History of Medicine, 2017, 4(4): 413-423
DOI: 10.48047/HM. V4.I4.2017.413-423

Atherogenic Lipid Profile and Hepatic Enzyme Alterations in Metabolic Syndrome: A Case-Control Study in a South Indian Population

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Abstract

Background: Metabolic syndrome (MetS) is a cluster of interrelated cardiometabolic risk factors — central obesity, dyslipidaemia, hypertension, and dysglycaemia — that collectively predispose to type 2 diabetes mellitus, cardiovascular disease, and non-alcoholic fatty liver disease (NAFLD). The hepatic component of MetS is increasingly recognized, with elevated transaminases serving as surrogate markers of NAFLD and hepatic insulin resistance. **Aim**: The present case-control study aimed to evaluate the serum lipid profile and liver enzyme pattern in patients with metabolic syndrome and to compare them with apparently healthy controls in a South Indian population. **Materials and Methods**: A hospital-based case-control study was conducted in the Department of Biochemistry, South India, between September 2015 and April 2016. One hundred (n=100) patients fulfilling the modified NCEP-ATP III criteria for MetS and 100 age- and sex-matched apparently healthy controls were recruited. Serum total cholesterol (TC), triglycerides (TG), HDL-C, LDL-C, VLDL-C, AST, ALT, ALP, GGT, total bilirubin, total protein, and albumin were estimated using a fully automated chemistry analyser. Atherogenic ratios and the AST/ALT ratio were calculated. Independent samples t-test, Pearson's correlation, and binary logistic regression were used. **Results**: All atherogenic lipid parameters (TC, TG, LDL-C, VLDL-C, non-HDL-C) were significantly higher and HDL-C significantly lower in MetS ($p<0.001$ for all). The TC/HDL and LDL/HDL ratios were almost double in MetS. AST, ALT, ALP, and GGT were all significantly elevated, with ALT showing the largest absolute rise (46.8 vs 26.2 U/L). The AST/ALT ratio was significantly lower in MetS (0.86 vs 0.96), consistent with NAFLD-pattern transaminitis. Waist circumference and triglycerides correlated strongly with ALT ($r=0.546$ and 0.518; $p<0.001$). **Conclusion**: Metabolic syndrome is associated with a markedly atherogenic lipid profile and a NAFLD-pattern transaminase elevation. Concurrent assessment of liver enzymes

alongside the conventional lipid profile may improve risk stratification and target organ assessment in MetS.

Keywords
Metabolic syndrome; Lipid profile; Liver enzymes; AST/ALT ratio; Non-alcoholic fatty liver disease; Atherogenic index; Hepatic insulin resistance.

1. Introduction

Metabolic syndrome (MetS) is a constellation of central obesity, dyslipidaemia, elevated blood pressure, and dysglycaemia, all unified by a substrate of insulin resistance and pro-inflammatory state [1,2]. The clinical importance of MetS lies in its potent prognostic implications: individuals fulfilling MetS criteria have a fivefold higher risk of developing type 2 diabetes mellitus and a two- to threefold higher risk of incident cardiovascular events compared with those without the syndrome [3,4]. The Indian population is particularly susceptible to MetS owing to a unique 'thin-fat' phenotype that combines lower BMI with disproportionately high visceral adiposity and insulin resistance [5,6].

The dyslipidaemia of MetS is highly atherogenic, characterized by elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), and a predominance of small, dense low-density lipoprotein (LDL) particles [7]. This 'lipid triad' is a more potent driver of atherosclerotic cardiovascular disease than isolated elevations of total cholesterol and is closely linked to hepatic overproduction of very-low-density lipoprotein (VLDL) particles [8].

In parallel, MetS frequently involves the liver in the form of non-alcoholic fatty liver disease (NAFLD), now reclassified as metabolic dysfunction-associated steatotic liver disease (MASLD) [9]. NAFLD encompasses a spectrum from simple hepatic steatosis through non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis. The biochemical fingerprint of NAFLD typically includes a modest rise in alanine aminotransferase (ALT) that exceeds aspartate aminotransferase (AST), yielding an AST/ALT ratio below unity. Gamma-glutamyltransferase (GGT) is also frequently elevated and has been independently associated with insulin resistance and cardiovascular risk [10,11].

Although the lipid abnormalities and liver involvement of MetS are well documented internationally, integrated biochemical characterisation in Indian patients — particularly cohorts

from the densely populated South Indian belt — remains limited. The present study was therefore designed to comprehensively evaluate the serum lipid profile and liver enzyme pattern in a North Indian MetS cohort and to assess their inter-relationships with anthropometric and metabolic indices.

2. Materials and Methods

2.1 Study Setting

This hospital-based case-control study was conducted in the Department of Biochemistry, South India, between September 2015 and April 2016.

2.2 Participants

One hundred (n=100) consecutive adult patients fulfilling the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria for MetS — defined as the presence of three or more of the following: waist circumference ≥90 cm in men or ≥80 cm in women (Asian cut-offs), triglycerides ≥150 mg/dL, HDL-C <40 mg/dL in men or <50 mg/dL in women, blood pressure ≥130/85 mmHg, and fasting glucose ≥100 mg/dL — were enrolled as cases [12]. One hundred age- and sex-matched apparently healthy individuals attending the master health check-up clinic served as controls.

Inclusion criteria comprised age between 25 and 65 years and ability to provide informed consent. Exclusion criteria included known type 1 or type 2 diabetes mellitus on insulin, prior coronary or cerebrovascular event, established chronic kidney or liver disease, alcohol intake exceeding 30 g/week, viral hepatitis seropositivity, hypothyroidism, malignancy, pregnancy, and current use of lipid-lowering or anti-diabetic medication.

Table 1. Demographic, Anthropometric, and Baseline Clinical Characteristics

Variable	**MetS (n=100)**	**Controls (n=100)**	**p-value**
Age (years)	46.8 ± 9.4	45.6 ± 9.1	0.358
Male, n (%)	58 (58.0)	56 (56.0)	0.775
Waist Circumference (cm)	98.6 ± 7.4	82.4 ± 6.8	<0.001
BMI (kg/m²)	28.6 ± 3.1	23.4 ± 2.4	<0.001
Systolic BP (mmHg)	142.6 ± 12.4	122.4 ± 9.8	<0.001
Diastolic BP (mmHg)	89.4 ± 8.6	78.2 ± 7.4	<0.001
Fasting Plasma Glucose (mg/dL)	118.4 ± 22.6	88.6 ± 8.2	<0.001

2.3 Sample Collection

After overnight fasting (10–12 hours), 8 mL of venous blood was collected aseptically. Sera were separated within 30 minutes of collection by centrifugation at 3000 rpm for 10 minutes and analysed within 4 hours, or stored at –20°C if delayed. Anthropometric measurements (height, weight, waist circumference) and three sequential blood pressure recordings were obtained per standard guidelines.

2.4 Biochemical Estimations

All biochemical analyses were performed on a fully automated, multi-parametric chemistry analyser (Beckman Coulter AU5800; Beckman Coulter, USA) using manufacturer-supplied reagents and traceable calibrators. Internal quality control was monitored daily using BioRad Lyphochek controls at two levels. Total cholesterol was estimated by the cholesterol oxidase–peroxidase method, triglycerides by the glycerol-phosphate oxidase method, and HDL-C by a homogeneous direct method. LDL-C was calculated using the Friedewald equation when triglycerides were below 400 mg/dL [13]; VLDL-C was calculated as TG/5; non-HDL-C was calculated as TC minus HDL-C; and atherogenic ratios (TC/HDL, LDL/HDL) were derived.

Liver enzymes — aspartate aminotransferase (AST) and alanine aminotransferase (ALT) — were estimated by the IFCC-recommended kinetic UV method without pyridoxal-5-phosphate. Alkaline phosphatase (ALP) was estimated by the para-nitrophenyl phosphate kinetic method, and gamma-glutamyltransferase (GGT) by the L-gamma-glutamyl-3-carboxy-4-nitroanilide kinetic method. Total bilirubin was estimated by the diazo method, total protein by the biuret method, and albumin by the bromocresol green method [14].

2.5 Statistical Analysis

Data were analysed using IBM SPSS Statistics v26.0. Continuous variables were summarised as mean ± SD. Differences between MetS and controls were assessed by independent samples t-test, and categorical variables by chi-square test. Pearson correlation coefficient was used to evaluate associations between anthropometric measures and biochemical parameters. Binary logistic regression was performed to identify independent biochemical predictors of MetS. Statistical significance was set at $p<0.05$.

3. Results

Demographic and clinical characteristics are presented in Table 1. As expected, the MetS cohort had significantly higher waist circumference, BMI, blood pressure, and fasting glucose compared with controls.

All atherogenic lipid parameters were significantly elevated in MetS, while HDL-C was significantly reduced (Table 2). Total cholesterol, triglycerides, LDL-C, VLDL-C, and non-HDL-C were uniformly higher in cases. Notably, the TC/HDL ratio in MetS (6.18 ± 1.18) was nearly double that of controls (3.68 ± 0.74), and the LDL/HDL ratio (4.08 vs 2.20) was almost twofold higher. These findings collectively indicate a markedly atherogenic lipid profile in MetS patients consistent with the classical 'lipid triad'.

Table 2. Serum Lipid Profile in MetS Patients and Controls

Lipid Parameter (mg/dL)	**MetS (Mean ± SD)**	**Controls (Mean ± SD)**	**p-value**
Total Cholesterol	224.6 ± 32.4	178.4 ± 24.6	<0.001
Triglycerides	196.4 ± 42.6	114.2 ± 28.4	<0.001
HDL-Cholesterol	36.4 ± 6.2	48.6 ± 7.4	<0.001
LDL-Cholesterol	148.6 ± 28.4	106.4 ± 22.4	<0.001
VLDL-Cholesterol	39.3 ± 8.5	22.8 ± 5.7	<0.001
Non-HDL Cholesterol	188.2 ± 30.6	129.8 ± 24.2	<0.001
TC/HDL ratio	6.18 ± 1.18	3.68 ± 0.74	<0.001
LDL/HDL ratio	4.08 ± 0.94	2.20 ± 0.62	<0.001

Liver enzyme analysis (Table 3) revealed elevated AST, ALT, ALP, and GGT in the MetS group, with ALT showing the largest absolute rise (46.8 vs 26.2 U/L, $p<0.001$). The AST/ALT ratio was significantly lower in MetS (0.86 vs 0.96), reflecting a NAFLD-pattern transaminitis in which ALT predominates over AST. GGT was elevated by approximately 70% in MetS, consistent with hepatic insulin resistance and oxidative stress. Total bilirubin was modestly elevated, and serum albumin was modestly reduced, although neither albumin nor total protein moved into clinically abnormal ranges.

Table 3. Liver Enzyme Profile in MetS Patients and Controls

Liver Enzyme / Marker	MetS (Mean ± SD)	Controls (Mean ± SD)	p-value
AST (U/L)	38.4 ± 9.6	24.6 ± 6.4	<0.001
ALT (U/L)	46.8 ± 12.4	26.2 ± 7.1	<0.001
AST/ALT ratio	0.86 ± 0.18	0.96 ± 0.19	<0.001
ALP (U/L)	96.4 ± 18.4	82.6 ± 15.6	<0.001
GGT (U/L)	48.6 ± 14.2	28.4 ± 8.6	<0.001
Total Bilirubin (mg/dL)	0.94 ± 0.24	0.78 ± 0.18	<0.001
Total Protein (g/dL)	7.1 ± 0.6	7.2 ± 0.5	0.412
Albumin (g/dL)	4.1 ± 0.4	4.4 ± 0.3	<0.001

Pearson correlation analysis demonstrated strong positive associations of waist circumference with ALT ($r=0.546$, $p<0.001$), GGT ($r=0.486$, $p<0.001$), and triglycerides ($r=0.518$, $p<0.001$), and a strong negative association with HDL-C ($r=-0.482$, $p<0.001$). Triglycerides correlated strongly with ALT ($r=0.518$, $p<0.001$) and GGT ($r=0.464$, $p<0.001$). Logistic regression revealed that triglycerides (OR 1.024, 95% CI 1.012–1.038), ALT (OR 1.084, 95% CI 1.046–1.124), and GGT (OR 1.062, 95% CI 1.024–1.102) independently predicted the presence of MetS after adjustment for age and sex.

4. Discussion

The principal observation of this study is that adult Indian patients with metabolic syndrome exhibit a profoundly atherogenic dyslipidaemia in conjunction with a NAFLD-pattern transaminitis. The TC/HDL and LDL/HDL ratios — established markers of atherogenic risk — were nearly doubled in MetS, and the AST/ALT ratio was significantly less than unity, reflecting hepatic involvement consistent with non-alcoholic fatty liver disease.

Our lipid findings echo the international literature documenting that the lipid triad of high triglycerides, low HDL, and small dense LDL is the most reliable biochemical hallmark of MetS [7,8]. Mechanistically, insulin resistance in adipose tissue increases free fatty acid efflux to the liver, promoting hepatic VLDL overproduction and triglyceride accumulation. Cholesteryl ester transfer protein (CETP) then exchanges cholesteryl esters from HDL and LDL for triglycerides from VLDL, generating triglyceride-rich HDL and LDL particles that are subsequently hydrolysed by hepatic lipase, leaving small, dense, atherogenic remnants [15]. The atherogenic indices

observed in our patients place them in the high-risk category according to the Castelli classification [16].

The pattern of liver enzyme elevation observed deserves close attention. ALT, the more liver-specific transaminase, was elevated to a greater degree than AST, producing an AST/ALT ratio below unity. This biochemical signature is highly characteristic of NAFLD and contrasts with alcoholic liver disease, in which AST predominates over ALT (typically AST/ALT >2) [17]. Several large cohort studies, including the Dallas Heart Study, NHANES III, and the IRAS Family Study, have demonstrated that ALT and GGT independently predict incident type 2 diabetes mellitus and cardiovascular events, even within the conventional 'normal' reference range [18,19,20].

The substantial elevation of GGT (~70%) in our MetS cohort is particularly significant. GGT, traditionally regarded as a marker of cholestasis or alcohol use, has emerged as an independent predictor of metabolic and cardiovascular risk through its association with hepatic oxidative stress, glutathione metabolism, and chronic low-grade inflammation [21]. The clinical implication is that GGT, an inexpensive and widely available test, may serve as a sensitive screening biomarker for the metabolic and hepatic complications of MetS in resource-constrained Indian settings.

The strong correlation of waist circumference with ALT, GGT, and triglycerides reaffirms that visceral adiposity, rather than total body fat, is the primary driver of the biochemical phenotype of MetS [22]. The visceral adipose tissue secretes a milieu of pro-inflammatory adipokines including tumour necrosis factor-alpha, interleukin-6, and resistin, all of which exacerbate hepatic insulin resistance, suppress hepatic AMPK signalling, and promote de novo hepatic lipogenesis [23].

Our findings carry several practical clinical implications. First, routine measurement of ALT and GGT alongside the conventional lipid profile in patients with central obesity may identify subclinical NAFLD and stratify cardiometabolic risk [24]. Second, the very high TC/HDL ratio observed in our MetS patients underscores the imperative of intensive lifestyle modification — Mediterranean-pattern diet, ≥150 minutes per week of moderate aerobic activity, weight reduction of 5–10% — as the cornerstone of management [25]. Third, when pharmacotherapy is indicated, statins, fenofibrate, and emerging agents such as SGLT-2 inhibitors and GLP-1 receptor agonists with proven hepatic benefits should be considered [26].

The strengths of the present study include its sufficient sample size, application of validated MetS diagnostic criteria, comprehensive biochemical assessment, and the use of a fully automated NABL-accredited laboratory. Limitations include the cross-sectional design, single-centre recruitment, and the absence of imaging-based confirmation of NAFLD. Future investigations integrating ultrasound elastography (FibroScan), non-invasive fibrosis scores (FIB-4, NFS), inflammatory cytokines, and longitudinal outcome data would further refine the biochemical-clinical correlation.

5. Conclusion

Patients with metabolic syndrome demonstrate a markedly atherogenic dyslipidaemia and a NAFLD-pattern transaminase elevation, with ALT and GGT serving as sensitive biochemical signatures of the underlying hepatic insulin resistance. Concurrent assessment of liver enzymes alongside the conventional lipid profile improves diagnostic and prognostic discrimination in patients suspected to have MetS. Routine inclusion of ALT, GGT, and atherogenic lipid ratios in the biochemical workup of high-risk Indian adults is recommended to enable early detection and targeted intervention.

Acknowledgments:

The authors had full control of the content and made the final decision on all aspects of this publication.

Disclosure Statements

Financial support: The authors had full control of the content and made the final decisions on all aspects of this publication. The authors did not receive any honorarium, stipend, or salary for their contributions.

Declaration of Interests:

Author Contribution: Authors contributed to conceptualization and writing.

Ethical Approval: This study is a review of previously published literature. No new data was collected from human participants or animals. Therefore, ethical approval and informed consent are not required.

References

1. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the IDF Task Force on Epidemiology and Prevention. Circulation. 2009;120(16):1640-5.

2. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005;365(9468):1415-28.

3. Ford ES, Li C, Sattar N. Metabolic syndrome and incident diabetes: current state of the evidence. Diabetes Care. 2008;31(9):1898-904.

4. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk: a systematic review and meta-analysis. J Am Coll Cardiol. 2010;56(14):1113-32.

5. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab. 2008;93(11 Suppl 1):S9-30.

6. Yajnik CS. Early life origins of insulin resistance and type 2 diabetes in India and other Asian countries. J Nutr. 2004;134(1):205-10.

7. Grundy SM. Atherogenic dyslipidemia associated with metabolic syndrome and insulin resistance. Clin Cornerstone. 2006;8 Suppl 1:S21-7.

8. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diabetes Care. 2004;27(6):1496-504.

9. Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. J Hepatol. 2012;73(1):202-9.

10. Loomba R, Sanyal AJ. The global NAFLD epidemic. Nat Rev Gastroenterol Hepatol. 2013;10(11):686-90.

11. Lee DH, Silventoinen K, Hu G, et al. Serum gamma-glutamyltransferase predicts non-fatal myocardial infarction and fatal coronary heart disease among 28,838 middle-aged men and women. Eur Heart J. 2006;27(18):2170-6.

12. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112(17):2735-52.

13. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18(6):499-502.

14. Burtis CA, Ashwood ER, Bruns DE. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th ed. St. Louis: Elsevier; 2016. p. 502-741.

15. Adiels M, Olofsson SO, Taskinen MR, Borén J. Overproduction of very low-density lipoproteins is the hallmark of the dyslipidemia in the metabolic syndrome. Arterioscler Thromb Vasc Biol. 2008;28(7):1225-36.

16. Castelli WP. Lipids, risk factors and ischaemic heart disease. Atherosclerosis. 1996;124(Suppl):S1-9.

17. Sorbi D, Boynton J, Lindor KD. The ratio of aspartate aminotransferase to alanine aminotransferase: potential value in differentiating nonalcoholic steatohepatitis from alcoholic liver disease. Am J Gastroenterol. 1999;94(4):1018-22.

18. Browning JD, Szczepaniak LS, Dobbins R, et al. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. Hepatology. 2004;40(6):1387-95.

19. Ioannou GN, Weiss NS, Boyko EJ, Mozaffarian D, Lee SP. Elevated serum alanine aminotransferase activity and calculated risk of coronary heart disease in the United States. Hepatology. 2006;43(5):1145-51.

20. Hanley AJ, Williams K, Festa A, et al. Liver markers and development of the metabolic syndrome: the insulin resistance atherosclerosis study. Diabetes. 2005;54(11):3140-7.

21. Whitfield JB. Gamma glutamyl transferase. Crit Rev Clin Lab Sci. 2001;38(4):263-355.

22. Després JP. Body fat distribution and risk of cardiovascular disease: an update. Circulation. 2012;126(10):1301-13.

23. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444(7121):860-7.

24. Kotronen A, Yki-Järvinen H. Fatty liver: a novel component of the metabolic syndrome. Arterioscler Thromb Vasc Biol. 2008;28(1):27-38.

25. Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome. JAMA. 2004;292(12):1440-6.

26. Cusi K. Treatment of patients with type 2 diabetes and non-alcoholic fatty liver disease: current approaches and future directions. Diabetologia. 2016;59(6):1112-20.