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Original Research Article

To Study the Association between Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) and Severity of Dengue Fever

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Abstract

Background: Early identification of patients at risk for severe dengue is a critical challenge in endemic regions. The Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) is a simple, non-invasive score using routine laboratory tests. We sought to evaluate the association between APRI and dengue severity in an adult population.

Methods: This cross-sectional observational study was conducted at a tertiary care hospital in South Gujarat, India. Eighty-two adult patients (age >18) with serologically confirmed dengue (NS1 or IgM positive) were enrolled. Patients with chronic liver disease, co-infections, or other causes of thrombocytopenia were excluded. APRI was calculated on admission. Patients were categorized as mild, moderate, or severe. Receiver Operating Characteristic (ROC) analysis was used to determine the optimal APRI threshold for predicting severe dengue.

Results: Of the 82 patients, 13.4% (n=11) had severe dengue, 41.5% (n=34) had moderate dengue, and 45.1% (n=37) had mild dengue. The mean APRI was 4.98 \pm 6.59. An optimal APRI threshold of >3.2 was identified for predicting severe dengue. All 11 severe dengue cases (100%) had an APRI > 3.2. The index demonstrated 100% sensitivity, 72.5% specificity, 100% negative predictive value (NPV), and 36.7% positive predictive value (PPV). The Area under the Curve (AUC) was 0.903 (95% CI, $p < 0.001$). A high APRI (> 3.2) was also significantly associated with the need for blood transfusion (36.6% vs. 0%, $p < 0.001$) and longer hospital stay (50% > 6 days vs. 25%, $p = 0.038$).

Conclusion: APRI is an excellent, highly sensitive, and universally accessible biomarker for risk stratification in adult dengue patients. Admission APRI > 3.2 is strongly associated with severe disease. Its 100% NPV makes it a valuable clinical tool to "rule out" severe dengue, thereby guiding resource allocation and de-escalation of care in resource-limited settings.

Introduction

Dengue fever, a mosquito-borne flaviviral infection, represents one of the most significant global public health challenges, with incidence dramatically increasing over the past two decades [1, 2]. India faces a substantial portion of this burden, with cyclical epidemics and significant morbidity and mortality reported annually by the National Vector Borne Disease Control (NVBDCP) [3]. The clinical spectrum of dengue is diverse, ranging from asymptomatic infection to a life-threatening illness. The 2009 World Health Organization (WHO) classification categorizes dengue into non-severe (with or without warning signs) and severe dengue [4]. Severe dengue is characterized by severe plasma leakage leading to shock (Dengue Shock Syndrome), severe bleeding, or severe organ impairment [5]. Hepatic involvement is one of the most common organ manifestations, ranging from asymptomatic transaminase elevation to, in rare cases, acute liver failure [6]. A characteristic finding is the predominance of aspartate aminotransferase (AST) elevation over alanine aminotransferase (ALT) [7]. A critical challenge in clinical management is the early identification of patients who will progress to severe disease [8]. While the WHO warning signs provide a framework, their predictive value can be moderate [9]. This highlights the need for simple, cost-effective, and reliable biomarkers for risk stratification, especially in resource-constrained settings. The Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) has emerged as a

potential predictor. First developed by Wai et al. (2003) to non-invasively assess hepatic fibrosis in hepatitis C [10], the index is calculated using two parameters routinely measured in all dengue patients: AST and platelet count. Its formula is:

APRI = [(AST level / AST Upper Limit of Normal) / Platelet count (10^9/L)] * 100.

The rationale for its use in dengue is strong: both components of the index, hepatic injury (rising AST) and thrombocytopenia, are individual hallmarks of dengue severity [11]. Combining them may provide enhanced predictive value. Recent studies have explored this, with promising results [12, 13, 14], but validation across different populations is required. Given this, the present study was designed to investigate the correlation between the APRI index and the severity of dengue fever in patients admitted to a tertiary care hospital in South Gujarat, India.

Materials & Methods

Study Design and Population: This was a cross-sectional observational study conducted among 82 adult patients (age >18 years) admitted to the Department of General Medicine at a tertiary care hospital in South Gujarat. Patients were enrolled over a 15-month period after obtaining institutional ethical approval and written informed consent.

Inclusion criteria were age >18 years, clinical symptoms consistent with dengue fever, and serological confirmation of dengue (positive for NS1 antigen or IgM dengue antibodies).

Exclusion criteria were: pregnant women, patients with known chronic liver disease (e.g., alcoholic liver disease, viral hepatitis B or C), patients with other co-infections (e.g., malaria, typhoid, UTI), patients taking known hepatotoxic drugs (e.g., anti-tubercular therapy), and patients with known pre-existing causes of thrombocytopenia (e.g., ITP, chemotherapy).

Data Collection and Definitions: A detailed history, general examination, and systemic examination were performed on all enrolled patients. Venous blood samples were collected at admission for complete blood count (CBC), liver function tests (LFTs), renal function tests (RFTs), and coagulation profile (PT, INR, APTT).

The APRI index was calculated using the formula: APRI = [(AST (IU/L) / 40 (IU/L)) / Platelet count (10^9/L)] * 100 (An AST Upper Limit of Normal of 40 IU/L was used as the standard).

Outcome Measures: The primary outcome was disease severity, categorized as Mild (non-severe dengue without warning signs), Moderate (non-severe dengue with warning signs), or Severe (severe plasma leakage, severe bleeding, or severe organ involvement) based on clinical and laboratory parameters as per WHO guidelines [4].

Secondary outcomes included the requirement for blood product transfusion, and the total length of hospital stay.

Statistical Analysis: Data was entered and analyzed using statistical software. Descriptive statistics were presented as mean \pm standard deviation (SD) for continuous variables and as frequencies and percentages for categorical variables. The association between APRI (as a categorical variable) and disease severity was assessed using the Chi-square test. A Receiver Operating Characteristic (ROC) curve was generated to determine the optimal cut-off value of APRI for predicting severe dengue. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. A p-value < 0.05 was considered statistically significant.

Result

Baseline Characteristics and Clinical Profile: A total of 82 patients were included in the study. The majority of patients were male (53.65%) and in the 18-30 year age group (51.22%).

The vast majority of patients (92.7%) had no pre-existing comorbidities. All patients (100%) are presented with fever, followed by malaise (53.66%), vomiting (52.44%), and headache (50.00%).

Serologically, 81.7% were positive for NS1 antigen only. The mean platelet count at admission was 132.77 ± 113.09 * 103 /mm3 .The mean AST and ALT were 120.66 ± 116.54 U/L and 63.49 ± 83.21 U/L, respectively, confirming AST predominance.

Disease Severity and Outcomes: Of the 82 patients, 45.1% (n=37) were classified as mild, 41.5% (n=34) as moderate, and 13.4% (n=11) as severe. A blood transfusion was required by 13.41% (n=11) of patients. The mean length of hospital stay showed a clear correlation with severity: 3.8 days for mild, 5.4 days for moderate, and 8.4 days for severe cases. (See Table 1).

Table 1: Baseline Characteristics, Severity, and Outcomes (N=82)

Characteristic	Subgroup	Value (N=82)
Gender	Male	44 (53.65%)
	Female	38 (46.35%)
Age Group (Years)	18-30	42 (51.22%)
	31-40	21 (25.61%)
	41-50	10 (12.20%)
	>50	9 (10.97%)
Comorbidities	None	76 (92.70%)
	Present (HTN, DM, IHD)	6 (7.30%)
Disease Severity	Mild	37 (45.10%)
	Moderate	34 (41.50%)
	Severe	11 (13.40%)
Mean Lab Values	Platelet Count (10^3/mm^3)	132.77
(Mean \pm SD)	AST (U/L)	120.66
	ALT (U/L)	63.49
Clinical Outcomes	Required Blood Transfusion	11 (13.41%)
	Mean Hospital Stay (Days)	5.5

Table 2: Correlation of APRI Score Categories with Disease Severity

APRI Score	Mild (n=37)	Moderate (n=34)	Severe (n=11)	Total
APRI < 3.2	28 (75.7%)	24 (70.6%)	0 (0%)	52
APRI => 3.2	9 (24.3%)	10 (29.4%)	11 (100%)	30
Total	37	34	11	82

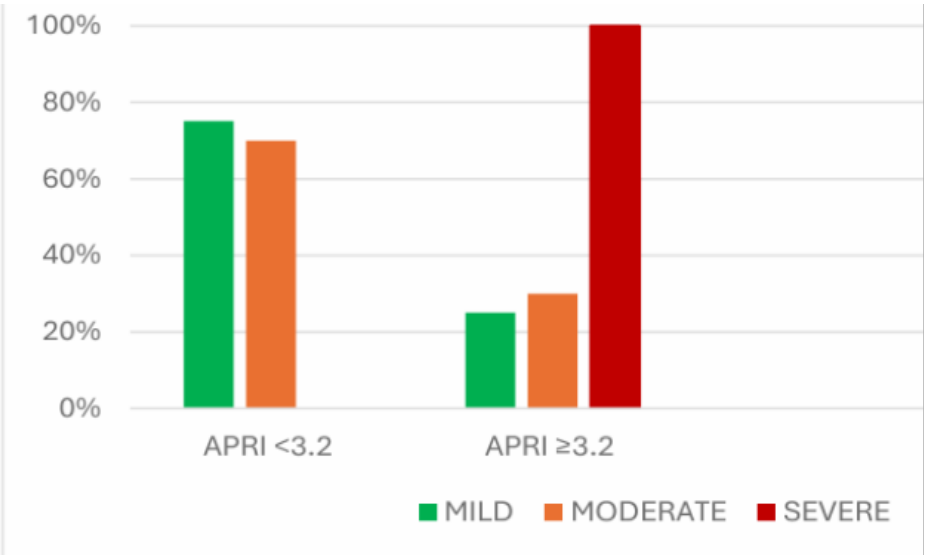

Figure 1: APRI Score

Table 3: Diagnostic Performance of APRI (>3.2) for Predicting Severe Dengue

Metric	Value
Sensitivity	100%
Specificity	72.5%
Positive Predictive Value (PPV)	36.7%
Negative Predictive Value (NPV)	100%
Area Under the Curve (AUC)	0.903
Optimal Threshold	3.2

APRI Performance in Predicting Severe Dengue: The mean APRI score for the cohort was 4.98 ± 1.43 ROC curve analysis was performed to identify the optimal APRI threshold for predicting severe dengue. The analysis yielded an optimal cut-off value of 3.2. The Area under the Curve (AUC) was 0.903 (95% CI, $p < 0.001$), indicating excellent discriminatory power.

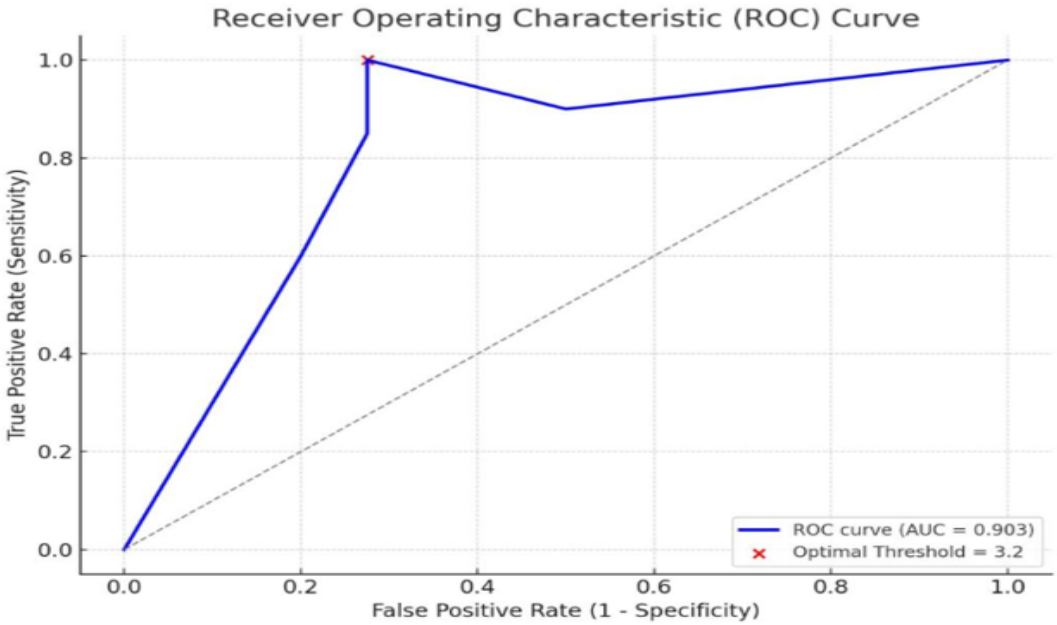

Figure 2: Receiver operating charateristic (ROC) Curve

APRI and Secondary Outcomes: The APRI score also correlated strongly with secondary outcomes. Among the 30 patients with APRI > 3.2, 11 (36.6%) required a blood transfusion. In contrast, 0% of the 52 patients with APRI < 3.2 required a transfusion. Furthermore, patients with a high APRI score were twice as likely to have a prolonged hospital stay (50% stayed - 6 days vs. 25% in the low-APRI group)

Table 4: Association of APRI Score with Secondary Outcomes

Outcome	APRI < 3.2 (n=52)	APRI > 3.2 (n=30)	p-value
Required Blood Transfusion	0 (0%)	11 (36.6%)	< 0.0001
Hospital Stay (6 Days)	13 (25.0%)	15 (50.0%)	0.038

Discussion

This study demonstrates that the APRI score, a simple index derived from routine admission labs, is an excellent predictor of severe dengue in an adult population. The primary finding is that an APRI cut-off of > 3.2 had 100% sensitivity and, most critically, a 100% negative predictive value (NPV) for identifying severe dengue, with a high overall accuracy (AUC 0.903).

The clinical implication of a 100% NPV is profound. In a busy, resource-limited setting, an admission APRI score < 3.2 can effectively "rule out" severe dengue, allowing clinicians to confidently de-escalate care, manage the patient in a lower-acuity setting, or consider safe outpatient management. This preserves critical hospital beds and resources for the 36.7% (PPV) of patients with a high APRI score who are at significant risk.

Our findings are consistent with and build upon existing literature. A 2024 study by Jayachandran et al. in South India also identified an identical optimal cut-off of >3.2, though with a lower sensitivity (69.2%) and higher specificity (84.2%) [13]. Other studies have reported different cut-offs (e.g., 2.5 by Harika et al. [15], 6.98 by Zhang et al. [12]), highlighting that while APRI is consistently useful, the optimal threshold may vary by population, timing of measurement, and local epidemiology. Our study's high AUC of 0.903 is among the best reported, confirming its strong diagnostic utility.

The APRI's strength lies in its pathophysiological basis. It combines two key processes of dengue pathogenesis: hepatic injury (releasing AST) and thrombocytopenia (from bone marrow suppression and peripheral destruction) [6, 11]. Our data confirms that a high APRI is strongly linked to its individual components, with 93% of the high-APRI group having elevated AST and 90% having thrombocytopenia. Furthermore, the strong association of high APRI with the need for blood transfusion (36.6% vs 0%) and prolonged hospital stay (50% vs 25% > 6 days) reinforces that APRI is not just a marker for a diagnostic classification but a robust indicator of overall disease burden and

resource utilization. We must acknowledge several limitations from the original study. First, this was a single-center study with a relatively small sample size, particularly for the severe dengue group (n=11). This small denominator can make sensitivity and NPV estimates (i.e., 100%) unstable, and these findings require validation in larger, multi-center cohorts. Second, the study excluded pediatric patients, a population with a high dengue burden, to whom these results cannot be extrapolated. Third, the APRI was measured at a single time point (admission). Studying the trend of APRI over time may offer even greater prognostic insight. Finally, by only including admitted patients, a selection bias may exist, excluding the mildest and most fulminant cases.

Table 5: Comparison of APRI Score Performance in Predicting Severe Dengue (Literature Review)

Study & Setting	Sample Size / Design	APRI Cut-off	Sensitivity	Specificity	AUC	Key Observations
Present Study (South Gujarat, 2024-25)	82 Adults / Cross-sectional	>3.2	100%	72.5 %	0.903	100% NPV. Strong link to transfusion need & hospital stay.
Jayachandran et al. (South India, 2024) [13]	224 Adults / Retrospective	> 3.2	69.2%	84.2 %	0.806	Identical cut-off. Also linked to longer hospital stay.
Harika et al. (Andhra Pradesh, 2022) [15]	180 Patients / Prospective	> 2.5	80.0%	76.8 %	N/A	Validated APRI's role in clinical risk stratification.
Zhang et al. (China, 2018) [12]	631 Adults / Retrospective	> 6.98	67.3%	76.2 %	0.769	Higher cut-off. Predictive accuracy improved (AUC 0.877) when combined with WBC & PT.

Conclusion

The APRI index is a simple, no-cost, and highly effective prognostic marker in adult patients with dengue fever. In this cohort, an admission APRI > 3.2 was strongly associated with severe disease classification, the need for blood product transfusion, and longer hospital stays.

With 100% sensitivity and 100% NPV at this cut-off, APRI serves as an outstanding clinical tool for early risk stratification.

It is particularly valuable for its ability to "rule out" severe dengue, thereby optimizing triage, resource allocation, and patient disposition in dengue-endemic regions.

Ethical Approval: Approved

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