



APRI AS A PREDICTOR OF SEVERE DENGUE FEVER

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ABSTRACT

Dengue fever poses a major public health burden in India, with severe cases requiring timely identification for effective management. This study aimed to evaluate the Aspartate Aminotransferase to Platelet Ratio Index (APRI) as a predictor of severe dengue. A total of 100 patients aged 18–50 years, confirmed positive for the NS1 antigen, were included in a cross-sectional study at Mandya Institute of Medical Sciences. Patients were categorized based on APRI scores (<3.2 and >3.22), and clinical outcomes were analyzed. Severe dengue occurred significantly more in the high APRI group (52.7%) compared to the low APRI group (3.1%). High APRI was also associated with prolonged hospital stay and increased need for platelet transfusions. APRI > 3.22 showed 90.5% sensitivity and 78.5% specificity in predicting severe dengue. These findings suggest that APRI, a simple and cost-effective marker, can aid in early identification and management of high-risk dengue patients, especially in resource-limited settings.

KEYWORDS :**INTRODUCTION**

Dengue fever remains a significant public health challenge in India, with periodic outbreaks placing immense pressure on healthcare systems. India recorded 1,86,567 dengue cases and 160 deaths were reported due to dengue in 2024.[1] The clinical spectrum of dengue ranges from mild febrile illness to severe forms characterized by plasma leakage, hemorrhage, and organ dysfunction.[2] Early identification of patients at risk of developing severe dengue is critical for timely intervention and reducing morbidity and mortality.[3] Conventional diagnostic parameters often fall short in reliably predicting disease severity, necessitating the exploration of novel, accessible biomarkers.[4]

The Aspartate Aminotransferase to Platelet Ratio Index (APRI), originally established as a non-invasive marker for liver fibrosis, has recently emerged as a potential prognostic tool in various infectious and inflammatory diseases.[5,6] Given that hepatic involvement and thrombocytopenia are common in dengue pathophysiology, APRI may offer a convenient and cost-effective indicator of disease severity. In the Indian context, where laboratory resources may be limited in many primary care settings, such a simple marker could significantly enhance early triage and management.[7,8]

Several international studies have hinted at the utility of APRI in predicting severe dengue; however, data from India remains sparse.[9,10] Considering the unique epidemiological patterns, viral serotype distribution, and demographic variations in the Indian population, it is imperative to assess the role of APRI specifically within this context.[12] This study aims to evaluate the correlation between APRI scores and the severity of dengue infection in Indian patients, thereby contributing to the development of evidence-based strategies for early identification and improved clinical outcomes.

MATERIALS AND METHODS**STUDY DESIGN**

Cross sectional study

STUDY SETTING

Mandya Institute of Medical Sciences, Mandya

STUDY POPULATION

Patients presenting to causality or medicine OPD of mandya institute of medical sciences.

STUDY DURATION

June 1, 2024 to october 1, 2024.

SAMPLE SIZE

100

SAMPLING TECHNIQUE

Consecutive sampling. All the patients positive for NS1 antigen test were included in the study.

INCLUSION AND EXCLUSION CRITERIA

- Inclusion criteria: patients aged 18-50 positive for NS1 antigen test were included in the study.
- Exclusion criteria: patients with pregnant women, history of alcohol consumption in past 1 month, any comorbidities, were excluded from the study.

METHODOLOGY

Patients who presented to OPD or casualty with history of fever and tested positive for NS1 antigen were included in the study. Basic demographic data and blood investigation at the time of admission was collected and patients were followed up throughout the hospital stay to and data regarding development of any complications, need for platelet transfusion and length of hospital stay were collected and analyzed.

Severe dengue was defined as dengue with any of the following symptoms: severe plasma leakage leading to shock or fluid accumulation with respiratory distress, severe bleeding, or severe organ impairment.

APRI was calculated using the following formula:

$$APRI = \frac{(AST/Upper\ Limit\ of\ AST) \times 100}{Platelet\ Count\ 10^9/L}$$

The upper limit of AST was defined as 40 IU/L.

STATISTICAL ANALYSIS

Data were analyzed using Statistical Package for Social Science (SPSS) version 20. The Chi-square test was used to find the statistical significance for the association of categorical variables. Student's t-test was used to compare continuous variables between the different groups in univariate analysis. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 100 patients were included in the study. Study population comprised of 57 (57%) males and 43 (43%) female and the majority 57% was in the age group of 20-40 years. Out of 100, 64% patients had APRI < 3.2 and 36% had APRI > 3.2.

Severe dengue was far more frequent in the APRI > 3.22 group (52.77%) versus the APRI < 3.2 group (3.12%), indicating a strong association between high APRI and severe disease. Sensitivity of APRI > 3.22 for predicting severe dengue was 90.5% and specificity was 78.5%. This suggests that APRI is a strong predictor of severe dengue, correctly identifying most true cases and reasonably excluding non-severe cases.

The average hospital stay was significantly longer in the APRI > 3.22 group (4.38 ± 1.12 days) compared to the APRI < 3.2 group (2.75 ± 1.51 days), with a highly significant p-value (1.81×10^{-7}), reflecting.

Table 1: comparison of sociodemographic and clinical profile of patients between 2 groups

Parameters	APRI<3.2 (n=64)	APRI>3.22 (n=36)	P-value
Age group			
<20	11 (17.1%)	5 (13.8%)	0.0771
20-40	35 (54.6%)	22 (61.1%)	0.0246
>40	18 (28.1%)	9 (25%)	0.0285
Gender			
Males	35 (54.6%)	22 (61.1%)	0.0246
Females	29 (45.3%)	14 (38.9%)	0.0025
AST	51.23 $\pm$ 239.57	214.62 $\pm$ 542.85	
Platelet count	127.57 $\pm$ 46.44 $\times 10^9$	85.90 $\pm$ 49.06 $\times 10^9$	
Severe dengue	2 (3.1%)	19 (52.7%)	
Hospital stay	2.75 $\pm$ 1.51 days	4.37 $\pm$ 1.12 days	<0.001
Platelet transfusion			
Yes	5 (7.8%)	12 (33.3%)	0.001
No	59	24 (66.6%)	

greater illness severity and need for extended care in high-APRI patients. Platelet transfusions were required in 4.68% patients in the APRI < 3.2 group and 33.33% patients in the APRI > 3.22 group. This difference was statistically significant ($p = 0.001$), supporting the idea that patients with higher APRI not only had lower platelet counts but also required more aggressive interventions.

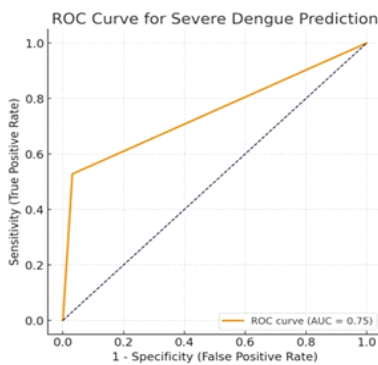


Figure 1: ROC curve of APRI in predicting severe dengue

DISCUSSION

Dengue fever remains a major public health challenge in tropical and subtropical regions, with a subset of cases progressing to severe dengue, characterized by plasma leakage, bleeding, and organ impairment. Early identification of patients at risk for severe dengue is crucial for optimizing management and resource allocation. The present study explores the utility of the Aspartate Aminotransferase to Platelet Ratio Index (APRI) in predicting the severity of dengue, and compares outcomes in patients stratified by an APRI threshold of 3.22.

Our analysis revealed a significantly higher incidence of severe dengue in the group with APRI > 3.22 (52.7%)

compared to those with APRI < 3.2 (3.1%). This sharp contrast underscores the potential of APRI as an early indicator of disease severity. AST elevation reflects hepatic inflammation or injury, while thrombocytopenia is a hallmark of dengue-related bone marrow suppression and immune-mediated platelet destruction.

In our cohort, patients with APRI > 3.22 had significantly lower platelet counts ($63.9 \pm 49.06 \times 10^9/L$) than those with

APRI < 3.2 ($127.6 \pm 46.4 \times 10^9/L$), with a highly significant p-value (< 0.00001). These results suggest that the APRI score effectively captures the dual insult of liver dysfunction and hematologic compromise seen in severe dengue.

Supporting this, 12 patients in the high APRI group required platelet transfusions, compared to only 3 in the lower APRI group ($p = 0.001$). Although the clinical benefit of platelet transfusions in dengue remains controversial, the increased requirement among patients with elevated APRI may reflect more severe thrombocytopenia or bleeding risk. In a randomized trial by Lye et al. (2017), prophylactic platelet transfusion was not associated with improved outcomes, highlighting the need for better markers to guide transfusion decisions. [12] APRI may help clinicians identify which patients are more likely to benefit from such interventions, rather than basing decisions solely on platelet count thresholds.

Hospital stay duration was also significantly longer in patients with APRI > 3.22 (4.38 ± 1.12 days) compared to those with APRI < 3.2 (2.75 ± 1.51 days). This aligns with previous literature suggesting that elevated APRI reflects greater systemic involvement and increased need for clinical monitoring. From a health systems perspective, early identification of such patients could aid in resource planning, especially during outbreaks.

Our findings are consistent with those of Jayachandran et al. (2024), who reported that elevated APRI scores correlated with severe dengue and increased clinical complications. While Jayachandran's study proposed a slightly different APRI cut-off, both studies highlight the robustness of APRI as a predictive marker across different populations. [13] Similarly, Jamil et al. (2024) demonstrated high sensitivity (84.9%) and specificity (89.0%) for severe dengue at an APRI cut-off of 9.04 (AUC = 0.93). [14]

Zhang et al. (2018) also identified APRI as an independent predictor of severe dengue (AUC = 0.785), emphasizing its potential as part of a multivariable risk assessment tool. In their study, APRI was analyzed alongside leukocytosis, serum albumin, and coagulopathy, further validating its clinical relevance. [15]

The mechanism linking APRI to severe dengue likely involves a combination of hepatic injury and hematological dysfunction. Dengue virus can directly infect hepatocytes and endothelial cells, resulting in transaminase elevation. Platelet destruction occurs through immune-mediated lysis and bone marrow suppression.

Despite these promising results, several limitations warrant discussion. The present study was conducted at a single center with a relatively small sample size, which may limit generalizability. While APRI is simple and cost-effective, it should not replace comprehensive clinical evaluation. Rather, it should be viewed as an adjunctive tool to enhance early risk stratification. Another limitation is the absence of serial APRI measurements. Future studies could investigate whether dynamic changes in APRI over time correlate with clinical deterioration or recovery.

CONCLUSION

APRI is a simple and useful index, which can be calculated from basic laboratory values such as AST and platelet count. APRI calculated at the time of admission showed 90.5% sensitivity and 78.5% specificity in predicting severe dengue. It also showed significant association with need for blood transfusion and length of hospital stay. In low resource settings APRI can be used to identify patients at risk of developing severe dengue, decide on appropriate treatment plan and identify need for referral to higher centres.

REFERENCES

1. National Center for Vector Borne Diseases Control. (2024). Dengue/DHF situation in India. <https://ncvdbc.mohfw.gov.in/index4.php?lang&level=0&linkid=431&lid=3715>
2. World Health Organization. (2009). Dengue: Guidelines for diagnosis, treatment, prevention and control. WHO Press.
3. Simmons, C. P, Farrar, J. J., Nguyen, V. V., & Wills, B. (2012). Dengue. *New England Journal of Medicine*, 366(15), 1423–1432.
4. Kittigul, L., Pitakarnjanakul, P., Sujirarat, D., & Siripanichgon, K. (2007). The usefulness of clinical and laboratory parameters for the diagnosis of dengue infection. *Southeast Asian Journal of Tropical Medicine and Public Health*, 38(3), 515–520.
5. Wai, C. T., Greenson, J. K., Fontana, R. J., Kalbfleisch, J. D., Marrero, J. A., Conjeevaram, H. S., et al. (2003). A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology*, 38(2), 518–526.
6. Lin, Z. H., Xin, Y. N., Dong, Q. J., Wang, Q., Jiang, X. J., Zhan, S. H., et al. (2011). Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: An updated meta-analysis. *Hepatology*, 53(3), 726–736.
7. Parkash, O., Almas, A., Jafri, S. M., Hamid, S., & Akhtar, J. (2010). Severity of hepatic involvement in dengue viral infection in a tertiary care hospital, Karachi, Pakistan (2008–2010). *BMC Infectious Diseases*, 10, 43.
8. Shepard, D. S., Undurraga, E. A., & Halasa, Y. A. (2013). Economic and disease burden of dengue in Southeast Asia. *PLoS Neglected Tropical Diseases*, 7(2), e2055.
9. Santos, J. I., Mondragón-Sánchez, R., Ochoa-Guzmán, A., López-Cruz, R., Zapata-Tarres, M., & Arredondo-García, J. L. (2016). Use of APRI and AST/ALT ratio as predictors of dengue severity. *American Journal of Tropical Medicine and Hygiene*, 95(5), 1244–1249.
10. Lee, I. K., Lee, W. H., Liu, J. W., & Yang, K. D. (2016). AST/ALT ratio and APRI score can predict severe dengue in adult patients. *Medicine*, 95(31), e4326.
11. Gupta, E., & Ballani, N. (2014). Current perspectives on the spread of dengue in India. *Infection and Drug Resistance*, 7, 337–342.
12. Lye, D. C., Archuleta, S., Syed-Omar, S. F., Low, J. G., Oh, H. M., Ferguson, D. J., et al. (2017). Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: A multicentre, open-label, randomised, controlled trial. *The Lancet*, 389(10079), 1611–1618.
13. Jayachandran, A., Rajendran, R., Kumar, V., & Karthikeyan, K. (2024). Clinical utility of APRI score in predicting severity in dengue fever: A prospective observational study. *Journal of Clinical and Diagnostic Research*, 18(2), OC01–OC05.
14. Jamil, B., Hasan, R. S., Arif, F., Kiyani, M., Khurshid, A., Ahsan, T., et al. (2024). Serum AST to platelet ratio index (APRI) in dengue patients: A useful marker for severity prediction. *Tropical Medicine & International Health*, 29(1), 45–52.
15. Zhang, H., Zhou, Y. P., Peng, H. J., Zhang, X. H., Zhou, F. Y., Liu, Z. H., et al. (2014). Predictive symptoms and signs of severe dengue disease for patients with dengue fever: A meta-analysis. *BioMed Research International*, 2014, 359308.