



LIMITED UTILITY OF THE ASPARTATE AMINOTRANSFERASE-TO-PLATELET RATIO INDEX FOR IDENTIFYING METABOLIC SYNDROME IN ADULTS WITH DIABETES MELLITUS: A HOSPITAL-BASED CROSS-SECTIONAL STUDY FROM CENTRAL INDIA

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ABSTRACT

Background: Metabolic syndrome is common in adults with diabetes and is closely linked to steatotic liver disease. The aspartate aminotransferase-to-platelet ratio index (APRI) is inexpensive and widely available, but its ability to identify metabolic syndrome in diabetic populations remains uncertain. **Methods:** We performed a hospital-based cross-sectional analysis of diabetes health-camp data. APRI was calculated as $[(AST/40) \times 100]/\text{platelet count}$ ($\times 10^9/L$). Metabolic syndrome was defined using modified NCEP ATP III criteria; because diabetes was already present, at least two additional components were required. Records with invalid core variables, reported alcohol use, or documented type 1 diabetes were excluded. Group comparisons, Spearman correlation, receiver operating characteristic (ROC) analysis and multivariable logistic regression were performed. **Results:** Of 220 screened records, 177 were included. Mean age was 53.28 ± 13.99 years, 117 (66.1%) participants were male, and metabolic syndrome was present in 153 (86.4%). Median APRI was 0.22 (IQR 0.16-0.30) in participants with metabolic syndrome and 0.27 (0.20-0.38) in those without it ($p=0.146$). APRI showed poor discrimination for metabolic syndrome (AUC 0.408; bootstrap 95% CI 0.294-0.526). In a parsimonious model that excluded variables used directly to define metabolic syndrome, APRI remained unassociated with metabolic syndrome (adjusted OR 0.90 per 0.1-unit increase, 95% CI 0.69-1.18; $p=0.447$). APRI correlated weakly with liver stiffness ($\rho=0.230$; $p=0.002$). **Conclusion:** APRI did not identify metabolic syndrome in this real-world diabetic cohort and should not be used as a standalone metabolic syndrome screening marker. Its association with liver stiffness supports a more plausible role in hepatic risk assessment.

KEYWORDS : APRI; Diabetes Mellitus; Metabolic Syndrome; Liver Fibrosis; FibroScan; Liver Stiffness; Cross-sectional Study

INTRODUCTION

Diabetes mellitus frequently coexists with central adiposity, hypertension and atherogenic dyslipidaemia. When these abnormalities cluster, they constitute metabolic syndrome and are associated with greater cardiovascular and hepatic risk.¹⁻⁵ Metabolic dysfunction-associated steatotic liver disease (historically termed NAFLD) is particularly common in people with type 2 diabetes, and progressive fibrosis is an important determinant of long-term liver-related outcomes.^{6,7}

Simple non-invasive fibrosis scores are attractive in resource-limited settings because they can be calculated from routine laboratory tests. APRI uses serum aspartate aminotransferase (AST) and platelet count and was developed primarily for liver fibrosis assessment.⁹⁻¹¹ Its low cost has encouraged evaluation beyond viral hepatitis, including cardiometabolic populations. De Matteis et al. found that higher APRI was associated with cardiovascular risk and metabolic abnormalities in a large metabolic cohort.¹² More recently, Jalisi et al. reported strong discrimination of metabolic syndrome by APRI among individuals with type 2 diabetes, with an AUC of 0.84.¹³

Those findings raise an important question of external validity. APRI reflects hepatocellular injury and platelet dynamics, whereas metabolic syndrome is defined by anthropometric, lipid and blood-pressure criteria. The relationship may therefore vary with population characteristics, hepatic disease burden, medication use, laboratory distributions and the operational definition of metabolic syndrome. Evidence from Indian diabetic populations also suggests that serum fibrosis indices may perform inconsistently when compared with elastography.¹⁵

We therefore examined whether APRI could distinguish participants with metabolic syndrome in a diabetes health-

camp cohort from Central India. We also explored its relationship with routine metabolic measures and FibroScan parameters, particularly liver stiffness, and repeated the analysis in participants whose records specifically documented type 2 diabetes.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional study used de-identified records collected during a diabetes health camp conducted in association with Kumar Saheb Late Shri Dilip Singh Judev Ji Government Super Speciality Hospital, Koni, Bilaspur, and Chhattisgarh Institute of Medical Sciences, Bilaspur, Chhattisgarh, India. The manuscript was prepared with reference to the STROBE recommendations for cross-sectional studies.¹⁴

Participants and Data Quality

A total of 220 camp records were screened. Valid assessment of the primary outcome required sex, waist circumference, triglycerides, HDL cholesterol, blood-pressure status, AST and platelet count. Values recorded as NA/N/A, physiologically implausible zero HDL values, or absent measurements were treated as missing rather than imputed. Seven records lacked valid core data. Among the remaining records, 33 reported alcohol use and three were explicitly documented as type 1 diabetes; these were excluded, leaving 177 participants for the primary analysis. Thirty-two of the included adult records did not specify diabetes type in the source registry. To avoid assigning an unrecorded diagnosis, the primary cohort is therefore described as adults with diabetes mellitus, with a prespecified sensitivity analysis restricted to 145 records explicitly labelled as type 2 diabetes.

Definitions

Metabolic syndrome was defined using modified NCEP ATP III

criteria. Because diabetes was already present, the glycaemic criterion was considered fulfilled and metabolic syndrome required at least two of four additional components: waist circumference ≥ 90 cm in men or ≥ 80 cm in women; triglycerides ≥ 150 mg/dL; HDL cholesterol < 40 mg/dL in men or < 50 mg/dL in women; and systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg, or a recorded history of hypertension.^{4,5}

APRI was calculated as $APRI = [(AST / \text{upper limit of normal AST}) \times 100] / \text{platelet count} (\times 10^9/L)$. The upper limit of normal AST was set at 40 IU/L, consistent with the laboratory convention used for this analysis. FibroScan variables included controlled attenuation parameter (CAP, dB/m) and liver stiffness measurement (LSM, kPa).

Statistical Analysis

Continuous variables were summarised using mean $\pm$ standard deviation and median with interquartile range (IQR). Categorical variables were expressed as number and percentage. Because several biochemical variables were non-normally distributed, comparisons between participants with and without metabolic syndrome used the Mann-Whitney U test. Spearman correlation assessed associations between APRI and selected metabolic or hepatic parameters. ROC analysis evaluated discrimination for metabolic syndrome, and the Youden index was used to describe the operating point for each marker. The 95% confidence interval for the APRI AUC was estimated by non-parametric bootstrap resampling. To avoid circular adjustment for variables that directly form the metabolic syndrome definition, the primary multivariable logistic regression was deliberately parsimonious and included APRI (per 0.1-unit increase), age, sex, BMI and HbA1c. Waist circumference, triglycerides, HDL cholesterol and blood pressure were not entered into this adjusted model because they were used to construct the outcome. A two-sided p-value < 0.05 was considered statistically significant. No missing values were imputed.

RESULTS

Participant Characteristics

Of 220 screened records, 177 were included in the primary analysis. The mean age was 53.28 $\pm$ 13.99 years, and 117 (66.1%) participants were male. Metabolic syndrome was present in 153 (86.4%). Low HDL cholesterol was present in 118 (66.7%), increased waist circumference in 120 (67.8%), raised blood pressure or a history of hypertension in 113 (63.8%), and raised triglycerides in 88 (49.7%). Baseline characteristics are shown in Table 1.

Table 1. Baseline Clinical and Laboratory Characteristics of the Primary Analysis Cohort. Comparison by Metabolic Syndrome Status

Variable	Mean $\pm$ SD	Median (IQR)	n
Age (years)	53.28 $\pm$ 13.99	54.00 (44.00-65.00)	177
BMI (kg/m ²)	26.19 $\pm$ 4.76	25.17 (23.00-28.00)	177
Waist circumference (cm)	90.46 $\pm$ 11.99	91.00 (86.00-98.00)	177
Systolic BP (mmHg)	125.93 $\pm$ 12.53	130.00 (120.00-130.00)	177
Diastolic BP (mmHg)	79.24 $\pm$ 8.76	80.00 (70.00-90.00)	177
HbA1c (%)	7.93 $\pm$ 2.08	7.60 (6.30-8.80)	177
Platelet count ($\times 10^9/L$)	257.79 $\pm$ 74.19	249.00 (210.00-304.00)	177
AST (IU/L)	25.61 $\pm$ 12.00	23.00 (17.00-31.00)	177
ALT (IU/L)	26.90 $\pm$ 15.93	22.10 (16.10-32.20)	177
Triglycerides (mg/dL)	171.44 $\pm$ 104.16	149.00 (104.80-216.00)	177
HDL cholesterol (mg/dL)	41.03 $\pm$ 21.44	39.00 (33.00-44.20)	177

CAP (dB/m)	248.02 $\pm$ 50.97	245.00 (212.00-281.25)	176
LSM (kPa)	7.80 $\pm$ 23.08	5.30 (4.35-6.80)	175
APRI	0.27 $\pm$ 0.16	0.22 (0.17-0.30)	177

Participants with metabolic syndrome had higher BMI, waist circumference, systolic and diastolic blood pressure, triglycerides, CAP and LSM, and lower HDL cholesterol. APRI did not differ significantly between groups: median APRI was 0.27 (IQR 0.20-0.38) without metabolic syndrome and 0.22 (0.16-0.30) with metabolic syndrome ($p=0.146$). AST and platelet count also did not differ significantly (Table 2).

Table 2. Comparison of Participants with and without Metabolic Syndrome. Values are Median (IQR). Diagnostic Discrimination

Variable	Without MetS (n=24)	With MetS (n=153)	p-value
Age (years)	54.50 (37.75-63.00)	54.00 (45.00-65.00)	0.347
BMI (kg/m ²)	23.73 (20.66-25.15)	25.80 (23.40-29.00)	< 0.001
Waist circumference (cm)	82.50 (76.00-87.25)	93.00 (86.36-99.00)	< 0.001
Systolic BP (mmHg)	120.00 (110.00-122.50)	130.00 (120.00-130.00)	0.002
Diastolic BP (mmHg)	70.00 (70.00-80.00)	80.00 (70.00-90.00)	0.023
HbA1c (%)	7.00 (5.83-8.95)	7.70 (6.40-8.80)	0.561
Platelet count ($\times 10^9/L$)	244.50 (210.25-290.00)	249.00 (210.00-308.00)	0.547
AST (IU/L)	24.30 (18.25-36.50)	22.40 (17.00-29.00)	0.127
ALT (IU/L)	24.00 (16.75-33.05)	22.00 (16.10-31.30)	0.579
Triglycerides (mg/dL)	84.15 (65.65-117.47)	156.00 (117.00-224.00)	< 0.001
HDL cholesterol (mg/dL)	44.10 (40.00-53.50)	38.00 (33.00-43.50)	< 0.001
CAP (dB/m)	216.50 (189.75-247.25)	250.00 (215.50-287.25)	0.005
LSM (kPa)	4.55 (4.00-5.60)	5.50 (4.50-6.80)	0.005
APRI	0.27 (0.20-0.38)	0.22 (0.16-0.30)	0.146

APRI showed poor discrimination for metabolic syndrome, with an AUC of 0.408 (bootstrap 95% CI 0.294-0.526). The Youden-derived APRI threshold was approximately 0.692, but this operating point had very low sensitivity (3.9%) despite 100% specificity and is not clinically useful. Waist circumference showed high apparent discrimination (AUC 0.820), followed by BMI, CAP and LSM. Because waist circumference is itself a defining component of metabolic syndrome, its ROC performance should be interpreted as an internal diagnostic benchmark rather than as an independent competing biomarker (Table 3).

Table 3. ROC Performance for Identifying Metabolic Syndrome. Multivariable Analysis

Marker	AUC	Youden cut-off	Sensitivity	Specificity
APRI	0.408	0.692	3.9%	100.0%
BMI	0.719	26.84	42.5%	95.8%
Waist circumference	0.820	90.0	64.7%	95.8%
CAP score	0.677	251	50.0%	83.3%
LSM score	0.679	5.0	62.9%	66.7%

In the parsimonious multivariable logistic regression, APRI remained unassociated with metabolic syndrome after adjustment for age, sex, BMI and HbA1c (adjusted OR 0.90 per 0.1-unit increase, 95% CI 0.69-1.18; $p=0.447$). BMI was independently associated with metabolic syndrome (adjusted OR 1.30 per kg/m², 95% CI 1.11-1.53; $p=0.001$), whereas age, sex and HbA1c were not statistically significant. Excluding

waist circumference, triglycerides, HDL cholesterol and blood pressure from the model avoids incorporation of the diagnostic components of metabolic syndrome into the predictor set and therefore provides a more defensible assessment of APRI's independent association (Table 4).

Table 4. Parsimonious Multivariable Logistic Regression for Metabolic Syndrome.

Variable	Adjusted OR	95% CI	p-value
APRI, per 0.1-unit increase	0.90	0.69-1.18	0.447
Age, per year	1.01	0.98-1.05	0.379
Male sex	0.58	0.19-1.74	0.328
BMI, per kg/m ²	1.30	1.11-1.53	0.001
HbA1c, per 1%	1.04	0.83-1.31	0.736

Correlation with Metabolic and Hepatic Parameters

APRI showed a weak positive correlation with liver stiffness ($\rho=0.230$; $p=0.002$) and HDL cholesterol ($\rho=0.256$; $p<0.001$), while correlations with BMI and triglycerides were weakly negative. APRI was not meaningfully correlated with HbA1c or CAP. These small correlations should be interpreted cautiously because several comparisons were performed and the study was not designed to infer causal relationships.

Table 5. Spearman Correlations of APRI with Selected Variables.

Parameter	Spearman rho with APRI	p-value
BMI	-0.180	0.016
Waist circumference	-0.145	0.053
HbA1c	0.015	0.840
Triglycerides	-0.184	0.014
HDL cholesterol	0.256	<0.001
CAP score	0.013	0.866
LSM score	0.230	0.002

Sensitivity Analysis Restricted to Documented Type 2 Diabetes

Among the 145 records explicitly labelled as type 2 diabetes, 131 (90.3%) met the modified metabolic syndrome definition. The negative primary finding was unchanged: APRI was 0.27 (IQR 0.23-0.36) in participants without metabolic syndrome and 0.22 (0.16-0.30) in those with metabolic syndrome ($p=0.084$), and the APRI AUC was 0.359. APRI retained a weak positive correlation with LSM ($\rho=0.198$; $p=0.018$). This sensitivity analysis reduces concern that inclusion of adult records with unspecified diabetes type explains the poor APRI discrimination.

DISCUSSION

The main observation in this cohort was straightforward: APRI did not distinguish participants with metabolic syndrome from those without it. Although metabolic syndrome was very common, APRI values were not higher in affected participants and the ROC curve showed poor discrimination. The same pattern persisted after adjustment for age, sex, BMI and HbA1c. Taken together, these findings do not support APRI as an independent marker of metabolic syndrome in this population.

This result contrasts with the report by Jalisi et al. In their type 2 diabetes cohort, APRI was higher in participants with metabolic syndrome and showed an AUC of 0.84, with 81.3% sensitivity and 67.7% specificity at a cut-off of 0.2458; APRI also remained independently associated with metabolic syndrome on regression analysis.¹³ In our cohort, the AUC was only 0.408 and the data-derived cut-off had very low sensitivity. Thus, the difference between the two studies involves not only statistical significance but also the direction and overall discriminatory performance of APRI.

There are several possible reasons for this difference. APRI was originally developed as a liver-related index: AST reflects hepatocellular injury, while platelet counts may decline as

fibrosis and portal hypertension advance. Metabolic syndrome, on the other hand, is defined using central obesity, triglycerides, HDL cholesterol, blood pressure and glycaemic status. Although hepatic and metabolic abnormalities share pathways such as insulin resistance and inflammation, a fibrosis-oriented index would not necessarily parallel the components used to diagnose metabolic syndrome in every population.⁹⁻¹¹

The composition of the study population may also have influenced the result. Metabolic syndrome was present in 86.4% of the primary cohort, leaving only 24 participants in the comparison group. This reflects a metabolically high-risk health-camp population and limits the precision with which discrimination can be estimated. The imbalance was even greater in the sensitivity analysis restricted to documented type 2 diabetes, where 90.3% met the metabolic syndrome definition.

Differences in setting and case mix are another consideration. Our data came from a health camp, whereas clinic- or hospital-based cohorts may differ in referral patterns, medication use, fasting status, obesity, underlying fibrosis and laboratory profiles. We also excluded participants with reported alcohol use because alcohol can alter AST and, consequently, APRI. Such differences in participant selection can change the distribution of APRI and its apparent relationship with metabolic syndrome.

The definition used for metabolic syndrome may also contribute to between-study differences. Because all participants had diabetes, the glycaemic component was considered fulfilled and at least two additional modified NCEP ATP III components were required. Other investigators have used different definitions and recruitment strategies. For example, De Matteis et al. used IDF-based criteria in a large metabolic cohort and found higher APRI values in participants with metabolic abnormalities, together with an association with cardiovascular risk.¹² This supports a cardiometabolic association in some populations, but does not mean that APRI will perform consistently as a diagnostic marker for metabolic syndrome.

Interestingly, APRI showed a weak but significant positive correlation with LSM, while its relationship with CAP was negligible. This is more consistent with the biological basis of APRI, because LSM is a measure related to liver stiffness and fibrosis rather than to the clinical definition of metabolic syndrome. Previous work in diabetes and NAFLD has likewise placed non-invasive fibrosis scores primarily in hepatic risk stratification rather than as replacements for standard metabolic syndrome criteria.^{7,15}

The correlations with HDL cholesterol and triglycerides were in directions that would not be expected if APRI behaved as a general metabolic-risk score. Both associations were weak and may reflect the distribution of AST and platelet counts in this sample, medication effects, residual confounding, sampling variation or multiple comparisons. These observations are therefore best regarded as exploratory.

In clinical practice, these results do not support using APRI to screen for metabolic syndrome in adults with diabetes. Waist circumference, blood pressure and lipid measurements are readily available and are directly incorporated into the diagnosis. APRI may still have value when the question is liver fibrosis risk, especially in settings where elastography is not easily accessible. Its correlation with LSM in this cohort suggests that future studies should examine APRI alongside FIB-4 and elastography using fibrosis-related outcomes.

Interpretive Context and Robustness

The overall pattern was consistent across the different

analyses. APRI was not higher in participants with metabolic syndrome, performed poorly on ROC analysis, and remained non-significant in the adjusted model. Restricting the analysis to records explicitly labelled as type 2 diabetes did not change the direction of the finding. The high prevalence of metabolic syndrome and the health-camp setting should be considered when applying these results to other populations. At the same time, the regression model deliberately excluded waist circumference, triglycerides, HDL cholesterol and blood pressure because these variables form part of the metabolic syndrome definition. This avoids a circular model and allows a cleaner assessment of whether APRI contributes independently. Overall, the difference from earlier reports appears more likely to reflect population characteristics and the liver-oriented nature of APRI than a single modelling choice.

CONCLUSION

In this diabetes health-camp cohort, metabolic syndrome was highly prevalent, but APRI did not discriminate participants with metabolic syndrome and was not independently associated with the condition. This differs from the strong diagnostic performance reported in an earlier type 2 diabetes cohort. Differences in study population, outcome prevalence, case mix and metabolic syndrome definitions may partly explain the contrasting results. The weak positive correlation between APRI and liver stiffness is more in keeping with its hepatic basis and suggests that APRI may be better suited to low-cost liver fibrosis risk assessment than to metabolic syndrome screening. Larger prospective, multicentre studies comparing APRI with FIB-4 and elastography for fibrosis-related outcomes would be useful.

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