and outcomes [1]. Dengue, a nonspecific infection, causes a spectrum of symptoms from no symptoms to life-threatening DHF/dengue shock syndrome. Early diagnosis and timely management are crucial for saving victims and preventing economic loss [2].

Dengue's acute phase begins with myalgia, making it difficult to differentiate between uneven and stormy infections. Medical studies use simple tests and lab investigations to predict illness course [3]. The 2009 WHO criteria highlight warning signs of dengue, including abdominal pain, mucosal bleeding, vomiting, clinical fluid collection, hepatomegaly, lethargy, and increased packed cell volume. These symptoms indicate a critical phase and severity of the disease, making proper treatment protocol challenging [4]. The government faces increased challenges in controlling mosquitoes due to unplanned urbanization and inefficient mosquito control methods in households [5].

Dengue fever presents in various ways, from asymptomatic to severe, and requires timely identification and referral. Its unpredictable course and early diagnosis are crucial for successful management [6]. Studies show patients with DHF have elevated serum transferases, creatinine kinase, lactate dehydrogenase, and aPTT levels, but these

biochemical markers have not been evaluated in early acute stages of disease. This study aims to study their potential in predicting severe dengue.

Aims and Objectives

The study investigates the potential of biochemical markers like serum LDH, Creatinine kinase, Albumin, aPTT, and aminotransferases as predictive indicators of severe dengue in adults, focusing on their correlation with dengue severity and their utility in this context.

Materials and Methods

The research is conducted on patients admitted to the Government Erode Medical College Hospital, Perundurai, throughout a one-year period from December 2023 to October 2024.

This research will be executed as a prospective clinical trial, with written informed permission obtained from participants once comprehensive information is provided about the study. Patients with dengue fever will undergo screening for biochemical markers including serum LDH, creatinine kinase, albumin, aPTT, SGOT, SGPT, and serum albumin by laboratory tests and clinical manifestations.

The study used a simple random sampling method to examine 50 patients admitted to the General Medical Ward and Fever Ward at Government Erode Medical College Hospital, Perundurai. The study was a prospective clinical study, focusing on dengue patients aged 13 and above, with a one-year observational period. The data was collected from patients admitted during the study period.

Selection Criteria

The study aims to include participants over 13 years old, either sex, with acute febrile syndrome testing positive for dengue infection with symptoms lasting less than 5 days, and cases meeting WHO 2009 dengue fever guidelines, while excluding those with fever but negative dengue, extremes of age, or comorbidities.

Procedure

After getting permission from the Ethical Committee, patients were selected after explaining the purpose of the study and procedure in detail and getting their informed consent in written format. Consent was obtained from parents for patients who were minors.

A detailed history of illness was taken, based on the WHO guidelines for diagnosis of dengue fever. A complete physical examination and necessary investigations were done to confirm the diagnosis.

Data Analysis

The statistical analysis for the required sample size per group was carried out using Statistical version 9 (StatSoft, Inc, 1984-2009, USA). All other statistical analyses were performed using the Statistical Package for Social Sciences for Windows 8.0 software. The results are presented as means with their respective standard deviations. To make comparisons, analysis of variance (ANOVA) was employed, followed by Tukey's post hoc test for multiple comparisons and the independent samples Student's t-test. Pearson correlation analysis was used to calculate correlations between variables. The results were evaluated within a 95% confidence interval, and significance was determined with a probability level of less than 0.05.

Results

The study reveals (Figure:1) that the majority of individuals (30%) fall within the 21-30 age group, followed by the 31-40 and >50 age groups (20%), the 41-50 age group (12%), and the ≤20 age group (18%), with the smallest proportion (only 18%) falling within the ≤20 age group.

Also the study population (50) comprise with males comprising 70% and females at 30%, (Table 1).

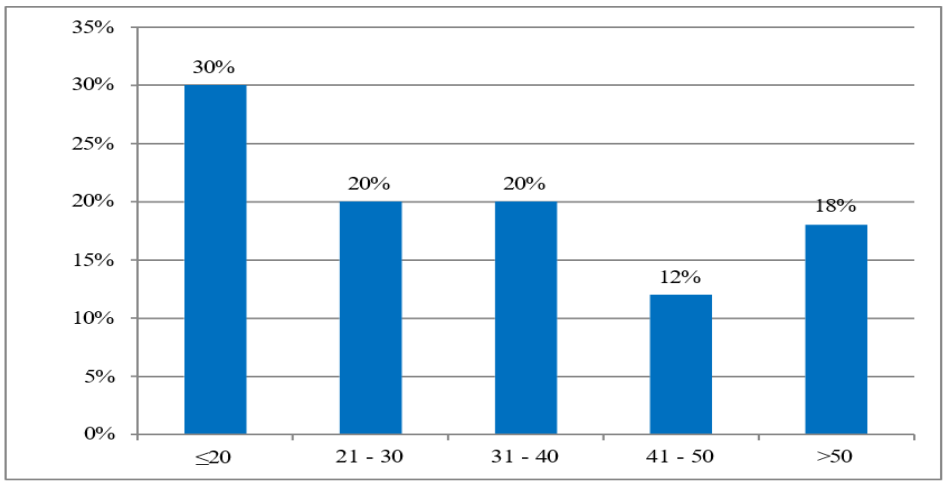

Figure 1: Bar chart of age group in study population (N=50)

Table 1: Descriptive analysis of gender in study population (N=50)

Gender	Frequency	Percentage
Male	35	70%
Female	15	30%
Total	50	100%

The study reveals the mean duration of fever observed was 2.86 days with a standard deviation (SD) of 0.88 days.

The median duration was 3 days, with the shortest recorded duration being 1 day and the longest 5 days. The 95% confidence interval (CI) for the mean duration of fever ranged from 2.61 to 3.10 days, suggesting that the true mean duration of fever in the population is likely to fall within this interval.

Table 2: Comparison of mean across type of dengue (N=50) (N=50)

Parameter	Type of Dengue	DNWS	DWWS	Severe Dengue	Statistical Test	P value	Significance
LDH (Mean ± SD)		225.91 ± 47.72	580.29 ± 290.33	735.46 ± 181.80	ANOVA	<0.001	Significant
LDH Levels	Normal (135-450 U/L)	21 (100%)	2 (28.6%)	1 (4.5%)	Fisher's Exact Test	<0.001	Significant
	Abnormal (>450 U/L)	0 (0%)	5 (71.4%)	21 (95.5%)			
CK (Mean ± SD)		88.71 ± 24.09	226.14 ± 104.66	262.91 ± 71.41	ANOVA	<0.001	Significant
CK Levels	Normal	21 (100%)	2 (28.6%)	0 (0%)	Fisher's Exact Test	<0.001	Significant
	Abnormal	0 (0%)	5 (71.4%)	22 (100%)			
Albumin (Mean ± SD)		4.49 ± 0.49	3.07 ± 0.56	3.06 ± 0.22	ANOVA	<0.001	Significant
Albumin Levels	Normal (3.5-5.4 g/dL)	21 (100%)	2 (28.6%)	1 (4.5%)	Fisher's Exact Test	<0.001	Significant
	Abnormal (<3.5 g/dL)	0 (0%)	5 (71.4%)	21 (95.5%)			
aPTT (Mean ± SD)		33.33 ± 2.21	41.97 ± 6.48	52.45 ± 6.93	ANOVA	<0.001	Significant
aPTT Levels	Normal (30-40 s)	21 (100%)	2 (28.6%)	0 (0%)	Fisher's Exact Test	<0.001	Significant
	Abnormal (>40 s)	0 (0%)	5 (71.4%)	22 (100%)			
SGOT (Median, IQR)		34 (32, 36)	68 (32, 102)	166 (98, 408)	Kruskal-Wallis	<0.001	Significant
SGOT Levels	Normal	13 (61.9%)	2 (28.6%)	0 (0%)	Fisher's Exact Test	<0.001	Significant
	Abnormal	0 (0%)	5 (71.4%)	22 (100%)			
SGPT (Median, IQR)		28 (26, 30.5)	56 (28, 98)	149 (80.5, 382.5)	Kruskal-Wallis	<0.001	Significant
SGPT Levels	Normal	21 (100%)	2 (28.6%)	0 (0%)	Fisher's Exact Test	<0.001	Significant
	Abnormal	0 (0%)	5 (71.4%)	22 (100%)			
Blood Transfusion	Normal	21 (100%)	6 (85.7%)	9 (40.9%)	Fisher's Exact Test	<0.001	Significant
	Abnormal	0 (0%)	1 (14.3%)	13 (59.1%)			

Table 2 compares the biochemical and hematological parameters across different types of dengue (DNWS, DWWS, and Severe Dengue) in a study population of 50 participants, using appropriate statistical tests to assess significance.

LDH Levels: The mean LDH levels showed a marked increase with disease severity, with values of 225.91 ± 47.72 in DNWS, 580.29 ± 290.33 in DWWS, and 735.46 ± 181.80 in Severe Dengue (ANOVA, $P < 0.001$).

Additionally, 100% of DNWS cases fell within the normal range (135-450 U/L), while a large majority of DWWS (71.4%) and Severe Dengue (95.5%) cases had abnormal LDH levels (Fisher's Exact Test, $P < 0.001$).

CK Levels: Mean CK levels were 88.71 ± 24.09 in DNWS, 226.14 ± 104.66 in DWWS, and 262.91 ± 71.41 in Severe Dengue, with significant variation across dengue types (ANOVA, $P < 0.001$). All DNWS cases had normal CK levels, while 71.4% of DWWS and 100% of Severe Dengue cases showed abnormal levels (Fisher's Exact Test, $P < 0.001$).

Albumin Levels: Mean albumin was highest in DNWS (4.49 ± 0.49) and significantly lower in both DWWS (3.07 ± 0.56) and Severe Dengue (3.06 ± 0.22) (ANOVA, $P < 0.001$). All DNWS cases had normal albumin levels, whereas the majority of DWWS (71.4%) and Severe Dengue (95.5%) cases were below the normal range (Fisher's Exact Test, $P < 0.001$).

aPTT: The mean aPTT was 33.33 ± 2.21 in DNWS, 41.97 ± 6.48 in DWWS, and 52.45 ± 6.93 in Severe Dengue, with a statistically significant difference (ANOVA, $P < 0.001$). All DNWS cases had normal aPTT, but most DWWS (71.4%) and all Severe Dengue cases had abnormal aPTT (Fisher's Exact Test, $P < 0.001$).

SGOT and SGPT: SGOT and SGPT levels, reported as median and interquartile range (IQR), were significantly elevated in Severe Dengue compared to DNWS and DWWS (Kruskal-Wallis, $P < 0.001$). The majority of DNWS cases had normal SGOT and SGPT levels, while nearly all DWWS and Severe Dengue cases had abnormal values (Fisher's Exact Test, $P < 0.001$).

Blood Transfusion Requirement: Blood transfusions were necessary in 14.3% of DWWS and 59.1% of Severe Dengue cases, but none of the DNWS cases required transfusion, indicating a statistically significant difference (Fisher's Exact Test, $P < 0.001$). Overall, these findings indicate that as the severity of dengue increases, there is a notable shift toward abnormal laboratory values across various biochemical and hematological parameters, with statistical tests confirming the significance of these differences. The study reveals a significant correlation between biomarkers like serum LDH, Creatinine kinase, Albumin, aPTT, and aminotransferases in dengue-like symptoms and severe dengue-like symptoms, suggesting timely use can predict progression and reduce mortality.

Discussion

The study included 50 cases, with 30% aged 13-20, 20% aged 21-30, 20% aged 31-40, 12% aged 41-50, and 18% aged over 50.The study found that 70% of the 35 cases were male, while 30% were female, a trend consistent with a previous study by Raza et al. 2014. [7]

The WHO guidelines 2009 classified patients based on severity, with 21 patients in DNWS, 7 in DWWS, and 22 in SD. The duration of fever at admission was determined. Samples were taken within 5 days of fever and biochemical marker analyses were performed. The mean LDH values in patients progressing to severe dengue were re-viewed [8].

Creatine kinase levels are significantly associated with severe dengue and DWWS, as shown in a study by Saiful et al. (2017). The study found that 27 patients had high creatine kinase levels, and all 22 patients who developed severe dengue had elevated levels. The mean creatine kinase value in severe dengue was 262.91+/-71.41, a significant association with severe dengue and DWWS, corroborating Saiful et al's large-scale study at Kaulalampur [9].

The study found that 26 patients had lower than normal serum albumin levels, and 95.5% of those who developed severe dengue had hypoalbuminemia. The mean albumin value for severe dengue was 3.06+/- 0.22. A p value of <0.001 indicates a significant association between severe dengue and DWWS, confirming a previous study by Kularatnam et al., where patients with lower albumin levels during critical illness phases progressed to severe dengue [10].

The study found a significant association between elevated serum aPTT levels in severe dengue patients and DWWS, with a mean value of 52.45+/-6.93s. This finding is consistent with a previous study by Simna et al., where patients with prolonged aPTT during the critical phase progressed to severe dengue. The current study confirms this association, with a P value of <0.001 indicating a significant association between aPTT levels and severe dengue [11].

The study found a significant association between elevated SGOT levels and severe dengue and DWWS, with a median level of 166 U/L in severe dengue patients. This finding is consistent with previous research by Jayanta and Vishal et al., where a median SGOT level of 168 U/L was observed in patients who progressed to severe dengue. The study's findings highlight the importance of monitoring SGOT levels in patients with severe dengue. The study found a significant association between elevated SGPT levels and severe dengue, with a median SGPT level of 149 in the severe dengue group. This finding is consistent with previous research by Jayanta and Vishal et al, where patients with a median SGPT value of 150 progressed to severe dengue. The study also found that high SGPT levels were present in patients

progressing to severe dengue. A study of 50 patients with confirmed dengue viral infection found that those with raised LDH, creatine kinase, hypoalbuminemia, prolonged aPTT, and SGOT levels progressed to severe dengue. Complications included persistent vomiting, increased hematocrit, mucosal bleeding, tosepsis, ARDS, renal failure, seizures, and encephalopathy. These biochemical markers could be used as predictive markers for severe dengue in adults.

Conclusion

The study reveals a significant association between biomarkers like Lactate Dehydrogenase, Creatinine Kinase, aPTT, aminotransferases, and albumin with dengue fever. Elevated serum LDH, Creatine Kinase, aPTT, and aminotransferases are found in severe dengue and DWWS, indicating the need for proper triage and monitoring of cases. Proper use of biochemical markers can reduce economic burden, morbidity, and mortality in severe dengue cases.

Limitations of the Study:

The study was conducted in a tertiary care center, where referral bias is inevitable, and nutritional factors were not studied.

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Ethical statement:

Institutional ethical committee accepted this study. The study was approved by the institutional human ethics committee, Government Erode Medical College Hospital, Perundurai. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. The confidentiality of the study participants was maintained.

Authors' contributions:

Dr. J.Saravana Priya - conceptualization, data curation, investigation, methodology, project administration, visualization, writing—original draft, writing—review and editing; **Dr. S.Rajesh Kumar** -conceptualization, methodology, writing—original draft, writing—review and editing; **Dr. C.Vignesh** - conceptualization, visualization, supervision, writing—original draft; **Dr. P.Srinivasan** - methodology, writing—original draft, writing, review and editing. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript**.**

Data Availability: All datasets generated or analyzed during this study are included in the manuscript.

Informed Consent: Written informed consent was obtained from the participants before enrolling in the study

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