RESEARCH PAPER

Association of the Uric Acid-to-HDL Cholesterol Ratio with Obesity in Patients with Type 2 Diabetes Mellitus and Non-Alcoholic Fatty Liver Disease: A Hospital-Based Cross-Sectional Study

Kanta Kumari[1], N. D. Soni[2], Aparna Garg[3], Manisha Choudhary[4], Harkesh[5], Sanjay[6]

[1]PhD Scholar, Department of Physiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

[2]Senior Professor, Department of Physiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

[3]Professor and Head, Department of Physiology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

[4]Assistant Professor, Department of Obstetrics and Gynaecology, Government Medical College, Jhunjhunu, Rajasthan, India

[5]Senior Resident, Department of Community Medicine, Government Medical College, Churu, Rajasthan, India.

[6]Consultant, Department of Orthopaedics, SMS Medical College, Jaipur, Rajasthan, India.

ABSTRACT

Background: Obesity is a central, modifiable driver of both type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD). The uric acid-to-high-density lipoprotein cholesterol ratio (UHR) has recently been proposed as a composite marker of systemic inflammation and metabolic dysfunction that may reflect cardiometabolic risk more faithfully than serum uric acid or HDL cholesterol alone.

Objective: To examine the association between the UHR and obesity in patients with coexisting T2DM and NAFLD.

Methods: In this hospital-based cross-sectional study, 422 adults with established T2DM and NAFLD were stratified by body mass index (BMI) into normal-weight, overweight, and obese groups. Sociodemographic, anthropometric, and biochemical variables, together with the UHR, were compared across BMI categories. Continuous variables were compared using one-way analysis of variance and categorical variables using the chi-square test, with a two-sided $p < 0.05$ taken as significant.

Results: Of the 422 participants, 56.2% were obese, 30.3% overweight, and 13.5% normal-weight. The mean UHR rose progressively across BMI categories, from 11.75 ± 3.53 in the normal-weight group to 15.88 ± 4.18 in the obese group ($p < 0.001$). A high UHR was present in 71.7% of obese participants, compared with 41.1% of normal-weight and 31.0% of overweight participants ($\chi^2 = 60.85$, $p < 0.001$). Obese participants also had significantly lower HDL cholesterol and higher blood urea and serum uric acid, together with greater waist circumference, whereas glycaemic indices did not differ across BMI groups.

Conclusion: The UHR showed a significant, graded positive association with obesity in patients with T2DM and NAFLD. As an inexpensive, routinely available index, the UHR may help identify obese individuals at heightened cardiometabolic risk.

Keywords: Type 2 diabetes mellitus; Non-alcoholic fatty liver disease; Uric acid-to-HDL cholesterol ratio; Obesity; Body mass index; Metabolic syndrome; Cross-sectional study.

How to cite this article: Kanta Kumari, N. D. Soni, Aparna Garg, Manisha Choudhary, Harkesh, Sanjay; Association of the Uric Acid-to-HDL Cholesterol Ratio with Obesity in Patients with Type 2 Diabetes Mellitus and Non-Alcoholic Fatty Liver Disease: A Hospital-Based Cross-Sectional Study, Int J Drug Deliv Technol. 2026;16(79s): 234-239. DOI: 10.25258/ijddt.16.79s.26

INTRODUCTION

Type 2 diabetes mellitus (T2DM) accounts for roughly 90% of all diabetes and is characterised by insulin resistance and progressive β-cell dysfunction leading to sustained hyperglycaemia. India carries one of the largest diabetes burdens in the world, with an estimated 77 million affected adults [1]. Among the recognised determinants of T2DM—including sedentary behaviour, urbanisation, unhealthy diet, advancing age, and genetic susceptibility—obesity is the strongest modifiable risk factor for both the onset and the progression of the disease [2].

Non-alcoholic fatty liver disease (NAFLD) is now the most common chronic liver disorder worldwide. It is defined by excessive triglyceride accumulation within hepatocytes in the absence of significant alcohol intake or other secondary causes of steatosis, and it spans a

spectrum from simple steatosis through non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis to hepatocellular carcinoma. NAFLD clusters strongly with obesity and T2DM, and current estimates indicate that approximately 45–55% of patients with T2DM have concomitant NAFLD [3,4].

The pathogenesis of NAFLD is multifactorial and tightly coupled to insulin resistance, obesity, dyslipidaemia, oxidative stress, and chronic low-grade inflammation. Hepatic fat accrues when lipid acquisition outpaces lipid disposal—through increased free fatty acid influx, enhanced de novo lipogenesis, impaired fatty acid oxidation, and reduced very-low-density lipoprotein (VLDL) export—driving hepatocellular injury and progression toward advanced liver disease [5].

Serum uric acid, the terminal product of purine metabolism, has attracted attention as a metabolic biomarker linked to insulin resistance, obesity, metabolic syndrome, cardiovascular disease, and NAFLD, promoting oxidative stress, endothelial dysfunction, and inflammation. High-density lipoprotein cholesterol (HDL-C), by contrast, exerts anti-inflammatory, antioxidant, and anti-atherogenic effects. Because uric acid and HDL-C act in opposing directions, the uric acid-to-HDL cholesterol ratio (UHR) has emerged as a composite index that may capture systemic inflammation and metabolic risk more sensitively than either component alone; the UHR has been associated with metabolic syndrome, poor glycaemic control, insulin resistance, and NAFLD [6,7].

Obesity remains the principal modifiable link between T2DM and NAFLD. Body mass index (BMI) is the most widely used measure of general adiposity owing to its simplicity and reproducibility, and higher BMI tracks with greater insulin resistance, adverse lipid profiles, systemic inflammation, and progression of hepatic steatosis. Although waist circumference, waist-to-hip ratio, and waist-to-height ratio better capture central adiposity, BMI remains the standard for classifying obesity in epidemiological and clinical studies [8].

Despite mounting evidence linking the UHR to metabolic disorders, data on its relationship with obesity in patients who have both T2DM and NAFLD remain scarce, particularly for Indian populations—a concern amplified by the rising prevalence of obesity across India [9]. Establishing this association could enable early identification of high-risk individuals using a simple, inexpensive, and routinely available biochemical index, improving risk stratification and enabling timely intervention. The present study was therefore undertaken to evaluate the association of the UHR with obesity in a hospital-based population of patients with T2DM and NAFLD, and to compare metabolic, biochemical, and anthropometric characteristics across BMI categories.

AIM

To determine the association between the uric acid-to-HDL cholesterol ratio and obesity among patients with type 2 diabetes mellitus and non-alcoholic fatty liver disease.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional study was conducted in the Department of Physiology, in collaboration with the Department of Medical Endocrinology, Mahatma Gandhi Medical College and Hospital, Sitapura, Jaipur, Rajasthan, India, between January 2023 and December 2025.

Study Participants and Sample Size

A total of 422 patients aged 40–50 years with established T2DM and NAFLD attending the endocrinology outpatient department were enrolled by consecutive sampling. The sample size was estimated using $n = Z^2PQ/E^2$, assuming an NAFLD prevalence among patients with T2DM of 48.48%, a 95% confidence level, and a 5% absolute margin of error; after allowing for a 10% non-response rate, the required sample size was 422.

Inclusion and Exclusion Criteria

Patients aged 40–50 years with confirmed T2DM and NAFLD were eligible. Individuals with significant alcohol intake, viral hepatitis (B or C), autoimmune liver disease, cirrhosis, hepatocellular carcinoma, other chronic liver diseases, diabetic ketoacidosis, pregnancy, or severe systemic illness were excluded.

Data Collection

Age, sex, residence, duration of diabetes, and relevant clinical history were recorded using a structured proforma. Anthropometric assessment comprised body weight, height, BMI, and waist circumference.

Biochemical Investigations

After an overnight fast of 8–12 hours, venous blood was drawn under aseptic conditions. Assays included fasting and postprandial blood glucose, glycated haemoglobin (HbA1c), serum uric acid, total cholesterol, triglycerides, HDL-C, low-density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea, and serum creatinine, all performed on a fully automated clinical chemistry analyser per the manufacturer's instructions. The UHR was calculated as UHR (%) = [serum uric acid (mg/dL) ÷ HDL-C (mg/dL)] × 100.

Diagnostic Criteria

T2DM was diagnosed by American Diabetes Association criteria (fasting plasma glucose ≥ 126 mg/dL, 2-hour plasma glucose ≥ 200 mg/dL on an oral glucose tolerance test, HbA1c ≥ 6.5%, or random plasma glucose ≥ 200 mg/dL with classic

hyperglycaemic symptoms). NAFLD was diagnosed by transient elastography (FibroScan®); hepatic steatosis was defined by a controlled attenuation parameter ≥ 274 dB/m after exclusion of secondary causes of steatosis.

Statistical Analysis

Data were entered in Microsoft Excel and analysed with appropriate statistical software. Continuous variables are expressed as mean ± standard deviation and categorical variables as frequencies and percentages. BMI categories were compared using one-way analysis of variance for continuous variables and the chi-square test for categorical variables; the association between BMI category and UHR status was further examined with Pearson and Spearman correlation. A two-sided $p < 0.05$ was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Mahatma Gandhi Medical College and Hospital, Jaipur, and written informed consent was obtained from every participant before enrolment.

RESULTS

A total of 422 patients with T2DM and NAFLD were studied. The mean age was 45.09 ± 3.12 years, the mean BMI was 31.08 ± 4.64 kg/m², and the mean waist circumference was 98.82 ± 11.61 cm. The sociodemographic profile is summarised in Table 1.

Table 1. Sociodemographic distribution of the study participants (N = 422).

Variable	Category	n	%
Residence	Rural	232	54.98
	Urban	190	45.02
Sex	Female	135	32.00
	Male	287	68.00
Age group (years)	40–45	222	52.61
	45–50	200	47.39
Diabetes duration (years)	0–5	160	37.91
	5–10	193	45.73
	10–15	65	15.40
	15–20	4	0.96
BMI category	Normal weight	57	13.51
	Overweight	128	30.33
	Obese	237	56.16
Total		**422**	**100.00**

Rural residents comprised 54.98% of the sample and urban residents 45.02%. Just over half the participants (52.61%) were aged 40–45 years. The commonest diabetes duration was 5–10 years (45.73%), followed by 0–5 years (37.91%). By BMI, most participants were obese (56.16%), while 30.33% were overweight and 13.51% were normal-weight.

Biochemical parameters across BMI categories are presented in Table 2. Liver enzymes (ALT and AST) did not differ significantly across groups ($p = 0.580$ and $p = 0.890$, respectively), and total cholesterol, LDL-C, triglycerides, and serum creatinine were likewise comparable (all $p > 0.05$). In contrast, HDL-C fell progressively with rising BMI, reaching its lowest mean in obese participants (35.45 ± 2.71 mg/dL) versus normal-weight (38.86 ± 6.18 mg/dL) and overweight (38.73 ± 6.84 mg/dL) participants ($p < 0.001$). Blood urea was highest in the obese group (29.70 ± 9.62 mg/dL; $p < 0.001$), and serum uric acid was significantly elevated in obese participants (5.60 ± 1.39 mg/dL; $p < 0.001$).

Table 2. Comparison of biochemical parameters across BMI categories (mean ± SD).

Parameter	Normal weight (n = 56)	Overweight (n = 126)	Obese (n = 240)	p value
ALT (U/L)	31.65 ± 13.82	33.38 ± 14.75	33.87 ± 14.34	0.580
AST (U/L)	24.28 ± 24.28	23.59 ± 23.59	22.80 ± 22.80	0.890
Total cholesterol (mg/dL)	220.21 ± 12.69	218.35 ± 16.85	221.07 ± 11.45	0.186
LDL-C (mg/dL)	130.91 ± 39.45	139.41 ± 34.64	141.50 ± 36.82	0.150
HDL-C (mg/dL)	38.86 ± 6.18	38.73 ± 6.84	35.45 ± 2.71	< 0.001
Triglycerides (mg/dL)	375.71 ± 122.23	385.29 ± 137.07	369.58 ± 131.29	0.556
Blood urea (mg/dL)	23.31 ± 10.90	26.51 ± 10.25	29.70 ± 9.62	< 0.001
Serum creatinine (mg/dL)	0.98 ± 0.26	0.95 ± 0.25	0.93 ± 0.24	0.321
Serum uric acid (mg/dL)	4.45 ± 1.08	4.33 ± 1.17	5.60 ± 1.39	< 0.001

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. p values from one-way analysis of variance.

The association between BMI category and UHR status (dichotomised at a cut-off of 13) is shown in Table 3. A statistically significant association was observed (χ^2 = 60.85, df = 2, $p < 0.001$): a high UHR was present in 71.7% of obese participants, compared with 41.1% of normal-weight and 31.0% of overweight participants. Both Pearson ($r = 0.313$, $p < 0.001$) and Spearman (ρ = 0.347, $p < 0.001$) correlations indicated a moderate positive relationship, with higher BMI categories associated with a greater proportion of high UHR values.

Table 3. Association between BMI category and UHR status (UHR cut-off = 13).

BMI category	Normal UHR, n (%)	High UHR, n (%)	Total, n (%)
Normal weight	33 (58.9)	23 (41.1)	56 (100.0)
Overweight	87 (69.0)	39 (31.0)	126 (100.0)
Obese	68 (28.3)	172 (71.7)	240 (100.0)
Total	**234 (55.5)**	**188 (44.5)**	**422 (100.0)**

χ^2 = 60.85, df = 2, $p < 0.001$; Pearson $r = 0.313$, $p < 0.001$; Spearman $\rho = 0.347$, $p < 0.001$. UHR, uric acid-to-HDL cholesterol ratio.

DISCUSSION

In this cohort of patients with coexisting T2DM and NAFLD, the majority were obese (56.16%), consistent with the well-established coupling of excess adiposity with T2DM [2]. HDL-C declined significantly in obese participants (35.45 ± 2.71 mg/dL) relative to normal-weight and overweight participants ($p < 0.001$). This pattern accords with current evidence that increasing adiposity profoundly alters HDL metabolism—lowering HDL-C and impairing HDL quality and function through triglyceride enrichment, reduced cholesterol efflux, and low-grade inflammation [10]. Total and LDL cholesterol did not differ across BMI groups, underscoring that the HDL fraction, rather than total cholesterol, discriminated between adiposity categories in this population.

Liver enzymes (ALT and AST) did not differ significantly across normal-weight, overweight, and obese groups, indicating that transaminases alone are an insensitive marker of BMI-related hepatic involvement in diabetic patients with NAFLD. This observation is in keeping with a systematic review and meta-analysis reporting that roughly a quarter of NAFLD patients—and about a fifth of those with NASH—have persistently normal ALT despite established disease, so that normal transaminases cannot exclude clinically significant steatohepatitis or fibrosis [11]. Blood urea rose across BMI categories (from 23.31 ± 10.90 mg/dL in normal-weight to 29.70 ± 9.62 mg/dL in obese participants; $p < 0.001$), consistent with the recognised adverse effect of obesity on renal haemodynamics and function and the resulting accumulation of nitrogenous waste [12].

Serum uric acid was significantly higher in obese participants (5.60 ± 1.39 mg/dL; $p < 0.001$). Obesity is a well-documented determinant of hyperuricaemia, operating through increased purine turnover, adipocyte-derived urate production, and reduced renal urate clearance in the setting of insulin resistance [13]. The non-monotonic pattern across categories—with the overweight group showing slightly lower values than the normal-weight group—may reflect metabolic and renal-clearance adaptations, differences in lean body mass, and treatment heterogeneity, but the substantial rise in the obese group aligns with the expected obesity–urate relationship.

A statistically significant, graded association was observed between BMI category and UHR status (χ^2 = 60.85, $p < 0.001$), corroborated by moderate positive Pearson ($r = 0.313$) and Spearman ($\rho = 0.347$) correlations. These findings are consistent with Cui et al., who reported a stepwise increase in NAFLD prevalence from 30.7% in the lowest to 73.68% in the highest UHR tertile among non-obese patients with T2DM, an association that persisted after adjustment for metabolic confounders including BMI and hepatic enzymes [14]. Population-based data in general adult cohorts similarly show that a higher UHR is independently associated with NAFLD risk [15], reinforcing the value of the ratio as a composite marker that integrates a pro-inflammatory, pro-oxidant substrate (uric acid) with a protective, anti-atherogenic one (HDL-C) [6,7]. Taken together, the concurrent decline in HDL-C and rise in serum uric acid with increasing adiposity provide a coherent mechanistic basis for the higher UHR observed in obese participants.

Limitations

This study has several limitations that should be considered when interpreting the findings. First, the cross-sectional design permits identification of an association between UHR and obesity but does not establish temporal or causal relationships. Second, the study was conducted at a single tertiary-care centre and included only participants aged 40–50 years; therefore, the findings may not be directly generalisable to younger or older individuals, community-based populations, or patients with different clinical characteristics. Third, obesity was primarily classified using BMI, which does not distinguish between fat and lean mass or adequately capture the distribution of central adiposity. Although waist circumference was recorded, other measures such as waist-to-height ratio and visceral adiposity were not incorporated into the primary analysis. Fourth, potential confounding factors

that can influence serum uric acid or HDL-C, including dietary patterns, physical activity, alcohol intake below the exclusion threshold, medication use, renal function, and other metabolic or inflammatory factors, may not have been fully accounted for. Fifth, the study evaluated a single biochemical ratio and did not determine whether UHR provides incremental predictive value over established anthropometric or metabolic risk markers. Finally, the present analysis did not assess longitudinal changes in UHR or whether elevated UHR predicts subsequent development of obesity-related complications, cardiovascular events, progression of hepatic disease, or changes following weight-loss and metabolic interventions. These limitations highlight the need for prospective, multicentre studies with broader populations and more comprehensive adjustment for potential confounders.

Future Directions

Future research should validate the observed association between UHR and obesity through prospective, multicentre studies involving broader age groups and more diverse populations. Longitudinal studies are particularly warranted to determine whether elevated UHR precedes the development or progression of obesity-related metabolic complications and whether changes in UHR parallel changes in body weight, central adiposity, glycaemic control, hepatic steatosis, and cardiovascular risk. Further studies should also evaluate UHR alongside waist-to-height ratio, visceral adiposity measures, insulin resistance indices, inflammatory biomarkers, and established cardiometabolic risk scores to determine whether UHR provides meaningful incremental predictive value.

An important future direction is the integration of UHR with routinely available clinical, anthropometric, biochemical, and imaging parameters into multivariable prediction models. Advances in artificial intelligence (AI) and machine learning may facilitate the analysis of large and multidimensional datasets and could potentially support individualized cardiometabolic risk stratification and clinical decision-making. AI-based approaches have increasingly been explored across healthcare for prediction, diagnosis, monitoring, and personalized care, although their clinical implementation requires standardized data, transparent and interpretable models, appropriate validation, and attention to ethical and privacy considerations [16]. Therefore, future studies could investigate whether AI-assisted models incorporating UHR, BMI, waist circumference, glycaemic parameters, lipid profile, renal indices, and liver-related measures can improve prediction of obesity-related complications beyond conventional statistical approaches. Such models should be externally validated across different populations before clinical implementation and should complement, rather than replace, clinician judgement.

CONCLUSION

In patients with T2DM and NAFLD, obesity was associated with significantly lower HDL cholesterol and higher blood urea and serum uric acid, denoting an unfavourable metabolic profile. BMI showed a significant, graded positive association with the UHR, with obese participants having the highest proportion of elevated values, and correlation analysis confirmed a moderate positive relationship. These findings indicate that the UHR is closely linked to obesity-related metabolic disturbance in this population and support its potential as a simple, inexpensive index for identifying obese individuals at increased cardiometabolic risk.

REFERENCES

1. World Health Organization. Diabetes – India. Geneva: World Health Organization; 2022. Available from: https://www.who.int/india/health-topics/diabetes
2. Yang T, Zhao B, Pei D. Evaluation of the association between obesity markers and type 2 diabetes: a cohort study based on a physical examination population. J Diabetes Res. 2021;2021:6503339.
3. Kalra S, Das AK, Tiwaskar M, Vg MP, Singh M. Assessment of prevalence and associated risk factors of NAFLD in people living with diabetes in India: a retrospective, multicenter, electronic medical records based study. J Assoc Physicians India. 2022;70(8):11-2.
4. Tanase DM, Gosav EM, Costea CF, et al. The intricate relationship between type 2 diabetes mellitus (T2DM), insulin resistance (IR), and nonalcoholic fatty liver disease (NAFLD). J Diabetes Res. 2020;2020:3920196.
5. Yang M, Geng CA, Liu X, Guan M. Lipid disorders in NAFLD and chronic kidney disease. Biomedicines. 2021;9(10):1405.
6. Kocak MZ, Aktas G, Erkus E, Sincer I, Atak B, Duman T. Serum uric acid to HDL-cholesterol ratio is a strong predictor of metabolic syndrome in type 2 diabetes mellitus. Rev Assoc Med Bras (1992). 2019;65(1):9-15.
7. Kosekli MA, Kurtkulagi O, Kahveci G, Duman TT, Tel BM, Bilgin S et al. The association between serum uric acid to high density lipoprotein-cholesterol ratio and non-alcoholic fatty liver disease: the ABUND study. Rev Assoc Med Bras. 2021;67(4):549-54.
8. Moltrer M, Pala L, Cosentino C, Mannucci E, Rotella CM, Cresci B. Body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR) and waist body mass index (wBMI): which is better? Endocrine. 2022;76(3):578-83.

9. Luhar S, Timæus IM, Jones R, Cunningham S, Patel SA, Kinra S et al. Forecasting the prevalence of overweight and obesity in India to 2040. PLoS One. 2020;15(2):e0229438.
10. Stadler JT, Marsche G. Obesity-related changes in high-density lipoprotein metabolism and function. Int J Mol Sci. 2020;21(23):8985.
11. Ma X, Liu S, Zhang J, Dong M, Wang Y, Wang M, et al. Proportion of NAFLD patients with normal ALT value in overall NAFLD patients: a systematic review and meta-analysis. BMC Gastroenterol. 2020;20(1):10.
12. Nawaz S, Chinnadurai R, Al-Chalabi S, Evans P, Kalra PA, Syed AA et al. Obesity and chronic kidney disease: a current review. Obes Sci Pract. 2023;9(2):61-74.
13. Feng X, Yang Y, Xie H, Zhuang S, Fang Y, Dai Y, et al. The association between hyperuricemia and obesity metabolic phenotypes in Chinese general population: a retrospective analysis. Front Nutr. 2022;9:773220.
14. Cui Y, Qu Z, Hu W, Shi H. Relationship between uric acid to high density lipoprotein cholesterol ratio and nonalcoholic fatty liver disease in nonoverweight/obese patients with type 2 diabetes. Int J Endocrinol. 2023;2023:2513175.
15. Zhao H, Qiu X, Li HZ, Cui JJ, Sun YY. Association between serum uric acid to HDL-cholesterol ratio and nonalcoholic fatty liver disease risk among Chinese adults. Biomed Environ Sci. 2023;36(1):1-9.
16. Joseph G, Bhatti N, Mittal R, Bhatti A. Current Application and Future Prospects of Artificial Intelligence in Healthcare and Medical Education: A Review of Literature. Cureus. 2025; 17(1).