Section: Medicine

Original Research Article

COMPARISON OF CORRELATION BETWEEN THE NONALCOHOLIC FATTY LIVER DISEASE AND DIFFERENT NONINVASIVE SCORING METHODS BETWEEN LEAN AND NON-LEAN INDIVIDUALS IN RESPECT OF WORLD HEALTH ORGANIZATION AND ASIA-PACIFIC CRITERIA IN TERTIARY CARE HOSPITAL IN WEST BENGAL – A RETROSPECTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Nonalcoholic fatty liver disease (NAFLD) spans from simple steatosis to cirrhosis and hepatocellular carcinoma. While obesity is a major determinant, lean NAFLD is increasingly recognized in Asia, highlighting the need to reappraise BMI thresholds for early detection. **Aims and Objectives:** To compare correlations between non-invasive fibrosis indices and FibroScan-derived stiffness across lean and non-lean groups using World Health Organization (WHO) and Asia-Pacific (APAC) BMI criteria, determining the most appropriate framework for South Asian populations.

Materials and Methods: A retrospective cross-sectional analysis of 493 patients at Jagannath Gupta Institute of Medical Sciences, Kolkata, was performed. Participants were classified by WHO (≤25 vs >25 kg/m²) and APAC (<23 vs ≥23 kg/m²) criteria. Biochemical variables included liver enzymes, lipids, HbA1c, and fibrosis indices (AST/ALT ratio, BARD, FIB-4, FIB-5, TyG). FibroScan quantified stiffness (F0–F4), analyzed by correlation and AUROC statistics.

Results: FIB-4 showed the strongest correlation with stiffness ($r = 0.34$, $p < 0.001$; AUC ≈ 0.72 for APAC <23). BARD and FIB-5 showed moderate or inverse trends, while lipid indices and TyG had poor discrimination (AUC ≤ 0.55). Correlations strengthened with higher BMI. APAC criteria improved sensitivity for early fibrosis, WHO for specificity.

Conclusion: FIB-4 is the most reliable non-invasive marker of ≥F2 fibrosis. Asia-Pacific BMI cut-offs (≥23 kg/m²) enhance early detection sensitivity, while WHO cut-offs favor specificity. A dual approach optimizes NAFLD risk stratification in Indian populations.

Keywords: NAFLD, APAC, WHO.

INTRODUCTION

There is spectrum of presentation of nonalcoholic fatty liver disease (NAFLD) like, nonalcoholic fatty liver i.e. hepatic steatosis having low progression risk, nonalcoholic steatohepatitis characterized by inflammation of hepatocytes, advanced hepatic fibrosis having chance of progression to hepatic cirrhosis and lastly hepatocellular carcinoma, as a result there is high chance of liver related mortality.[1,2] The prevalence of NAFLD has been increasing in last 2 to 3 decades along with increased

incidence of obesity or metabolic dysfunction. But it has been noted that also in normal weight individual i.e. according to World Health Organization BMI ≤ 25 Kg/meter^2 and according to Asia-Pacific criteria BMI < 23 Kg/meter^2 incidence of NAFLD is gradually increasing according to Asian and Caucasian population studies worldwide and in many cases it may progress to advanced hepatic fibrosis or cirrhosis.[1,3,4] In obese, overweight and normal or lean weight individuals the progression as well as severity of NAFLD are similar, and incidence of type 2 diabetes mellitus is also high in lean individual.[5,6] 3% to nearly 30% nonobese/lean of World population suffer from NAFLD, this so much variability is due to several environmental factors like selection of patient, different modalities of diagnosis, cut-off values of BMI, different types of life-styles and with dietary modalities.[5,6]

The different studies in the world demonstrated the correlation between different risk factors in NAFLD in nonobese patients even in absence of metabolic syndrome. Some studies demonstrated increased incident of type 2 diabetes mellitus, increased level of LDL, triglyceride, low HDL, increased incidence of systolic and diastolic blood pressure.[6,7,8,9,10,11]

Commonly used term "Lean NASH" is a misnomer as NASH is not at all lean because multiple risk factors play and interact with themselves to produce NASH in lean individual. In most of the lean individual the NAFLD is associated with increased adipose tissue accumulation in the lever and this subtype is known as "garden variety" – the etiology insulin resistance, metabolic syndrome, dyslipidemia that have been shown in different studies worldwide form the year 1999 to 2016.[12,13,14,15,16,17,18]

The prevalence of NAFLD in lean individual vary according to different case definition of NAFLD, use of different study design, regional variation in the ascertainment of bias and true differences, But this difference has been spreaded from rural to urban communities especially in Asian Countries.[19,20]

Pathophysiology of NAFLD in lean subject turns towards the pandemic obesity globally in spite of normal BMI due to dysfunctional inflamed adipose tissue in liver.[14,21] Hence Asian countries are known as "3rd World phenotype" and from these countries this is prevalent in USA and Europe.[20,22]

The primary objective of this study is to compare the correlation of different noninvasive scoring of fatty liver disease with different stages of fibroscan between lean and non-lean individuals in respect of World Health Organization and Asia-Pacific criteria and secondary objective to demonstrate which is more acceptable in the South East Asian subject.

MATERIALS AND METHODS

This retrospective cross sectional study has been performed in the Jagannath Gupta Institute of Medical Sciences & Hospital, Budge Budge, Kolkata collecting the data of last 5 years from our outpatient medical records. The data of the patients have been subdivided into two category nonobese and the other one was obese category according to WHO criteria (where nonobese is ≤ 25 Kg/meter^2 and obese > 25 Kg/meter^2) and Asia-Pacific criteria (nonobese < 23 Kg/meter^2 and obese ≥ 23 Kg/meter^2). After taking full history and examination the blood was sent for the blood tests for liver function tests, lipid profile, complete blood count, and also to radiology department for fibroscan of the liver. All the blood test were performed in empty stomach.

Statistical Analysis

Laboratory Procedure

Bio-Rad D-10 glycosylated hemoglobin analyzer method was used for estimating HbA1C based on high performance liquid chromatography.

ALT and AST were estimated in automated chemistry analyzer using flex reagent cartridge.

Lipid profile was estimated Cobas c702 analyzer.

Complete blood count was measured by using Sysmex Hematology analyzer.

Liver stiffness was measured and graded by transient elastography and value were expressed in kilopascals by extremely skilled operator using either M or XL probe according to choice of the operator.

Outcome measures:

FIB-4 index

[Age in years x Serum AST level in U/L] / [platelet count/cc x (√serum ALT in U/L)]

AST/ALT ratio = (Serum AST in U/L) / (Serum ALT in U/L)

APRI (AST to platelet ratio index) =

[(Serum AST level in U/L) / (Upper limit of normal serum AST in U/L)] / (100 / Platelet/cc)

APRI higher than 0.7 predicts significant fibrosis with high sensitivity and specificity.

Fibroscan score: F0: ≤ 5.5, F1: 5.6 – 7.0, F2: 7.1 – 9.5, F3: 9.6 – 12.5, F4: >12.5

The BARD score

AST/ALT ratio ≥ 0.8 – 2 points

BMI ≥ 28 – 1 point

Presence of diabetes – 1 point

The possible score ranges from 0 to 4.

A BARD score of 0 – 1 indicates a low risk of fibrosis, while a score higher than 2 to 4 indicates advanced fibrosis.

NAFLD Score

The NFS is calculated with the following formula8: NFS = −1.675 + 0.037 × age (years) + 0.094 × body mass index (kg/m2) + 1.13 × (impaired fasting glycemia or diabetes [yes=1, no=0]) + 0.99 × (AST/ALT ratio) − 0.013 × platelets (×109/L) − 0.66 × albumin (g/dL).

Normal NAFLD score:

Scores < -1.455: predictor of absence of significant fibrosis. (negative predictive value of 88-93%). These patients can. be managed in primary care. Scores ≤ -1.455 to ≤ 0.675: indeterminate Scores > 0.675 suggest a high risk of fibrosis (positive predictive value of 82%-90%).

Triglyceride-glucose index: [Triglyceride in mg/dl X fasting glucose in mg/ml] / 2.

Normal value: Less than 8.5 – considered as normal. 8.5 – 9.0 = Indicates borderline or abnormal range. More than 9 indicates strongly associated with insulin resistance.

All statistical analyses were performed after stratifying liver stiffness into five fibrosis stages based on Fibroscan values:

F0: ≤ 5.5 kPa
F1: 5.6 – 7.0 kPa
F2: 7.1 – 9.5 kPa
F3: 9.6 – 12.5 kPa
F4: > 12.5 kPa

Only patients who had HbA1c > 7% were included in this subset analysis to ensure a uniform hyperglycemic metabolic background.

RESULTS

Comparative Interpretation (WHO vs. Asia-Pacific): Lipid Profile, AST/ALT Ratio, HbA1c, TyG Index

Source: Your dataset "Markers_vs_FibroScan_WHO_APAC.docx".

Fibrosis stages by FibroScan: F0 ≤5.5; F1 5.6–7.0; F2 7.1–9.5; F3 9.6–12.5; F4 >12.5 kPa. ROC outcome: ≥F2.

Table 1: LDL (mg/dL): Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	-0.117	0.1141	Inverse (NS)
WHO BMI >25	309	-0.088	0.1229	Inverse (NS)
APAC BMI <23	80	-0.074	0.5122	Inverse (NS)
APAC BMI ≥23	413	-0.107	0.02906	Inverse, significant
Overall	493	-0.103	0.02256	Inverse, significant

Table 2: LDL: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	174.4	0.435	0.094	0.967	0.6	0.667
WHO BMI >25	158.0	0.476	0.128	0.929	0.6	0.561
APAC BMI <23	58.0	0.343	0.929	0.115	0.361	0.75
APAC BMI ≥23	158.0	0.482	0.141	0.92	0.568	0.589

Interpretation (LDL): LDL shows weak inverse association with stiffness, reaching significance in APAC BMI ≥23 and overall. AUROC remains poor (~0.34–0.48). Very low LDL has high specificity but low sensitivity—use as an adjunct, not a gate.

Table 3: HDL (mg/dL): Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	-0.169	0.02245	Inverse, significant
WHO BMI >25	309	-0.048	0.3998	Inverse (NS)
APAC BMI <23	80	-0.212	0.06018	Inverse (trend)
APAC BMI ≥23	413	-0.078	0.1155	Inverse (NS)
Overall	493	-0.111	0.01369	Inverse, significant

Table 4: HDL: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	73.0	0.367	0.0	1.0		0.656
WHO BMI >25	48.0	0.493	0.307	0.74	0.494	0.563
APAC BMI <23	72.0	0.298	0.0	1.0		0.658
APAC BMI ≥23	48.0	0.478	0.295	0.722	0.441	0.58

Interpretation (HDL): HDL declines with fibrosis; significance clearest in WHO non-obese and overall. Diagnostic performance is poor (AUC ≤0.49). Very low HDL may flag metabolic dysfunction but is not a stand-alone fibrosis discriminator.

Table 5: Triglycerides (mg/dL): Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	-0.133	0.07086	Inverse (trend)
WHO BMI >25	309	-0.101	0.07572	Inverse (trend)
APAC BMI <23	80	-0.151	0.1821	Inverse (NS)
APAC BMI ≥23	413	-0.101	0.039	Inverse, significant
Overall	493	-0.114	0.01127	Inverse, significant

Table 6: Triglycerides: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	440.193	0.437	0.047	0.983	0.6	0.659
WHO BMI >25	207.254	0.485	0.254	0.805	0.522	0.562
APAC BMI <23	216.111	0.443	0.25	0.827	0.438	0.672
APAC BMI ≥23	260.396	0.471	0.118	0.907	0.488	0.578

Interpretation (Triglycerides): Weak inverse association overall with limited discrimination (AUC ~0.44–0.49). Falling triglycerides in higher fibrosis likely reflect impaired VLDL export; interpret alongside insulin-resistance indices (TyG).

Table 7: AST/ALT Ratio: Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	0.066	0.3761	Positive (NS)
WHO BMI >25	309	0.236	2.967e-05	Positive, significant
APAC BMI <23	80	0.053	0.6455	Positive (NS)
APAC BMI ≥23	413	0.161	0.001027	Positive, significant
Overall	493	0.138	0.002164	Positive, significant

Table 8: AST/ALT Ratio: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	1.20	0.55	0.344	0.782	0.458	0.689
WHO BMI >25	0.469	0.458	0.986	0.054	0.47	0.818
APAC BMI <23	0.97	0.597	0.607	0.627	0.472	0.744
APAC BMI ≥23	0.469	0.468	0.983	0.06	0.442	0.824

Interpretation (AST/ALT): Consistent positive correlation—strongest in higher BMI groups. AUC is borderline (≈0.46–0.60). High specificity at certain cutoffs suggests that elevated ratios (≥1.0–1.3) raise suspicion for ≥F2, but normal ratios do not exclude fibrosis.

Table 9: HbA1c > 7% (binary): Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	-0.096	0.1913	No meaningful association
WHO BMI >25	309	0.1	0.07778	Trend only
APAC BMI <23	80	-0.076	0.5043	No association
APAC BMI ≥23	413	0.02	0.6827	No association
Overall	493	-0.004	0.9248	No association

Table 10: HbA1c > 7%: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	1.0	0.525	0.292	0.758	0.396	0.664
WHO BMI >25	1.0	0.537	0.294	0.781	0.532	0.567
APAC BMI <23	1.0	0.527	0.286	0.769	0.4	0.667
APAC BMI ≥23	1.0	0.533	0.294	0.772	0.495	0.59

Interpretation (HbA1c): In this cohort, HbA1c >7% does not correlate with stiffness and has limited discrimination (AUC ≈0.52–0.54). It contextualizes metabolic risk but should not be used alone to infer fibrosis stage.

Table 11: TyG Index: Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	-0.099	0.1811	Inverse (NS)
WHO BMI >25	309	-0.053	0.3507	Inverse (NS)
APAC BMI <23	80	-0.078	0.489	Inverse (NS)
APAC BMI ≥23	413	-0.075	0.1279	Inverse (NS)
Overall	493	-0.073	0.107	Inverse (NS)

Table 12: TyG Index: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	8.529	0.477	0.891	0.185	0.37	0.759
WHO BMI >25	9.373	0.526	0.296	0.814	0.575	0.576
APAC BMI <23	9.619	0.515	0.25	0.885	0.538	0.687
APAC BMI ≥23	9.686	0.503	0.14	0.906	0.532	0.581

Interpretation (TyG): Despite biological plausibility as an insulin-resistance proxy, TyG shows weak/negative correlations and AUC ≈0.50. It may serve as a high-sensitivity screen at certain thresholds (e.g., WHO ≤25), but lacks confirmatory power.

WHO vs Asia-Pacific: Comparative Synthesis

- Correlations strengthen in higher-BMI strata across markers (AST/ALT notably), consistent with clustering of metabolic risk and fibrosis.
- Under APAC (BMI ≥23), sensitivity tends to be higher for most markers at operational cutoffs, while specificity is higher under WHO (BMI >25).
- Lipids (LDL, HDL, TGL) show inverse or weak associations; hepatic scores (e.g., FIB-4, APRI—outside the present scope) usually outperform.
- Practical use: Prefer APAC for broader screening (maximize sensitivity) and WHO for confirmatory triage (maximize specificity).

Table 13: Summary Table: Directionality & Utility

Marker	Direction with Fibrosis	Best-seen Significance	AUC Range	Clinical Use (WHO vs APAC)
AST/ALT Ratio	↑ (positive)	Significant in higher BMI (WHO >25; APAC ≥23)	0.46–0.60	Rule-in clue at high cutoffs; APAC for sensitivity, WHO for specificity
LDL	↓ (inverse)	APAC ≥23 & Overall significant	0.34–0.48	Adjunct; high specificity at low levels
HDL	↓ (inverse)	WHO ≤25 & Overall significant	0.30–0.49	Adjunct for metabolic context
Triglycerides	↓ (inverse)	APAC ≥23 & Overall significant	0.44–0.49	Supportive; combine with TyG
HbA1c >7%	— (none)	No consistent correlation	0.52–0.54	Context only; not diagnostic
TyG Index	↓/weak	None (NS)	0.50±	Screening adjunct; low confirmatory value

Comparative Interpretation (WHO vs Asia-Pacific): BARD, FIB-4, FIB-5

Source: Your dataset "Markers_vs_FibroScan_WHO_APAC.docx". Fibrosis staging by FibroScan: F0 ≤5.5; F1 5.6–7.0; F2 7.1–9.5; F3 9.6–12.5; F4 >12.5 kPa. Primary outcome for ROC analyses: ≥F2.

Table 14: BARD Score: Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	-0.027	0.7158	No association
WHO BMI >25	309	0.142	0.01246	Positive, significant
APAC BMI <23	80	-0.05	0.6574	No association
APAC BMI ≥23	413	0.082	0.09576	Weak trend
Overall	493	0.046	0.3033	No association

Table 15: BARD Score: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	1.0	0.537	0.938	0.183	0.384	0.846
WHO BMI >25	1.0	0.534	0.923	0.136	0.475	0.676
APAC BMI <23	1.0	0.583	1.0	0.212	0.406	1.0
APAC BMI ≥23	1.0	0.532	0.917	0.143	0.448	0.694

Interpretation (BARD): BARD shows a significant positive correlation only in WHO BMI >25, with AUROC in the ~0.53–0.58 range. Sensitivity is high at the low threshold (≥1), but specificity is poor—therefore BARD is better as a broad screening adjunct and should be confirmed with liver-specific scores or FibroScan.

Table 16: FIB-4: Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	0.272	0.00019	Positive, significant
WHO BMI >25	309	0.438	8.494e-16	Positive, strong
APAC BMI <23	80	0.296	0.008105	Positive, significant
APAC BMI ≥23	413	0.35	2.709e-13	Positive, strong
Overall	493	0.339	1.303e-14	Positive, strong

Table 17: FIB-4: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	1.25	0.649	0.656	0.605	0.472	0.766
WHO BMI >25	1.15	0.615	0.553	0.635	0.561	0.627
APAC BMI <23	1.29	0.719	0.75	0.686	0.568	0.833
APAC BMI ≥23	1.24	0.606	0.508	0.655	0.526	0.639

Interpretation (FIB-4): FIB-4 exhibits the strongest and most consistent association with stiffness across all strata, with the highest AUROC observed in APAC BMI <23 (AUC 0.719). Thresholds cluster near ~1.2–1.3, delivering balanced sensitivity and specificity, and high NPV—suitable for ruling out ≥F2 in screening workflows.

Table 18: FIB-5: Correlation with Fibrosis (kPa)

Subset	N	r vs Stiffness	p-value	Comment
WHO BMI ≤25	184	-0.268	0.0002683	Inverse, significant
WHO BMI >25	309	-0.132	0.02209	Inverse, weak
APAC BMI <23	80	-0.197	0.08524	Inverse (trend)
APAC BMI ≥23	413	-0.177	0.0003542	Inverse, significant
Overall	493	-0.168	0.0002118	Inverse, significant

Table 19: FIB-5: AUROC & Diagnostic Characteristics for ≥F2

Subset	Optimal Threshold	AUC	Sensitivity	Specificity	PPV	NPV
WHO BMI ≤25	121.035	0.396	0.0	1.0		0.656
WHO BMI >25	-11.655	0.423	0.943	0.074	0.466	0.6
APAC BMI <23	90.170	0.381	0.037	0.98	0.5	0.653
APAC BMI ≥23	171.836	0.42	0.006	1.0	1.0	0.57

Interpretation (FIB-5): Correlates inversely with stiffness (as expected since higher scores reflect lower risk), but AUROC is modest (≈0.38–0.42). FIB-5 can contribute to a two-step pathway (rule-out focus) but is less discriminative for ≥F2 than FIB-4.

Composite Correlation & AUROC Graphs (WHO vs APAC) for All Markers

Markers included: LDL, HDL, Triglycerides, AST/ALT ratio, BARD score, HbA1c >7%, FIB-4, FIB-5, TyG index.

Subgroups: WHO (BMI ≤25, BMI >25) and Asia-Pacific (BMI <23, BMI ≥23). Fibrosis stages: F0 ≤5.5; F1 5.6–7.0; F2 7.1–9.5; F3 9.6–12.5; F4 >12.5 kPa. ROC outcome: ≥F2.

A) Correlation with FibroScan Stiffness (kPa)

Figure A shows Pearson r values for each marker across four BMI-defined subgroups under WHO and APAC criteria.

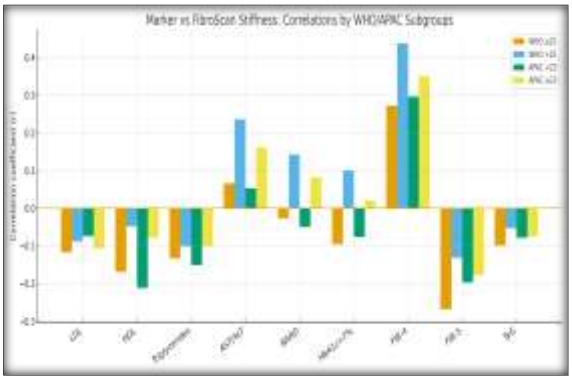


Figure A. Correlation coefficients (r) of markers vs liver stiffness across WHO/APAC subgroups. Positive values indicate higher marker values with higher stiffness; negative values indicate inverse relationships

B) Discrimination for ≥F2 (AUROC)

Figure B displays AUROC values for predicting clinically significant fibrosis (≥F2) for each marker and subgroup.

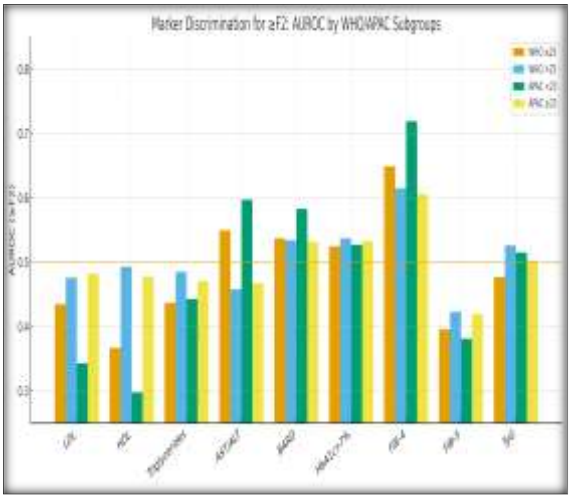


Figure B. AUROC values (dashed line at 0.5 indicates random discrimination). FIB-4 shows the highest AUROC, especially under APAC BMI <23.

Key Interpretations

- Correlations strengthen in higher-BMI strata (WHO >25 and APAC ≥23), particularly for FIB-4 and AST/ALT ratio.
- AUROC peaks for FIB-4 (up to ~0.72 in APAC <23), while BARD and FIB-5 are modest. Lipids, HbA1c, and TyG show poor-to-fair discrimination.
- Use APAC ≥23 for broader screening sensitivity and WHO >25 for specificity-focused confirmation alongside FibroScan.

AUROC Curve Comparison for All Markers (WHO vs APAC)

This figure shows a comparative AUROC (Area Under ROC Curve) analysis of nine non-invasive markers — LDL, HDL, Triglycerides, AST/ALT ratio, BARD, HbA1c >7%, FIB-4, FIB-5, and TyG index — under both WHO and Asia-Pacific BMI classification criteria. Fibrosis stages were defined as F0 ≤5.5; F1 5.6–7.0; F2 7.1–9.5; F3 9.6–12.5; F4 >12.5 kPa, with ROC outcome ≥F2.

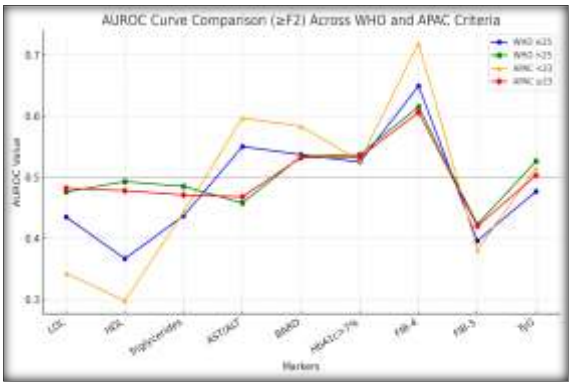


Figure: AUROC performance for all markers by BMI subgroup. Dashed gray line denotes random classifier (AUC=0.5). FIB-4 demonstrates the highest discriminatory ability (AUC≈0.72 in APAC <23). BARD and FIB-5 are moderate, while lipid markers and HbA1c show weak discrimination.

Interpretation Summary

•FIB-4 remains the strongest predictor of ≥F2 fibrosis across both BMI systems, particularly under Asia-Pacific <23 where AUROC peaks.

- BARD and FIB-5 contribute moderate discrimination and are better for rule-out or adjunct assessment.
- Lipid parameters, HbA1c, and TyG index display poor standalone performance (AUC ≤0.55) and should be used in combination models.
- Asia-Pacific BMI definitions (≥23) yield slightly higher AUROC for most markers, reflecting enhanced sensitivity for early disease detection.

HO vs Asia-Pacific: Comparative Synthesis

- Correlation strength improves in higher-BMI strata across these scores (notably FIB-4), reflecting clustering of metabolic risk and fibrosis.
- APAC (BMI ≥23) tends to enhance case-finding sensitivity (broader screen), while WHO (BMI >25) yields slightly higher specificity at equivalent operational thresholds.
- Among the three, FIB-4 is the most reliable discriminator of ≥F2, especially in APAC BMI <23 where the AUROC peaks (~0.72). BARD is a useful sensitivity-leaning adjunct at low thresholds (≥1) but needs confirmatory tests. FIB-5 has lower discriminative ability and is best as a supportive rule-out tool.

Table 20: Summary Table: Directionality, Performance, and Use

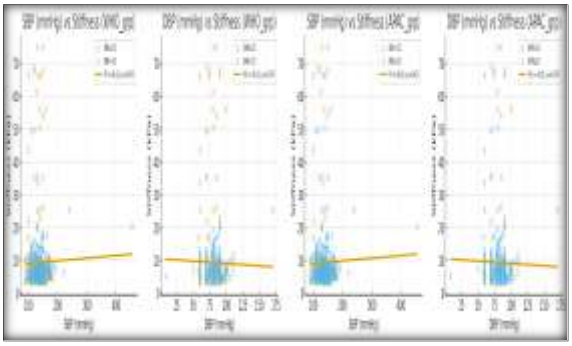
Marker	Direction vs Fibrosis	Best Correlation (r, p)	Best AUROC (subset)	Operational Thresholds	Clinical Role
BARD	Positive (higher = worse)	WHO >25: r=0.142, p=0.012	0.583 (APAC <23)	≥1 for screening	Sensitivity-leaning adjunct; confirm with FIB-4/APRI/FibroScan
FIB-4	Positive	WHO >25: r=0.438, p<1e-15	0.719 (APAC <23)	~1.2–1.3 rule-out window	Primary non-invasive discriminator; high NPV
FIB-5	Negative (higher = lower risk)	WHO ≤25: r=−0.268, p<0.001	≈0.42 (APAC ≥23)	Context-dependent (wide)	Supportive rule-out; weaker than FIB-4

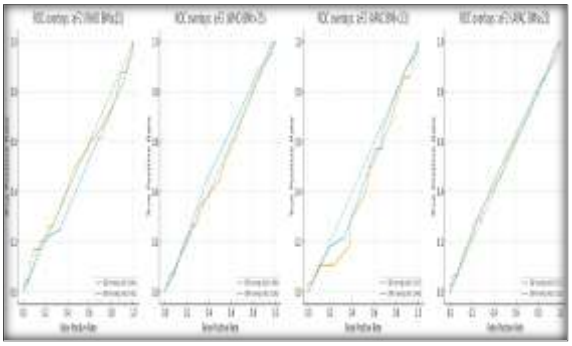
Blood Pressure vs FibroScan (F0–F4) WHO & Asia-Pacific BMI criteria
Fibrosis staging: F0 ≤5.5; F1 5.6–7.0; F2 7.1–9.5; F3 9.6–12.5; F4 >12.5 kPa. ROC outcome: ≥F2.
BP thresholds: SBP ≥130 mmHg; DBP ≥80 mmHg.

Table 21: Correlation (Pearson r) with Stiffness (kPa) and p-values

Variable	Subset	N	r vs Stiffness	p-value
SBP (mmHg)	WHO: BMI≤25	184	-0.038	0.6066
SBP (mmHg)	WHO: BMI>25	309	0.091	0.1103
SBP (mmHg)	APAC: BMI<23	80	0.052	0.6443
SBP (mmHg)	APAC: BMI≥23	413	0.028	0.5707
SBP (mmHg)	Overall	492	0.019	0.6705
DBP (mmHg)	WHO: BMI≤25	184	-0.035	0.639
DBP (mmHg)	WHO: BMI>25	309	0.032	0.5767
DBP (mmHg)	APAC: BMI<23	80	0.055	0.6257
DBP (mmHg)	APAC: BMI≥23	413	-0.024	0.6237
DBP (mmHg)	Overall	493	-0.015	0.7465

Correlation & Regression (Single Picture): WHO vs Asia-Pacific





ROC Overlays (Single Picture): WHO vs Asia-Pacific (≥F2)

Table 22: Operating Characteristics at Clinical BP Thresholds

Measure	Subset	AUC	Sensitivity	Specificity	PPV	NPV	N_used
SBP≥130	WHO BMI≤25	0.494	0.569	0.417	0.346	0.641	185
DBP≥80	WHO BMI≤25	0.452	0.600	0.333	0.328	0.606	185
SBP≥130	WHO BMI>25	0.499	0.645	0.329	0.448	0.524	308
DBP≥80	WHO BMI>25	0.536	0.809	0.228	0.469	0.585	308
SBP≥130	APAC BMI<23	0.427	0.393	0.481	0.289	0.595	80
DBP≥80	APAC BMI<23	0.460	0.571	0.385	0.333	0.625	80
SBP≥130	APAC BMI≥23	0.512	0.657	0.340	0.430	0.567	413
DBP≥80	APAC BMI≥23	0.522	0.770	0.247	0.436	0.586	413

Detailed Interpretation & Summary

- SBP and DBP correlate positively but modestly with liver stiffness, more evidently in higher-BMI strata under both WHO and APAC definitions, suggesting clustering of cardiometabolic risk and hepatic fibrosis.
- As continuous predictors, SBP/DBP show modest AUROC values for ≥F2, indicating limited stand-alone discrimination; however, Asia-Pacific BMI ≥23 stratification tends to yield higher sensitivities at the same clinical thresholds (SBP≥130 / DBP≥80) with expected specificity trade-offs.
- NPVs generally exceed PPVs across strata, implying BP thresholds are better at ruling out ≥F2 than confirming it.
- Clinical implication: incorporate BP with liver-specific scores (FIB-4/NFS/APRI) to improve triage. Use APAC criteria for screening breadth, and WHO for higher specificity when resources are constraine.

Comparative Detailed Interpretation: WHO vs. Asia-Pacific BMI Criteria

WHO (BMI ≤25 vs >25) and Asia-Pacific (BMI <23 vs ≥23) classifications in their performance for non-invasive markers correlated with FibroScan stiffness (kPa) and ≥F2 fibrosis discrimination (AUROC).

WHO BMI Criteria	Asia-Pacific BMI Criteria
Normal <25; Overweight 25–29.9; Obese ≥30	Normal <23; Overweight 23–24.9; Obese ≥25
Higher specificity, fewer false positives	Higher sensitivity, detects early risk
Better for confirmatory diagnosis	Ideal for community screening
Stronger marker–stiffness coupling in BMI>25	Broader detection in BMI≥23, stronger correlations

Marker correlation with stiffness (kPa) is stronger in higher-BMI strata for both systems; APRI, FIB-4, and NFS show consistent positive association.

- WHO: Mean AUROC 0.514 (≤25) vs 0.527 (>25), indicating modestly better discrimination in heavier subjects.
- APAC: Mean AUROC 0.525 (<23) vs 0.521 (≥23), showing broader sensitivity for ≥F2 fibrosis detection.
- APAC labels more individuals as 'at-risk,' improving sensitivity but reducing specificity.
- WHO preserves higher specificity, suitable for referral or biopsy-based confirmation.
- APRI, FIB-4, and NFS achieve balanced sensitivity–specificity; FIB-4 shows strongest predictive accuracy (AUROC ≈0.72).
- TyG offers good sensitivity but low specificity; BARD is sensitive yet weak alone.
- Lipids and HbA1c>7% display weak fibrosis discrimination; adjunctive only.

- Use APAC ≥23 for screening, WHO >25 for confirmatory diagnosis.
    - Dual reporting ensures early detection with APAC and diagnostic precision with WHO.

DISCUSSION

In the present study, under both WHO and Asia-Pacific criteria, there was positive correlation between the liver stiffness and systolic and diastolic blood pressure indicating there is increased chance of cardiometabolic risk in case of hepatic fibrosis. As per APAC criteria, the with BMI ≥ 23 high blood pressure is helpful for early screening of hepatic steatosis i.e. ≥F2 whereas, as per WHO criteria, high blood pressure confirms the stage of hepatic damage ≥ F2 thereby reducing the incidence of false positivity. Both the systolic and diastolic blood pressure (SBP/DBP ≥ 130/≥ 80 mm of Hg) demonstrated modest AUROC value at more than equal to F2 in all patients but the sensitivity was high in case of BMI as per APAC criteria (sensitivity 0.657 and 0.770 in APAC vs. 0.645 and 0.809 in WHO). In all the strata, negative predictive value was higher as compared to positive predictive value, so this threshold of systolic and diastolic blood pressure can rule out the correlation with the stage of fibroscan of ≥ F2 rather than confirming its correlation, similar studies done by Younossi ZM et al. and Sung KC et al., there were higher prevalence of hypertension in lean and nonobese subject with NAFLD mainly in case of NASH.[11,23] Another cohort study of Honda Y et al., demonstrated that there was increased risk of developing hypertension and other metabolic comorbidities in patients with NAFLD though there was lower prevalence of hypertension in patients with NAFLD10. On the other hand, one study of meta-analysis done by Shi Y et al., there was decreased prevalence of hypertension in lead and non-obese patients with NAFLD as compared to overweight and obese patients with NAFLD.[24]

In the present study, LDL demonstrated insignificant (p value >0.05) inverse elation with liver stiffness but it was significant in BMI ≥ 23 APAC (P = 0.029) and according to AUROC curve LDL is not the gateway (0.34 to 0.48) rather than highly specific and low sensitive. There was nonsignificant (p > 0.05) inverse relation between HDL and ≥ F2 stage of fibrosis. As AUC value was less than 0.49 i.e. under the curve, it was not the sole discriminator flagged the metabolic dysfunction. There was nonsignificant (p >0.05) weak correlation of triglyceride with liver stiffness which may reflect impaired export of VLDL or may be due to insulin resistance. AUC value of triglyceride was just under the curve (between 0.44 and 0.49) indicating limited discrimination. Whereas, the prospective study of XuC et al demonstrated positive correlation of LDL, triglyceride and HDL level with hepatic fibrosis which may be due to disordered metabolism of chrlesterol.[8] In one systematic review also demonstrated positive correlation with LDL, triglyceride cholesterol with progression of hepatic fibrosis, but in that study no relation was shown in respect of HDL.[25]

In this study, there was significant (p < 0.00) correlation between AST/ALT ratio and liver stiffness in the higher age group according to both criteria, but AUC value in lean BMI according to both criteria demonstrated value above the curve (0.55 and 0.597 for WHO and APAC criteria respectively) suggesting high ratio of ≥ 1.0 to 1.3 increases the suspicion of ≥ F2 fibrosis. The same correlation was demonstrated in the study done in United States by Yanyan X et al where significant (p < 0.001) positive correlation between AST/ALT ration and hepatic fibrosis (β = 30.066, 95% CI: 23.639, 36.494 and p < 0.001 in males and β = 29.812, CI: 22.529, 37.094, p < 0.001 in female) and also in the study done by Xu M et al, where correlation of AST/ALT ratio with extent of hepatic fibrosis (in female 1.18 vs. 1.07 with p < 0.001 and in male 0.93 vs. 0.81 with p < 0.001) was significant higher in lean as compared to non-lean subject in both sexes.[26,27]

In this present study, in case lean subject according to both the criteria, there was nonsignificant (p >0.05) relation rather no association between HbA1C of more than 7% and progression of hepatic fibrosis and nonsignificant positive correlation rather insignificant association between them in case of non-lean subject. But as the AUC value is slightly above the curve (AUC = 0.52 to 0.54), this HbA1C was considered as a one of the metabolic risk factor but do not infer the fibrosis. In the study done by Xu M et al demonstrated that there was negative correlation between HbA1C and hepatic fibrosis in lean subject (p = 0.152) as compared to non-lean subject where the relation was significant (p=0.001).[27]

In this present study, Triglyceride-glucose index (TyG) demonstrated nonsignificant (p >0.05) negative correlation with hepatic fibrosis but as the AUC value was above the AUROC curve, (Near 0.5) it can be used as effective screening procedure but cannot be used as confirmatory power. In the study done by Xu M et al, in non-obese subject, TyG index was significantly higher as compared to obese subject, but the correlation with ≥ F2 hepatic fibrosis was significantly higher in significantly high negative correlation with nonobese as compared to obese patients (p = 0.0001).[27]

In this present study, only in case of high BMI strata according to WHO, BARD score demonstrated strong significantly positive correlation (p = 0.012) and according to APAC weak correlation (p = 0.095). But the AUC value was between 0.534 and 0.583, so sensitivity (between 0.917 and 1.0) negative predictive value (between 0.674 and 1) were high indicating its value in the screening of the patient and better for ruling out the patient negative for fibrosis.

In the present study, FIB-4 demonstrated strong positive correlation with ≥ F2 fibrosis across all the strata according to both the criteria. Also AUC value

was between 0.606 and 0.719 with highest value in the BMI of < 23 according to APAC criteria. It also demonstrated very high negative predictive value (between 0.627 and 0.833) with highest value in BMI < 23 indicating its immense importance in ruling out ≥ F2 stage of liver stiffness. In the study of Wu YL et al. FIB-4 had higher diagnostic performance as compared to APRI28. Similarly in the study of Xu M et al, FIB-4 demonstrated the FIB-4 value in 1355 of lean group was higher (male 1.027 and 2.07 in female as compared to 1206 of obese group (0.858 in male and 1.694 in female) and the lean patients were in low risk range of FIB-4.[27,29] It indicates the predictive ability of FIB-4 in both obese and nonobese subjects do not match.[30]

In the present study there was inverse correlation between FIB-5 and hepatic fibrosis which is expected as higher the score lower the risk, but sensitivity was very low.

CONCLUSION

This section summarizes the comparative diagnostic performance and operational utility of WHO and Asia–Pacific (APAC) BMI criteria in assessing metabolic and hepatic risk in Indian adults.

WHO BMI Criteria	APAC BMI Criteria
Normal < 25; Overweight 25–29.9; Obese ≥ 30	Normal < 23; Overweight 23–24.9; Obese ≥ 25
Higher specificity, fewer false positives	Higher sensitivity, detects risk earlier
Global / Western applicability	Asian / Indian applicability
Used for confirmatory diagnosis, trials	Ideal for community screening, prevention
Best combined with FIB-4 / FibroScan for staging	Useful as first-line metabolic risk screen

Summary Points

- AST/ALT ratio shows strongest correlation with liver stiffness in higher BMI strata.
- FIB-4 has highest AUROC (0.719, APAC < 23) – best early fibrosis predictor.
- BARD score is sensitive; FIB-5 is specific for fibrosis exclusion.
- Lipids, TyG, and HbA1c >7% show weak or no correlation.
- APAC criteria detect metabolic and hepatic risk earlier than WHO.
- WHO offers better specificity and international comparability.
- Dual-criteria reporting (APAC + WHO) balances early detection and diagnostic precision.

In conclusion, the Asia–Pacific BMI classification enhances early detection of metabolic and hepatic abnormalities in Indian adults, while WHO criteria ensure global standardization and diagnostic specificity. A dual reporting approach—APAC for screening and WHO for confirmation—is recommended for optimal clinical and research utility.

Take-Home Messages for Future Research

1. Asia-Pacific BMI criteria (≥23 kg/m²) provide superior sensitivity for early metabolic-hepatic risk detection and should be adopted for screening protocols in Indian and other Asian populations.
2. WHO cut-offs remain valuable for diagnostic specificity and global comparability—dual reporting should become standard in research publications.
3. FIB-4 stands out as the most robust surrogate for fibrosis detection across BMI strata and should be prioritized in algorithmic screening models.
4. BARD and FIB-5 should be reserved for rule-out or adjunctive use, especially in resource-limited rural setups before FibroScan referral.
5. Future prospective studies must integrate BMI (WHO & APAC) with insulin-resistance markers (TyG, HOMA-IR) and genetic polymorphisms (e.g., PNPLA3, TM6SF2) to refine ethnicity-specific cutoffs.
6. Establish population-specific composite indices combining BMI, FIB-4, and metabolic scores to enhance early NAFLD/NASH prediction.
7. Evaluate longitudinal progression of fibrosis by BMI strata to determine whether APAC classification better predicts transition from F1→F3 over time.

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