International Journal of Science and Healthcare Research
[Indexed, Peer-Reviewed Journal]
Vol. 11; Issue: 1; Jan.-March 2026
Website: ijshr.com
Original Research Article *ISSN: 2455-7587*

Atherogenic Index of Serum and Non-HDL Cholesterol as Predictors of Cardiometabolic Risk in Type 2 Diabetes Mellitus

Sreeja Shanker J[1], Vibha C[2], Parvathi M[3]

[1]Assistant Professor, Department of Biochemistry, Government Medical College (IIMS), Palakkad
[2]Professor, Department of Biochemistry, Bangalore Medical College & Research Institute, Bangalore
[3]Assistant Professor, Department of General Medicine, Bangalore Medical College & Research Institute, Bangalore.

Corresponding Author- Dr Sreeja Shanker J
ORCID ID: 0000-0001-5643-499X

DOI: https://doi.org/10.52403/ijshr.20260108

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is strongly associated with increased cardiovascular risk. While conventional lipid measurements such as LDL-cholesterol (LDL-C) are well-established markers of atherosclerosis, they do not fully explain the excess cardiovascular disease (CVD) risk observed in T2DM. Non-HDL-cholesterol (non-HDL-C) and composite lipid ratios like Atherogenic Index of Plasma (AIP), Castelli Risk Index-I (CRI-I), Castelli Risk Index-II (CRI-II), Atherogenic Coefficient (AC), and triglyceride-to-HDL ratio (TG/HDL) may better reflect the burden of atherogenic lipoproteins.
Objective: To evaluate non-HDL-C and selected atherogenic indices in adults with T2DM and compare them with healthy controls.
Methods: A case control study including 40 T2DM patients and 40 age-matched controls. Fasting glucose, HbA1c, and lipid parameters were measured. Non-HDL-C was calculated as TC−HDL. Derived indices included AIP=log10(TG/HDL), CRI-I=TC/HDL, CRI-II=LDL/HDL, AC=(TC−HDL)/HDL, and TG/HDL ratio. Independent t-tests were applied.
Results: T2DM subjects had significantly higher TC (202.8±33.1 mg/dL), TG (168.7±71.4 mg/dL), LDL-C (134.7±35.9 mg/dL), and lower HDL-C (33.8±5.8 mg/dL) than controls ($p<0.001$). Non-HDL-C was markedly elevated (168.9±34.0 vs. 102.9±32.3 mg/dL, $p=1.6\times10^{-13}$). Atherogenic indices were significantly higher in T2DM: AIP (0.66±0.23 vs. 0.40±0.16), CRI-I (6.20±1.56 vs. 3.41±0.90), CRI-II (4.17±1.49 vs. 2.47±0.68), AC (5.20±1.56 vs. 2.41±0.90), and TG/HDL (5.11±2.14 vs. 2.69±1.07).
Conclusion: Non-HDL-C and atherogenic indices were significantly higher in T2DM and reflect the atherogenic burden associated with diabetic dyslipidaemia. Incorporating these indices into routine assessment may enhance early detection of CVD risk.

Keywords: Non-HDL cholesterol, T2DM, AIP, Castelli Index, atherogenic indices, dyslipidaemia.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major global health challenge characterized by a substantially increased risk of cardiovascular disease (CVD). Despite advances in glycaemic management, individuals with T2DM continue to experience higher rates of

myocardial infarction, stroke, and atherosclerotic complications compared with non-diabetic individuals [1,2]. Traditional lipid markers, particularly LDL-cholesterol (LDL-C), only partially explain this elevated risk, and many patients develop cardiovascular events even after achieving guideline-recommended LDL-C targets indicating a significant "residual risk" [3].

Dyslipidaemia in T2DM typically presents as elevated triglycerides (TG), reduced HDL-cholesterol (HDL-C), and increased small dense LDL particles, all of which contribute to a more atherogenic lipid profile [4]. This has led to growing interest in alternative lipid indices that offer better risk prediction.

Non-HDL-cholesterol (non-HDL-C), calculated as total cholesterol minus HDL-C, reflects the total burden of apoB-containing atherogenic lipoproteins. Several studies demonstrate that non-HDL-C is a stronger predictor of future CVD events than LDL-C, particularly in individuals with diabetes and hypertriglyceridaemia [1–3].

Another important marker is the Atherogenic Index of Plasma (AIP), defined as log10(TG/HDL-C). AIP correlates with small dense LDL particles, endothelial dysfunction, and insulin resistance, and has been shown to predict metabolic syndrome and cardiometabolic risk [4–7]. Furthermore, AIP has been associated with future development of diabetes and increased vascular risk in diverse populations [8,9].

Classical lipid ratios such as the Castelli Risk Index-I (CRI-I: TC/HDL-C) and Castelli Risk Index-II (CRI-II: LDL-C/HDL-C) reflect the balance between atherogenic and protective lipoproteins. Elevated CRI-I and CRI-II levels have been associated with carotid atherosclerosis and coronary artery disease [10–12].

Other indices including the Atherogenic Coefficient (AC: [TC−HDL-C]/HDL-C) and TG/HDL-C ratio serve as practical surrogate markers of insulin resistance and metabolic syndrome. Both have been linked with subclinical atherosclerosis and adverse cardiovascular outcomes [13–15].

Given their strong association with metabolic derangements and cardiovascular pathology, these atherogenic indices may offer improved discrimination of cardiometabolic risk in T2DM compared with conventional lipid parameters.

Because Indian and South-Asian populations possess a high cardiometabolic susceptibility, evaluating these indices may provide enhanced insight into CVD risk in T2DM.

The present study evaluates the comparative performance of non-HDL-C and selected atherogenic indices versus conventional lipid parameters in T2DM subjects and healthy controls.

MATERIALS AND METHODS

Study Design and Setting

A case–control study was conducted to evaluate lipid parameters in patients with diagnosed type 2 diabetes mellitus (T2DM) and age-matched healthy controls at the Outpatient and Inpatient Departments of the Department of General Medicine, Victoria Hospital, attached to Bangalore Medical College and Research Institute (BMCRI), Bengaluru. Ethical approval was obtained from the Institutional Ethics and Research Committee of BMCRI, and written informed consent was obtained from all participants.

Selection of Study Subjects

A total of 80 subjects were included in the study, comprising 40 cases (T2DM patients) and 40 age- and sex-matched healthy controls, selected based on predefined inclusion and exclusion criteria.

Inclusion Criteria

1. Individuals aged 40–60 years diagnosed with T2DM as per the American Diabetes Association (ADA) 2018 criteria:
   - Fasting blood sugar ≥ 126 mg/dL
   - Postprandial blood sugar ≥ 200 mg/dL
   - HbA1c ≥ 6.5%
2. Age- and sex-matched apparently healthy, non-diabetic individuals serving as controls.

Exclusion Criteria

1. Individuals with Type 1 diabetes mellitus
2. History of cardiac disease, hepatic disease, typhoid, epilepsy, stroke, asthma, allergies, anaemia, malignancy, tuberculosis, or thyroid disorders
3. Individuals with a history of alcoholism or smoking
4. Individuals with severe combined immunodeficiencies
5. Those receiving statins, insulin, thiazide diuretics, anti-hyperuricaemia medications, or multivitamin supplements
6. Pregnant women, women with gestational diabetes, and those on hormone replacement therapy

Collection of Blood Samples

After obtaining written informed consent, 6 mL of venous blood was collected from each participant under aseptic conditions. The sample was divided into two portions:

- Part 1: Collected in a sterile EDTA tube and used for estimation of HbA1c.
- Part 2: Collected in a plain tube, centrifuged, and the separated serum was used for the estimation of lipid profile and other biochemical parameters.

  Clinical history and physical examination findings were recorded for all subjects.

Parameters Analysed

Fasting blood sugar
Postprandial blood sugar
HbA1c
Lipid profile

Derived Atherogenic Indices

- Non-HDL-C = TC − HDL
- AIP = log10(TG/HDL)
- CRI-I = TC/HDL
- CRI-II = LDL/HDL
- AC = (TC − HDL)/HDL
- TG/HDL ratio = TG/HDL

Analytical methods used:

- Biochemical parameters: Standard enzymatic methods
- HbA1c: Ion-exchange high-performance liquid chromatography (HPLC)

STATISTICAL ANALYSIS

Data were analysed using SPSS software (version 17.0). Descriptive statistics such as range, mean, and standard deviation (SD) were calculated for all biochemical parameters in both groups.

The student's t-test was applied to assess the significance of differences in mean values between cases and controls. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1. Conventional Lipid Parameters

Parameter	T2DM (mean ± SD)	Controls (mean ± SD)	p-value
TC	202.8 ± 33.1	147.4 ± 32.5	p < 0.001
TG	168.7 ± 71.4	116.0 ± 40.3	p < 0.001
HDL-C	33.8 ± 5.8	44.5 ± 8.2	p < 0.001
LDL-C	134.7 ± 35.9	107.2 ± 25.6	p < 0.001
VLDL-C	33.7 ± 14.3	23.2 ± 8.1	p < 0.001

Table 2. Atherogenic Indices

Index	T2DM	Controls	p-value
Non-HDL-C	168.9 ± 34.0	102.9 ± 32.3	p < 0.001
AIP	0.66 ± 0.23	0.40 ± 0.16	p < 0.001
CRI-I	6.20 ± 1.56	3.41 ± 0.90	p < 0.001
CRI-II	4.17 ± 1.49	2.47 ± 0.68	p < 0.001
AC	5.20 ± 1.56	2.41 ± 0.90	p < 0.001
TG/HDL	5.11 ± 2.14	2.69 ± 1.07	p < 0.001

Diabetic subjects exhibited significantly higher FPG, PPBG, and HbA1c levels, along with a classical dyslipidaemia pattern characterised by elevated TC, TG, LDL-C,

and VLDL-C and markedly reduced HDL-C, with all differences being statistically significant ($p < 0.001$).

DISCUSSION

This study demonstrates that individuals with T2DM exhibit significantly higher non-HDL-cholesterol levels and elevated atherogenic lipid indices including AIP, CRI-I, CRI-II, AC, and TG/HDL-C ratio compared with healthy controls. These findings are consistent with established evidence highlighting the unique lipid abnormalities characteristic of diabetes.

Non-HDL-Cholesterol and Residual Risk

Non-HDL-C showed a marked elevation in T2DM participants. This supports previous research demonstrating that non-HDL-C is a more reliable indicator of atherogenic lipoprotein burden and a superior predictor of cardiovascular events compared with LDL-C. Because non-HDL-C includes all apoB-containing particles, it captures the full scope of diabetic dyslipidaemia and has been recommended as a primary therapeutic target in several lipid management guidelines [16]. Large epidemiological and clinical data reinforce that overreliance on LDL-C alone may underestimate cardiovascular risk in diabetes, and incorporating non-HDL-C improves prediction of long-term outcomes [17].

Atherogenic Lipoproteins and Diabetic Dyslipidaemia

The atherogenic shifts seen in T2DM including increased small dense LDL particles and remnant cholesterol are central contributors to vascular disease [18]. The marked elevation of AIP in our diabetic population aligns with prior evidence showing that AIP strongly correlates with atherogenic dyslipidaemia, insulin resistance, and vascular dysfunction. AIP has been suggested as a practical and reliable tool for stratifying cardiometabolic risk, especially in patients with obesity or diabetes [19].

Castelli Indices and Insulin Resistance-Related Atherogenicity

CRI-I and CRI-II were significantly higher among diabetic subjects, reflecting a profound imbalance between pro-atherogenic lipoproteins and HDL-mediated reverse cholesterol transport. Prior studies have demonstrated that elevated Castelli indices are associated with increased carotid intima-media thickness and coronary risk [12]. Our findings support their usefulness as simple but meaningful clinical risk markers.

Atherogenic Coefficient and TG/HDL-C Ratio

The elevated AC and TG/HDL-C ratio observed in this study reflect underlying insulin resistance, a key pathological driver in T2DM. Existing research highlights these indices as reliable indicators of metabolic syndrome, endothelial dysfunction, and cardiovascular morbidity [14,20,21]. The TG/HDL-C ratio, in particular, integrates two major lipid abnormalities, hypertriglyceridemia and low HDL-C and has been shown to correlate with both hepatic and peripheral insulin resistance.

Clinical Implications

- Non-HDL-C may be a useful lipid marker for CVD risk reduction in diabetes.
- AIP, Castelli indices, AC, and TG/HDL-C ratio offer cost-effective, easily calculated markers that can enhance risk stratification.
- Incorporating these indices into routine reports could improve early detection of high-risk metabolic states.

Limitations

The study is limited by a modest sample size, single-centre design, and absence of longitudinal cardiovascular outcomes. However, the results remain consistent with robust international data and reinforce the validity of using composite lipid indices in T2DM.

CONCLUSION

Non-HDL-cholesterol and atherogenic indices including AIP, CRI-I, CRI-II, Atherogenic Coefficient, and TG/HDL ratio are significantly higher in T2DM and show useful discrimination in the study population. Incorporating these markers into routine assessments may enhance cardiovascular risk stratification.

Declaration by Authors

Ethical Approval: Approved

Acknowledgement: The authors acknowledge the healthcare staff of BMCRI, Bengaluru.

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Robinson JG, Wang S, Jacobson TA. Meta-analysis of comparison of effectiveness of lowering apolipoprotein B versus low-density lipoprotein cholesterol and nonhigh-density lipoprotein cholesterol for cardiovascular risk reduction in randomized trials. Am J Cardiol. 2012 Nov 15;110(10):1468-76. doi: 10.1016/j.amjcard.2012.07.007. Epub 2012 Aug 17. PMID: 22906895.
2. Cui Y, Blumenthal RS, Flaws JA, Whiteman MK, Langenberg P, Bachorik PS, Bush TL. Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. Arch Intern Med. 2001 Jun 11;161(11):1413-9. doi: 10.1001/archinte.161.11.1413. PMID: 11386890.
3. Ghandehari H, Kamal-Bahl S, Wong ND. Prevalence and extent of dyslipidemia and recommended lipid levels in US adults with and without cardiovascular comorbidities: the National Health and Nutrition Examination Survey 2003-2004. Am Heart J. 2008 Jul;156(1):112-9. doi: 10.1016/j.ahj.2008.03.005. Epub 2008 May 15. PMID: 18585505.
4. Li, YW., Kao, TW., Chang, PK. *et al.* Atherogenic index of plasma as predictors for metabolic syndrome, hypertension and diabetes mellitus in Taiwan citizens: a 9-year longitudinal study. *Sci Rep* 11, 9900 (2021). https://doi.org/10.1038/s41598-021-89307-z
5. Cai, G., Shi, G., Xue, S. and Lu, W. (2017) The Atherogenic Index of Plasma Is a Strong and Independent Predictor for Coronary Artery Disease in the Chinese Han Population. Medicine (Baltimore),96, e8058.https://doi.org/10.1097/MD.0000000000008058
6. Niroumand S, Khajedaluee M, Khadem-Rezaiyan M, Abrishami M, Juya M, Khodaee G, Dadgarmoghaddam M. Atherogenic Index of Plasma (AIP): A marker of cardiovascular disease. Med J Islam Repub Iran. 2015 Jul 25; 29:240. PMID: 26793631; PMCID: PMC4715400.
7. Milada Dobiášová, Atherogenic Index of Plasma [Log (Triglycerides/HDL-Cholesterol)]: Theoretical and Practical Implications, *Clinical Chemistry*, Volume 50, Issue 7, 1 July 2004, Pages 1113–1115, https://doi.org/10.1373/clinchem.2004.033175
8. Liao Y, Han Y, Cao C, Song H, Hu H. Association between atherogenic index of plasma and risk of type 2 diabetes mellitus and the mediating effect of BMI: a comparative analysis in Chinese and Japanese populations. Diabetol Metab Syndr. 2025 Aug 22;17(1):349. doi: 10.1186/s13098-025-01907-1. PMID: 40847426; PMCID: PMC12372214.
9. Assempoor R, Daneshvar MS, Taghvaei A, Abroy AS, Azimi A, Nelson JR, Hosseini K. Atherogenic index of plasma and coronary artery disease: a systematic review and meta-analysis of observational studies. Cardiovasc Diabetol. 2025 Jan 22;24(1):35. doi: 10.1186/s12933-025-02582-2. PMID: 39844262; PMCID: PMC11756160.
10. Castelli WP. Cholesterol and lipids in the risk of coronary artery disease--the Framingham Heart Study. Can J Cardiol. 1988 Jul;4 Suppl A:5A-10A. PMID: 3179802.
11. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. Circulation. 1997 Oct 21;96(8):2520-5. doi: 10.1161/01.cir.96.8.2520. PMID: 9355888.
12. Raaj I, Thalamati M, Gowda M N V, Rao A. The Role of the Atherogenic Index of Plasma and the Castelli Risk Index I and II in Cardiovascular Disease. Cureus. 2024 Nov 28;16(11): e74644. doi: 10.7759/cureus.74644. PMID: 39735061; PMCID: PMC11681972.

13. Andraschko LM, Gazi G, Leucuta DC, Popa SL, Chis BA, Ismaiel A. Atherogenic Index of Plasma in Metabolic Syndrome-A Systematic Review and Meta-Analysis. Medicina (Kaunas). 2025 Mar 27;61(4):611. doi: 10.3390/medicina61040611. PMID: 40282902; PMCID: PMC12028871.
14. Kosmas CE, Rodriguez Polanco S, Bousvarou MD, Papakonstantinou EJ, Peña Genao E, Guzman E, Kostara CE. The Triglyceride/High-Density Lipoprotein Cholesterol (TG/HDL-C) Ratio as a Risk Marker for Metabolic Syndrome and Cardiovascular Disease. Diagnostics (Basel). 2023 Mar 1;13(5):929. doi: 10.3390/diagnostics13050929. PMID: 36900073; PMCID: PMC10001260.
15. Murguía-Romero M, Jiménez-Flores JR, Sigrist-Flores SC, Espinoza-Camacho MA, Jiménez-Morales M, Piña E, Méndez-Cruz AR, Villalobos-Molina R, Reaven GM. Plasma triglyceride/HDL-cholesterol ratio, insulin resistance, and cardiometabolic risk in young adults. J Lipid Res. 2013 Oct;54(10):2795-9. doi: 10.1194/jlr.M040584. Epub 2013 Jul 17. PMID: 23863983; PMCID: PMC3770092.
16. Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, Witztum JL. Lipoprotein management in patients with cardiometabolic risk: consensus conference report from the American Diabetes Association and the American College of Cardiology Foundation. J Am Coll Cardiol. 2008 Apr 15;51(15):1512-24. doi: 10.1016/j.jacc.2008.02.034. PMID: 18402913.
17. Vazirian F, Darroudi S, Rahimi HR, Latifi M, Shakeri B, Abolbashari S, Mohammadpour AH, Esmaily H, Mouhebati M, Samadi S, Mobarhan MG. Non-HDL cholesterol and long-term follow-up outcomes in patients with metabolic syndrome. Lipids Health Dis. 2023 Oct 4;22(1):165. doi: 10.1186/s12944-023-01923-y. PMID: 37794473; PMCID: PMC10548659.
18. Taskinen MR, Borén J. New insights into the pathophysiology of dyslipidemia in type 2diabetes. *Atherosclerosis*.2015;239(2):483-495. doi: 10.1016/j.atherosclerosis.2015.01.039
19. Sun Y, Lin X, Zou Z, Zhao C, Liu A, Zhou J, Li Z, Wu X, Dou S, Zhu J, Li T, Lv X, Wang Y, Li Y. Baseline atherogenic index of plasma and its trajectory predict onset of type 2 diabetes in a health screened adult population: a large longitudinal study. Cardiovasc Diabetol. 2025 Feb 7;24(1):57. doi: 10.1186/s12933-025-02619-6. PMID: 39920728; PMCID: PMC11806864.
20. Ni, W., Ni Q, Jiang R, et al. Association of insulin resistance indices with major adverse cardiovascular events in patients with acute myocardial infarction and chronic kidney disease: a retrospective cohort study. Ann Med. 2026 Dec;58(1):2612790. doi: 10.1080/07853890.2026.2612790.
21. Wu, S., Gao, Y., Liu, W. *et al.* The relationship between atherogenic index of plasma and plaque vulnerabilities: an optical coherence tomography study. *Cardiovasc Diabetol* 23, 442 (2024). https://doi.org/10.1186/s12933-024-02532-4

How to cite this article: Sreeja Shanker J, Vibha C, Parvathi M. Atherogenic index of serum and non-HDL cholesterol as predictors of cardiometabolic risk in type 2 diabetes mellitus. *Int. J. Sci. Healthc. Res.* 2026; 11(1): 73-78. DOI: *https://doi.org/10.52403/ijshr.20260108*

******