



SERUM ADIPONECTIN AND THE DEGREE OF HEPATIC FIBROSIS IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE WITH METABOLIC SYNDROME: A HOSPITAL-BASED CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Hepatic fibrosis is the strongest determinant of liver-related outcome in metabolic dysfunction-associated steatotic liver disease (MASLD), yet liver biopsy is seldom feasible in routine care. Adiponectin, an adipocyte-derived hormone with insulin-sensitising and anti-fibrotic properties, has been proposed as a circulating marker of fibrosis, but data from Indian patients remain limited. **Methods:** Fifty adults with imaging-proven hepatic steatosis fulfilling MASLD criteria and at least three metabolic syndrome components were enrolled in a cross-sectional study at a tertiary centre in northern India between March 2025 and March 2026. Serum adiponectin was measured by sandwich ELISA. Liver stiffness and steatosis were assessed by vibration-controlled transient elastography with controlled attenuation parameter, and APRI and FIB-4 were calculated. Spearman correlation, Kruskal-Wallis, chi-square and multiple linear regression were used. **Results:** Mean serum adiponectin was $5.65 \pm 2.25 \mu\text{g/mL}$ and mean liver stiffness $9.18 \pm 3.89 \text{ kPa}$; 62% of patients had fibrosis stage F2 or higher. Adiponectin correlated inversely with liver stiffness ($\rho = -0.725, p < 0.001$), APRI ($\rho = -0.566, p < 0.001$) and FIB-4 ($\rho = -0.328, p = 0.020$), and declined stepwise across fibrosis stages ($H = 31.57, p < 0.001$). Every patient with advanced fibrosis (F3-F4) was diabetic ($\chi^2 = 17.04, p < 0.001$). On multivariable analysis, adiponectin remained an independent inverse predictor of liver stiffness ($\beta = -0.299, p < 0.001$). **Conclusion:** Low serum adiponectin tracks fibrosis severity in MASLD with metabolic syndrome and may assist non-invasive risk stratification, particularly in patients with diabetes.

KEYWORDS : Adiponectin; Metabolic Dysfunction-Associated Steatotic Liver Disease; Liver Fibrosis; Metabolic Syndrome; Transient Elastography; Non-Invasive Biomarkers.

INTRODUCTION

Fatty liver disease related to metabolic dysfunction is now the commonest chronic liver disorder worldwide, affecting close to a quarter of the adult population [1]. Pooled estimates over the past decade show the figure still rising, in step with obesity and type 2 diabetes [2]. In 2023 a multisociety Delphi process replaced the term non-alcoholic fatty liver disease with metabolic dysfunction-associated steatotic liver disease (MASLD), defined as hepatic steatosis together with at least one cardiometabolic risk factor [3]. Besides removing language that many patients found stigmatising, the new definition moved metabolic dysfunction from the margins of the diagnosis to its centre [4]. Burden estimates using the revised criteria place the number affected worldwide beyond a billion [5].

MASLD does not behave as a purely hepatic problem. It keeps company with hypertension, atherogenic dyslipidaemia and insulin resistance, and it raises cardiovascular risk over and above those companions [6]. Current thinking frames the disease in immunometabolic terms, with dysfunctional adipose tissue, low-grade systemic inflammation and lipotoxicity acting jointly on the liver [7].

Whatever the extrahepatic consequences, liver-related outcome is governed by the stage of fibrosis. In long-term follow-up of biopsied cohorts, fibrosis stage, and no other histological feature, predicted mortality and transplantation [8], and risk climbs steeply from stage F2 onwards [9].

Steeptoe hepatitis with fibrosis has become one of the fastest-growing indications for liver transplantation [10]. Finding out who has significant fibrosis therefore matters considerably more than finding out who has steatosis.

Biopsy remains the reference standard for staging [11], but sampling variability, cost and procedural risk rule it out for screening or repeated assessment. Vibration-controlled transient elastography and magnetic resonance elastography perform well, yet both need dedicated equipment and trained operators, which restricts their availability in district hospitals and primary care [12]. Serum-based indices such as the aspartate aminotransferase to platelet ratio index (APRI) and the fibrosis-4 index (FIB-4) are inexpensive and reproducible, and have been deployed successfully within automated care pathways for patients with diabetes [13], although a substantial proportion of results fall in an indeterminate zone. A blood marker that carries biological information about fibrogenesis, rather than merely reflecting transaminase and platelet values, would be a useful addition.

Adiponectin is one candidate. It is secreted almost exclusively by adipocytes and, unusually among adipokines, its circulating concentration falls as adiposity rises. In experimental models it reverses the insulin resistance of both obesity and lipodystrophy [14], and reduced levels in type 2 diabetes were described more than two decades ago [15]. Within the liver, adiponectin restrains hepatic stellate cell activation, suppresses pro-fibrogenic gene expression and

promotes fatty acid oxidation, which gives it a credible anti-fibrotic role [16]. Adipokine dysregulation more generally is thought to link adipose tissue stress to the transition from simple steatosis to steatohepatitis [17], and hypo-adiponectinaemia has been reported repeatedly in patients with fatty liver disease [18].

What is less settled is how closely adiponectin tracks the degree of fibrosis in patients who already carry the full metabolic syndrome phenotype, and whether it adds anything to indices already in routine use. Reports from Indian cohorts are few. We therefore measured serum adiponectin in patients with MASLD and metabolic syndrome and examined its relationship with fibrosis assessed by three separate methods.

MATERIALS AND METHODS

This hospital-based cross-sectional observational study was carried out in the Department of Medicine in collaboration with the Department of Gastroenterology and Hepatology at Moti Lal Nehru Medical College and Swaroop Rani Nehru Hospital, Prayagraj, over one year (March 2025 to March 2026). The protocol was approved by the Institutional Ethics Committee before recruitment began, and written informed consent was obtained from every participant in a language they understood. Consecutive adults older than 18 years attending the gastroenterology and medicine outpatient and inpatient services with imaging evidence of hepatic steatosis were screened. Patients were eligible if they fulfilled the diagnostic criteria for MASLD, met at least three of the five metabolic syndrome criteria, and reported no alcohol intake. We excluded patients with significant alcohol consumption, reactive viral markers (HBsAg, anti-HCV or HIV), a family history of chronic liver disease, chronic liver disease of another aetiology (autoimmune hepatitis, congestive hepatopathy, primary biliary cholangitis, primary sclerosing cholangitis or Wilson disease), acute hepatitis or acute liver failure, current use of drugs known to cause secondary steatosis (corticosteroids, tamoxifen or amiodarone), and any past hepatic or extrahepatic malignancy. The required sample size was calculated from the standard formula for a single proportion at a 95% confidence level, and 50 patients were recruited by consecutive sampling.

A structured case record form was used to document demographic details, duration and treatment of diabetes and hypertension, smoking status, physical activity, drug history and family history. Height, weight, waist and hip circumference were measured by a single observer using standard technique, and body mass index was derived as weight in kilograms divided by height in metres squared. Blood pressure was recorded in the seated position after at least five minutes of rest. Metabolic syndrome was defined by the presence of three or more of the following: central obesity by South Asian waist circumference thresholds, raised triglycerides, reduced high-density lipoprotein (HDL) cholesterol, raised blood pressure or antihypertensive treatment, and raised fasting glucose or established diabetes.

Venous blood was drawn after an overnight fast of at least eight hours. Complete blood count, liver and kidney function tests, serum electrolytes, fasting and postprandial blood sugar, glycated haemoglobin, fasting lipid profile and viral markers were processed in the institutional central laboratory using routine automated methods. Serum for adiponectin estimation was separated, aliquoted and stored at -80°C until batch analysis. Adiponectin was measured by sandwich enzyme-linked immunosorbent assay using a commercial human adiponectin kit (Fine Test, EH2593, V4.0, 96T) strictly according to the manufacturer's protocol, with all samples assayed in the same laboratory. Ultrasonography of the whole

abdomen was performed on a Samsung HS50 system, and steatosis was graded from one to three on the basis of hepatic echogenicity, beam attenuation and clarity of intrahepatic vasculature. Liver stiffness and controlled attenuation parameter (CAP) were measured by vibration-controlled transient elastography (FibroScan Mini Plus 430) in the fasting state by a single trained operator, and fibrosis was staged from the liver stiffness value according to established METAVIR-equivalent cut-offs (F1 to F4). APRI was calculated as $[\text{AST} / \text{upper limit of normal AST}] \div [\text{platelet count} (\times 10^9/\text{L}) \times 100]$, and FIB-4 as $[\text{age (years)} \times \text{AST (U/L)}] \div [\text{platelet count} (\times 10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}]$.

Statistical Analysis:

Data were entered in Microsoft Excel and analysed with standard statistical software. Continuous variables are presented as mean $\pm$ standard deviation with range, and categorical variables as counts and percentages. Because liver stiffness, adiponectin and the fibrosis indices were not normally distributed, associations between continuous variables were examined using the Spearman rank correlation coefficient (ρ). Adiponectin concentrations across the four fibrosis stages were compared using the Kruskal-Wallis test. Associations between categorical variables were tested with the chi-square test. Variables plausibly related to fibrosis, namely body mass index, glycated haemoglobin, triglyceride to HDL ratio, serum adiponectin, APRI and FIB-4, were entered simultaneously into a multiple linear regression model with liver stiffness in kilopascals as the dependent variable. A two-sided p value below 0.05 was taken as statistically significant.

RESULTS

Fifty patients were studied. The mean age was 49.52 ± 12.84 years, and almost half the cohort fell in the fifth and sixth decades. Men slightly outnumbered women, giving a ratio of about 1.17 to 1. The group was uniformly overweight or obese, with a mean body mass index of $29.84 \pm 3.03 \text{ kg/m}^2$ and a mean waist circumference of $95.67 \pm 6.21 \text{ cm}$, comfortably above the South Asian thresholds for central obesity in both sexes. Metabolic comorbidity was heavy: dyslipidaemia was present in 98%, hypertension in 86% and type 2 diabetes in 58%, and by design all 50 patients met the criteria for metabolic syndrome. Tobacco exposure was also common, with 78% being current or former smokers (Table 1).

Table 1: Baseline Demographic, Anthropometric and Clinical Characteristics of the Study Population (n = 50)

	Value
Age (years), mean $\pm$ SD	49.52 $\pm$ 12.84
20–40 years, n (%)	16 (32.0)
41–60 years, n (%)	22 (44.0)
61–80 years, n (%)	12 (24.0)
Male sex, n (%)	27 (54.0)
Female sex, n (%)	23 (46.0)
Body mass index (kg/m^2), mean $\pm$ SD (range)	29.84 $\pm$ 3.03 (25.3–40.0)
Waist circumference (cm), mean $\pm$ SD (range)	95.67 $\pm$ 6.21 (80.0–108.2)
Systolic blood pressure (mmHg), mean $\pm$ SD (range)	134.72 $\pm$ 11.71 (100–162)
Diastolic blood pressure (mmHg), mean $\pm$ SD (range)	83.10 $\pm$ 8.22 (70–102)
Current smoker, n (%)	24 (48.0)
Former smoker, n (%)	15 (30.0)
Never smoker, n (%)	11 (22.0)
Type 2 diabetes mellitus, n (%)	29 (58.0)
Hypertension, n (%)	43 (86.0)
Dyslipidaemia, n (%)	49 (98.0)
Metabolic syndrome, n (%)	50 (100.0)

Glycaemic control was poor overall: mean fasting blood sugar was 142.32 ± 32.34 mg/dL and mean glycated haemoglobin $7.56 \pm 1.33\%$. The lipid pattern was distinctly atherogenic, with high triglycerides (222.18 ± 47.47 mg/dL), low HDL cholesterol (43.30 ± 5.42 mg/dL) and a mean triglyceride to HDL ratio of 5.22 ± 1.33 , well above the value of 3.0 generally taken to indicate insulin resistance. Both transaminases were raised, and mean AST exceeded mean ALT, a pattern that tends to appear as fibrosis advances. Synthetic function and renal function were preserved. Mean platelet count was $234.85 \pm 65.68 \times 10^9/L$, with the lower end of the range reflecting patients with more advanced disease. Mean serum adiponectin was 5.65 ± 2.25 μ g/mL, and individual values varied more than eightfold, from 1.2 to 10.0 μ g/mL (Table 2). All 50 patients were non-reactive for HBsAg, anti-HCV and HIV.

Table 2: Biochemical, Haematological and Adiponectin Profile of the Study Population (n = 50)

Parameter	Mean $\pm$ SD	Range
Fasting blood sugar (mg/dL)	142.32 ± 32.34	93.8–197.1
Postprandial blood sugar (mg/dL)	195.75 ± 40.81	130.9–278.0
Glycated haemoglobin (%)	7.56 ± 1.33	5.4–10.1
Total cholesterol (mg/dL)	212.49 ± 24.97	162.2–264.0
LDL cholesterol (mg/dL)	124.66 ± 21.69	91.1–168.8
HDL cholesterol (mg/dL)	43.30 ± 5.42	33.5–54.6
Triglycerides (mg/dL)	222.18 ± 47.47	141.2–299.3
Triglyceride/HDL ratio	5.22 ± 1.33	3.0–8.8
Total bilirubin (mg/dL)	0.94 ± 0.24	0.5–1.4
ALT (U/L)	53.91 ± 14.01	29.2–80.0
AST (U/L)	62.19 ± 19.72	30.1–117.7
Alkaline phosphatase (U/L)	113.29 ± 18.93	82.3–153.7
Total protein (g/dL)	7.62 ± 0.47	6.6–8.5
Serum albumin (g/dL)	4.09 ± 0.44	3.2–4.8
Serum creatinine (mg/dL)	0.98 ± 0.15	0.7–1.3
Blood urea (mg/dL)	34.67 ± 10.07	18.6–54.5
Haemoglobin (g/dL)	13.18 ± 1.59	11.0–16.0
Total leucocyte count (cells/mm ³)	7638.86 ± 2062.07	4007–10752
Platelet count ($\times 10^9/L$)	234.85 ± 65.68	116.4–350.3
Serum adiponectin (μ g/mL)	5.65 ± 2.25	1.2–10.0

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; LDL, low-density lipoprotein;

Ultrasonography demonstrated definite steatosis in 46 of 50 patients (92%), most often of grade 2. CAP-based grading gave an identical distribution, with 40% at S2 and 30% at S3, and the mean CAP value of 277.45 ± 30.14 dB/m sat well above the 248 dB/m threshold usually taken to indicate steatosis. Mean liver stiffness was 9.18 ± 3.89 kPa, with individual values spanning 4.0 to 19.3 kPa. Nineteen patients (38%) had stage F1 disease, but 31 (62%) had significant fibrosis of stage F2 or worse, and 16 (32%) had advanced fibrosis or cirrhosis (F3–F4). Mean APRI was 0.76 ± 0.45 and mean FIB-4 was 2.07 ± 1.22 ; the latter exceeds the 1.45 lower cut-off, and both indices showed wide dispersion consistent with the spread of fibrosis stages (Table 3).

Table 3: Hepatic Steatosis and Fibrosis Assessment by Ultrasonography, Transient Elastography and Serum Fibrosis Indices (n = 50)

	Value
Liver stiffness measurement (kPa), mean $\pm$ SD (range)	9.18 ± 3.89 (4.0–19.3)
Controlled attenuation parameter (dB/m), mean $\pm$ SD (range)	277.45 ± 30.14 (214.1–336.4)
APRI score, mean $\pm$ SD (range)	0.76 ± 0.45 (0.23–1.95)
FIB-4 score, mean $\pm$ SD (range)	2.07 ± 1.22 (0.44–5.31)

Ultrasound steatosis grade, n (%)	
None or minimal	4 (8.0)
Grade 1	11 (22.0)
Grade 2	20 (40.0)
Grade 3	15 (30.0)
CAP-derived steatosis grade, n (%)	
S0	4 (8.0)
S1	11 (22.0)
S2	20 (40.0)
S3	15 (30.0)
Fibrosis stage by transient elastography, n (%)	
F1	19 (38.0)
F2	15 (30.0)
F3	10 (20.0)
F4	6 (12.0)
Significant fibrosis ($\geq$ F2), n (%)	31 (62.0)

Serum adiponectin was inversely related to every measure of fibrosis tested. The association was strongest with liver stiffness ($\rho = -0.725$, $p < 0.001$), intermediate with APRI ($\rho = -0.566$, $p < 0.001$) and weakest, though still significant, with FIB-4 ($\rho = -0.328$, $p = 0.020$). The three fibrosis measures themselves correlated closely with one another, most strongly between APRI and FIB-4 ($\rho = 0.838$) and between liver stiffness and APRI ($\rho = 0.837$), which supports their internal consistency in this cohort (Table 4, Panel A).

When patients were grouped by fibrosis stage, adiponectin fell in a stepwise fashion from F1 through to F4 (Kruskal–Wallis $H = 31.57$, $df = 3$, $p < 0.001$). The mean rank dropped from 38.16 at F1 to 4.67 at F4, a gradient with no overlap in direction at any stage, which is what one would expect of a dose-response relationship rather than a threshold effect (Table 4, Panel B).

Table 4: Relationship Between Serum Adiponectin and Hepatic Fibrosis. Panel A: Spearman Rank Correlations. Panel B: Comparison of Serum Adiponectin Across Fibrosis Stages (Kruskal–Wallis test)

Panel A — Correlation pair	Spearman ρ	p value
Serum adiponectin vs liver stiffness (kPa)	–0.725	< 0.001
Serum adiponectin vs APRI score	–0.566	< 0.001
Serum adiponectin vs FIB-4 score	–0.328	0.020
Liver stiffness (kPa) vs APRI score	0.837	< 0.001
Liver stiffness (kPa) vs FIB-4 score	0.560	< 0.001
APRI score vs FIB-4 score	0.838	< 0.001
Panel B — Fibrosis stage (n)	Mean rank of adiponectin	Test statistic
F1 (n = 19)	38.16	$H = 31.57$
F2 (n = 15)	24.60	$df = 3$
F3 (n = 10)	15.30	$p < 0.001$
F4 (n = 6)	4.67	

Patients were dichotomised into those with non-advanced fibrosis (F1–F2, $n = 34$) and those with advanced fibrosis or cirrhosis (F3–F4, $n = 16$). Diabetes separated the two groups sharply: all 16 patients with advanced fibrosis were diabetic, against 13 of 34 (38.2%) in the non-advanced group ($\chi^2 = 17.04$, $p < 0.001$). Hypertension was borderline ($\chi^2 = 3.83$, $p = 0.050$) and dyslipidaemia showed no association at all ($\chi^2 = 0.48$, $p = 0.488$), but in both cases the near-universal prevalence of the condition across the whole cohort left little room to discriminate between groups (Table 5). These two comparisons should therefore be read with caution rather than as evidence of absence of an effect.

Table 5: Association Between Components of the Metabolic Syndrome and Advanced Hepatic Fibrosis

Component	Non-advanced fibrosis, F1-F2 (n = 34), n (%)	Advanced fibrosis, F3-F4 (n = 16), n (%)	χ^2	p value
Diabetes mellitus	13 (38.2)	16 (100.0)	17.04	< 0.001
Hypertension	27 (79.4)	16 (100.0)	3.83	0.050
Dyslipidaemia	33 (97.1)	16 (100.0)	0.48	0.488

Six variables were entered simultaneously into a multiple linear regression model with liver stiffness as the dependent variable. Serum adiponectin remained an independent inverse predictor after adjustment ($B = -0.519$, $\beta = -0.299$, $p < 0.001$), meaning that each 1 $\mu\text{g/mL}$ rise in adiponectin corresponded to a fall of roughly 0.52 kPa in liver stiffness with the other covariates held constant. APRI was the strongest predictor in the model ($\beta = 0.797$, $p < 0.001$) and body mass index also contributed independently ($\beta = 0.173$, $p = 0.006$). Glycated haemoglobin fell just short of conventional significance ($\beta = 0.126$, $p = 0.052$), while the triglyceride to HDL ratio and FIB-4 did not contribute once the other variables were accounted for (Table 6).

Table 6: Multiple Linear Regression Analysis with Liver Stiffness (kPa) as the Dependent Variable

Predictor	B (unstandardised)	Standard error	β (standardised)	t	p value
Body mass index (kg/m^2)	0.223	0.078	0.173	2.863	0.006
Glycated haemoglobin (%)	0.369	0.184	0.126	2.002	0.052
Triglyceride/HDL ratio	-0.297	0.177	-0.101	-1.680	0.100
Serum adiponectin ($\mu\text{g/mL}$)	-0.519	0.130	-0.299	-3.978	< 0.001
APRI score	6.967	1.188	0.797	5.863	< 0.001
FIB-4 score	-0.600	0.376	-0.188	-1.597	0.118

DISCUSSION

In this cohort of 50 patients with MASLD and metabolic syndrome, serum adiponectin fell as hepatic fibrosis worsened. The relationship held across three different ways of assessing fibrosis, persisted after adjustment for adiposity, glycaemic control and the serum fibrosis indices, and followed a stepwise gradient across METAVIR-equivalent stages. Diabetes was the metabolic syndrome component most closely tied to advanced disease.

Mean adiponectin of 5.65 $\mu\text{g/mL}$ in our patients is low by comparison with healthy populations and consistent with what has been described in metabolic liver disease. Mohamed and colleagues, studying Egyptian patients with fatty liver, reported a comparable inverse relationship between adiponectin and biopsy-assessed fibrosis stage [19]. Zhang and co-workers followed 1,325 initially disease-free Chinese adults and found that those in the lowest baseline adiponectin quartile were substantially more likely to develop fatty liver over three years, with an adjusted odds ratio of 1.89 against the highest quartile [20]. Their prospective design supplies something a cross-sectional study cannot: evidence that the fall in adiponectin precedes the liver disease rather than merely accompanying it. Cho and colleagues, working in a community-based Korean cohort, showed that low adiponectin combined with high visceral fat area predicted incident metabolic syndrome independently of the usual clinical variables [21]. Our findings sit comfortably alongside all three.

The comparison with Radwan and colleagues is more instructive for what it does not show. In their Egyptian series, patients with chronic liver disease had a mean adiponectin of 12.4 $\mu\text{g/mL}$, roughly double the value we recorded, and levels were higher still in the earlier stages of disease [22]. That cohort was largely hepatitis C related. Adiponectin behaves differently in viral and metabolic liver disease: in advanced viral hepatitis and cirrhosis, concentrations tend to rise, probably reflecting reduced hepatic clearance and a compensatory response to ongoing injury, whereas in metabolic disease the dominant signal is suppression of adiponectin by dysfunctional adipose tissue [16,23]. Any attempt to use adiponectin as a fibrosis marker has to take aetiology into account; a value that suggests advanced fibrosis in MASLD may mean something quite different in hepatitis C. A recent 17-year Korean cohort study reinforced the point for the metabolic phenotype specifically, finding baseline adiponectin predictive of incident MASLD [24].

The biology gives the association a plausible footing. Adiponectin acts through AdipoR1 and AdipoR2, both of which are expressed in the liver and both of which are downregulated in steatotic tissue, so hypoadiponectinaemia and receptor loss compound one another [25]. Signalling through AMP-activated protein kinase promotes fatty acid oxidation and restrains gluconeogenesis and triglyceride synthesis, while adiponectin also suppresses NLRP3 inflammasome activation in experimental steatohepatitis [26] and, through peroxisome proliferator-activated receptor pathways, reduces hepatic triglyceride accumulation and improves insulin sensitivity [27]. Acting directly on hepatic stellate cells, adiponectin inhibits proliferation and migration, suppresses transcription of collagen I, transforming growth factor β 1 and α -smooth muscle actin, and promotes stellate cell apoptosis [16]. A falling adiponectin concentration therefore removes a brake on fibrogenesis at the same time as it worsens the metabolic environment that drives it.

That every patient with advanced fibrosis in our study was diabetic deserves comment. The finding matches a large body of evidence linking type 2 diabetes to fibrosis progression in fatty liver disease; pooled analyses put the prevalence of fatty liver in diabetes at around two thirds [28], and adipose tissue insulin resistance is now regarded as a principal driver of the transition from steatosis to steatohepatitis [29]. The corollary is practical: a patient with MASLD and diabetes warrants fibrosis assessment as a matter of routine, not as an afterthought. Our regression model puts body mass index alongside adiponectin as an independent contributor, and glycated haemoglobin came very close, which points in the same direction. By contrast, hypertension and dyslipidaemia showed little or no relationship with fibrosis stage, but this almost certainly reflects the design of the study rather than the underlying biology. Requiring three metabolic syndrome criteria for entry left 86% hypertensive and 98% dyslipidaemic, so there was scarcely any variation left to detect an effect.

The wider literature supports adiponectin as a marker of metabolic derangement in its own right, in mixed populations [30] and in specific groups such as postmenopausal women [31], and adipocytokine panels have been proposed as predictors of MASLD in patients with type 2 diabetes [32]. Where adiponectin might earn a place clinically is as an adjunct rather than a replacement. In our data it correlated with liver stiffness ($p = -0.725$) more strongly than FIB-4 did ($p = 0.560$), which is notable given that FIB-4 is widely used as a first-line triage tool and is known to perform poorly in the indeterminate range. Whether adding adiponectin to FIB-4 improves discrimination is a question our sample size cannot answer, but it is a reasonable hypothesis to test. It is also relevant that adiponectin is potentially modifiable: weight loss raises it, and several agents under development for steatohepatitis act on overlapping pathways [33].

Several limitations qualify these findings. The cross-sectional design means we can describe association but not sequence; adiponectin was measured once, at a single point in a chronic disease. Fibrosis was staged by transient elastography rather than biopsy, and although this is now standard practice and arguably more representative of the whole organ, elastography can be affected by hepatic congestion, inflammation and a high body mass index, all of which were present in some of our patients. Fifty patients from one tertiary hospital in northern India is a small and selected sample; patients reaching a referral gastroenterology service are likely to have more advanced disease than those in the community, which may explain the high proportion with significant fibrosis. The chi-square comparisons for hypertension and dyslipidaemia involved small expected cell counts and are correspondingly unreliable. We did not measure insulin, HOMA-IR or leptin, so we could not examine the adiponectin to leptin ratio, which some workers consider more informative than adiponectin alone. Finally, adiponectin assays are not standardised across manufacturers, and absolute values are not directly comparable between studies; only the direction and strength of association travel well.

CONCLUSION

Serum adiponectin was inversely and independently related to hepatic fibrosis severity in patients with MASLD and coexistent metabolic syndrome, with a consistent stepwise fall from mild fibrosis through to cirrhosis. The association held across transient elastography, APRI and FIB-4, and survived adjustment for body mass index, glycaemic control and the serum fibrosis indices. Diabetes emerged as the metabolic syndrome component most strongly linked to advanced fibrosis, and every patient in the study with F3 or F4 disease was diabetic.

Taken together, these observations suggest that serum adiponectin deserves evaluation as an adjunctive non-invasive marker for fibrosis risk stratification in metabolic liver disease, particularly where elastography is unavailable and where existing serum indices return indeterminate results. Larger prospective multicentre studies, ideally with biopsy or paired elastography over time and with assay standardisation, are needed before the measurement can be recommended for routine use. In the meantime, the strength of the association between diabetes and advanced fibrosis argues for systematic fibrosis assessment in every patient with MASLD and type 2 diabetes.

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