Original Article

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HsCRP and Atherogenic Index as Markers of Cardiovascular Risk in Type 2 Diabetes Mellitus: A Cross-Sectional Analysis

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is associated with increased cardiovascular risk due to chronic inflammation and atherogenic dyslipidemia. High-sensitivity C-reactive Protein (hsCRP) and the Atherogenic Index of Plasma (AIP) have emerged as potential biomarkers for identifying cardiometabolic risk, however, their combined relationship with ischemic heart disease remains inadequately explored. To evaluate the association of hsCRP and Atherogenic Index of Plasma with lipid profile and ischemic heart disease among patients with type 2 diabetes mellitus.

Materials and methods: A hospital-based cross-sectional observational study was carried out in the Department of Biochemistry, Chittagong Medical College, Department of Endocrinology of Chittagong Medical College Hospital and Chattogram Diabetic Hospital. 'One hundred (100) type 2 diabetes mellitus patient were included in the study by nonprobability consecutive sampling. Serum hsCRP, lipid profile parameters and AIP were measured using standard laboratory methods.' 'Comparative analysis, Pearson correlation, independent sample t-test, and multiple logistic regression were performed to assess relationships between inflammatory status and atherogenic lipid indices.'

Results: 'Patients with type 2 diabetes mellitus ischemic heart disease demonstrated significantly higher hsCRP, triglyceride, and LDL-cholesterol levels compared with those without ischemic heart disease ($p < 0.01$).' 'Correlation analysis revealed significant positive relationships between hsCRP and total cholesterol ($r = 0.292$) triglycerides ($r = 0.325$), LDL-cholesterol ($r = 0.279$) and AIP ($r = 0.286$). Individuals with hsCRP >3 mg/L showed a significantly higher prevalence of ischemic heart disease ($p = 0.009$) and greater mean AIP values ($p = 0.0001$).' 'Multiple logistic regression analysis identified triglycerides and LDL-cholesterol as independent predictors of elevated hsCRP, while AIP remained a strong predictor after adjustment for ischemic heart disease (OR = 9.35, $p = 0.002$).'

Conclusion: 'Elevated hsCRP is strongly associated with atherogenic lipid abnormalities and increased cardiovascular risk in patients with type 2 diabetes mellitus. The combined assessment of inflammatory markers and Atherogenic Index of Plasma may enhance early cardiovascular risk stratification beyond traditional lipid profile parameters.'

Key words: Atherogenic index of plasma; Dyslipidemia; hsCRP; Ischemic heart disease; Inflammation; Type 2 diabetes mellitus.

Introduction

'Type 2 Diabetes Mellitus (T2DM) is a major metabolic disorder associated with accelerated atherosclerosis and a significantly increased risk of Cardiovascular Disease (CVD) which remains the leading cause of morbidity and mortality among diabetic patients worldwide.' 'Chronic hyperglycaemia contributes to endothelial dysfunction, oxidative stress, and persistent low-grade inflammation, ultimately promoting vascular injury and plaque formation.' 'Traditional lipid parameters alone do not fully explain cardiovascular risk in T2DM and recent research has emphasised the role of inflammatory biomarkers and composite lipid indices in improving cardiometabolic risk stratification.[1,2]'

'High-sensitivity C-reactive Protein (hsCRP) is a well-established marker of systemic inflammation and has emerged as an important predictor of cardiovascular events.' 'Elevated hsCRP reflects activation of inflammatory pathways that contribute to endothelial dysfunction, plaque progression and instability. Evidence suggests that inflammation plays a central role in all stages of atherogenesis, highlighting the clinical significance of hsCRP as a non-traditional cardiovascular risk marker, particularly in individuals with metabolic disorders such as T2DM.'[3]

'In patients with T2DM, chronic inflammation frequently coexists with atherogenic dyslipidaemia characterised by elevated triglycerides, reduced HDL-cholesterol and increased small dense LDL particles.' 'The Atherogenic Index of Plasma (AIP)

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calculated as the logarithmic ratio of triglycerides to HDL-cholesterol, has emerged as a valuable indicator reflecting the balance between atherogenic and protective lipoproteins. 'Several recent studies have demonstrated that AIP is strongly associated with cardiovascular outcomes and mortality, suggesting that this index may provide superior predictive value compared with traditional lipid parameters alone.[1,4,5']

Emerging evidence indicates that AIP is not only linked with cardiovascular disease but also associated with metabolic complications such as diabetic nephropathy and insulin resistance. A recent systematic review reported that higher AIP values significantly increased the risk of diabetic nephropathy, supporting the concept that atherogenic lipid abnormalities contribute to microvascular as well as macrovascular complications in diabetes.[6] Furthermore, longitudinal cohort studies have shown that elevated AIP and its dynamic changes over time are closely related to cardiometabolic risk, indicating that AIP may serve as a useful marker for monitoring disease progression.[7,8]

The interaction between inflammation and lipid metabolism is particularly relevant in T2DM. Chronic inflammatory activation may alter lipid handling, promote oxidative modification of lipoproteins, and accelerate the development of atherosclerotic plaques. Cross-sectional and cohort studies have demonstrated that increased AIP is associated with vascular calcification and adverse cardiovascular outcomes, suggesting that integrating inflammatory markers such as hsCRP with lipid-derived indices may improve early identification of high-risk individuals.[9]

Despite growing interest in these biomarkers, studies evaluating the combined relationship between hsCRP and AIP in diabetic populations remain limited, especially in clinical cross-sectional settings. Assessing both inflammatory and atherogenic lipid indices may provide a more comprehensive understanding of cardiovascular risk beyond traditional clinical parameters such as blood pressure or total cholesterol levels. Therefore, the present cross-sectional analysis aims to evaluate the role of high-sensitivity C-reactive protein and the atherogenic index of plasma as markers of cardiovascular risk in patients with type 2 diabetes mellitus, with the goal of improving biochemical risk stratification and supporting preventive cardiometabolic strategies.

Materials and methods

This cross-sectional study was conducted in conjunction between Chattogram Diabetic Hospital and the outpatient Department of Endocrinology at Chittagong Medical College Hospital. The research period for this study spanned the years 2022 and 2023. Following approval from the relevant departments and the ethical review committee, the study was carried out. Every participant was asked to give their informed consent.

Inclusion criteria

Patients with Type 2 Diabetes Mellitus.

Exclusion criteria

'Chronic liver disease, Acute infection, malignancy, Sepsis, Pregnancy.'

Participants were enlisted from the Outpatient Department (OPD) of Endocrinology at Chittagong Medical College Hospital and Chattogram Diabetic Hospital during standard diabetes appointments. Following the acquisition of a concise clinical history and preliminary screening, verbal informed consent was obtained, and the participants were instructed to report to the Department of Biochemistry, Chittagong Medical College, between 8:00 and 9:00 am after an overnight fast of 8–12 hours. Upon arrival, written informed permission was secured from each participant. A cut-off threshold of < 3 mg/L was established for Hs-CRP. Serum Hs-CRP was quantified utilizing a commercially available chemiluminescence immunoassay kit on a MAGLUMI 2000 fully automated analyzer, whereas fasting serum lipid profile parameters were assessed through an enzymatic kinetic technique employing the Siemens Dimension EXL 200 analyzer.

All gathered data were processed and statistically evaluated utilizing IBM SPSS (Statistical Package for Social Sciences) version 26.0 for Windows, with a p-value < 0.05 considered statistically significant. Continuous variables were presented as mean ± SEM or SD. The Kolmogorov–Smirnov test was employed to evaluate data normality, with

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a p-value beyond 0.05 signifying a normal distribution. Pearson's correlation analysis was utilized where necessary to ascertain statistical correlations.

Results

Table I Comparison of Inflammatory Marker, Blood Pressure, Lipid Profile and Clinical Characteristics Between Patients of Type 2 diabetes mellitus With or Without having ischemic heart disease (n=100).

Parameter	Overall Mean ± SD	Ischemic Heart disease Present (n=69) Mean ± SD	Ischemic Heart disease Absent (n=31) Mean ± SD	p-value
HsCRP (mg/L)	5.35 ± 2.30	5.83 ± 2.27	4.28 ± 2.01	0.002*
SBP mmhg	141.30 ± 9.60	141.38 ± 9.66	141.13 ± 9.64	0.90
DBP mmHg	89.45 ± 6.66	89.57 ± 6.95	89.19 ± 6.07	0.79
TC (mg/dl)	205.41 ± 49.37	209.29 ± 55.10	196.77 ± 32.41	0.24
TG (mg/dl)	210.18 ± 90.59	222.09 ± 88.47	183.68 ± 91.03	0.049*
LDL (mg/dl)	101.64 ± 32.40	105.39 ± 34.09	93.29 ± 26.96	0.008*
HDL (mg/dl)	35.43 ± 10.78	35.16 ± 10.99	36.03 ± 10.44	0.71
Duration of diabetes mellitus (Years)	6.15 ± 4.10	6.12 ± 3.87	6.21 ± 4.65	0.91

*p-value highly significant at <0.01.

HsCRP, triglycerides and LDL cholesterol were significantly higher in patients with ischemic heart disease ($p < 0.01$) indicating increased inflammation and dyslipidemia. No significant differences were observed in blood pressure, total cholesterol, HDL or duration of diabetes ($p > 0.05$). These findings suggest that inflammatory status and specific lipid abnormalities are more strongly associated with ischemic heart disease in this study population.

Table II Pearson correlation of Hs-CRP with study variable between Patients of Type 2 diabetes mellitus With or Without having ischemic heart disease (n=100)

Variable	Correlation (rho, p)	p-value
SBP	0.110	0.27
DBP	0.079	0.43
TC	0.292	0.003*
TG	0.325	0.001*
LDL-C	0.279	0.004*
HDL-C	-0.117	0.24
Atherogenic index of plasma (AIP)	0.286	0.006*
DODM	0.015	0.88

*p-value significant at <0.01.

Correlation analysis showed that hs-CRP had significant positive correlations with TC, TG and LDL-C and AIP indicating that higher inflammatory status is correlated with an atherogenic index in patients with type 2 diabetes mellitus. However, SBP, DBP, HDL and DODM did not show statistically significant correlations with hs-CRP. These findings suggest that inflammation is more closely related to dyslipidemia rather than blood pressure or duration of diabetes in this study population.

Table III Association of hsCRP Level with Ischemic Heart Disease among Patients with Type 2 Diabetes Mellitus (n=100)

Variables			Ischemic heart disease absent	present	Total	p-value
HsCRP	≤3 mg/L	Count	13	12	25	0.009
		% of Total	13.0%	12.0%	25.0%	
	>3 mg/L	Count	18	57	75	
		% of Total	18.0%	57.0%	75.0%	
	Total	Count	31	69	100	
		% of Total	31.0%	69.0%	100.0%	

Patients with hsCRP >3 mg/L showed a significantly higher proportion of ischemic heart disease compared to those with hsCRP ≤3 mg/L ($p=0.009$). This finding suggests that elevated hsCRP is strongly associated with increased cardiovascular risk in this study population.

Table IV Multiple Logistic Regression Analysis of Lipid Parameters and AIP Group Associated with Elevated hsCRP (>3 mg/L) among Patients with Type 2 Diabetes Mellitus

Variables	B	S.E.	Wald	p-value	EXP(B)/ odds ratio	95% C.I.for EXP(B) Lower	Upper
TC	0.005	0.006	0.533	0.465	1.005	0.992	1.018
TG	0.010	0.004	5.238	0.022	1.010	1.001	1.019
LDL-C	0.025	0.010	6.230	0.013	1.025	1.005	1.045
HDL-C	-0.015	0.030	0.233	0.629	0.986	0.929	1.045
AIP group (Adjusted for IHD)	2.234	0.739	9.143	0.002	9.35	2.19	39.1

Dependent variable: HsCRP > 3 mg/L=1 & ≤ 3 mg/L =0.

Multiple logistic regression analysis demonstrated that triglycerides and LDL-C were significant independent predictors of elevated hsCRP (>3 mg/L) while TC and HDL-C showed no significant association. The AIP group remained a strong predictor after adjustment for ischemic heart disease, with patients having 9-fold higher odds of elevated hsCRP (OR=9.35, p=0.002) indicating a significant association between atherogenic index and inflammation in type 2 diabetes mellitus.

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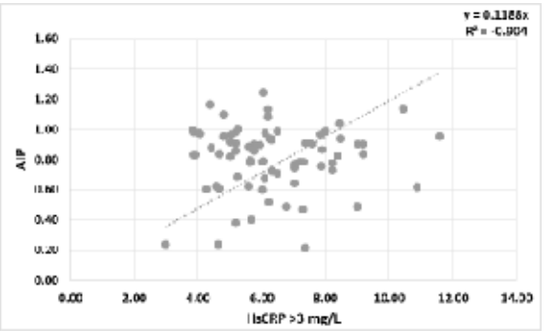

Figure 1 Linear Relationship between hsCRP >3 mg/L and Atherogenic Index of Plasma (AIP) among Patients with Type 2 Diabetes Mellitus (n=75)

Figure 1 demonstrates a positive linear relationship between hsCRP and Atherogenic Index of Plasma (AIP) among patients with type 2 diabetes mellitus. The upward trend indicates that higher hsCRP levels are associated with increased AIP, suggesting that systemic inflammation may contribute to a more atherogenic index of plasma and elevated cardiovascular risk in this population.

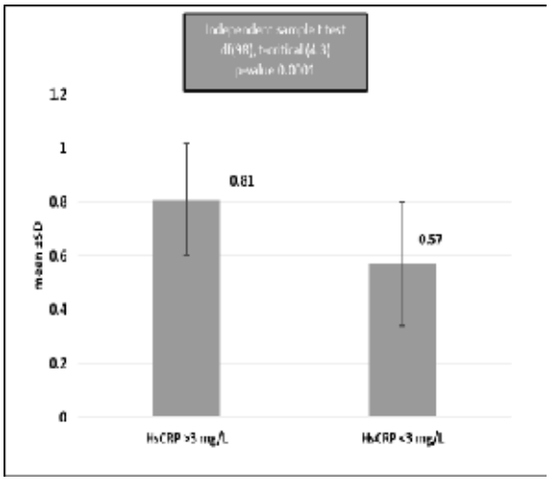

Figure 2 Comparison of Mean Atherogenic Index of Plasma (AIP) between hsCRP >3 mg/L and hsCRP <3 mg/L Groups among Patients with Type 2 Diabetes Mellitus

Figure 2 shows that patients with hsCRP >3 mg/L had a significantly higher mean AIP compared to those with hsCRP <3 mg/L (p=0.0001). This finding suggests that elevated inflammatory status is associated with a more atherogenic index of plasma and increased cardiovascular risk in patients with type 2 diabetes mellitus.

Discussion

The current investigation revealed that hsCRP levels were markedly elevated in individuals with ischemic heart disease relative to those without, signifying an augmented inflammatory burden in the high-risk diabetic cohort. Table I. This discovery aligns with current cardiovascular research indicating that hsCRP is significantly correlated with atherosclerotic progression and forecasts cardiovascular events via persistent low-grade inflammation and endothelial dysfunction.[1,7] Increased hsCRP indicates systemic inflammatory activation that aids in plaque development and instability, affirming its status as an independent marker of cardiovascular risk in individuals with type 2 diabetes mellitus.[6]

Patients with ischemic heart disease had considerably higher triglyceride levels in this study, indicating the existence of atherogenic dyslipidaemia in this category. Hypertriglyceridaemia, low HDL-cholesterol and small dense LDL particles all contribute to diabetic dyslipidaemia and expedite up atherogenesis. Recent studies have also shown that increased triglycerides raise the risk of cardiovascular complications in diabetic coronary disease, even after lowering LDL cholesterol levels, indicating that triglyceride-rich lipoproteins are significant.[4,5]

LDL-cholesterol levels were also significantly elevated among patients with ischemic heart disease in this study. LDL particles, particularly oxidised and small dense forms, promote foam cell formation and vascular inflammation, thereby accelerating coronary plaque development. Previous investigations in diabetic populations have reported comparable results, showing that higher LDL levels are associated with coronary artery disease severity and increased cardiovascular mortality.[2] However, there was no significant difference in diastolic or systolic blood pressure across the groups, indicating that hemodynamic variables may not be as strongly associated with ischemic heart disease in this cohort as inflammatory and lipid-mediated processes. Despite the fact that hypertension is known to increase the risk of cardiovascular disease, some research suggest that inflammatory markers and atherogenic lipid indices could be more accurate in determining the residual risk of cardiovascular disease in type 2 diabetic individuals.[1,7]

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Similarly, HDL-cholesterol did not show a significant difference between groups in the present study. This observation aligns with recent literature suggesting that functional quality and anti-inflammatory properties of HDL may be more relevant than absolute HDL concentration in determining cardiovascular risk, particularly in diabetic individuals where HDL dysfunction is common.[4]

Duration of diabetes mellitus also showed no significant association with ischemic heart disease in this analysis. While longer disease duration is often linked with increased cardiovascular complications, some cross-sectional studies suggest that biochemical markers such as hsCRP and atherogenic lipid indices may reflect current inflammatory and metabolic status more accurately than disease duration alone.[6,9]

Table II showed significant positive correlations between hs-CRP and total cholesterol, triglycerides, LDL-cholesterol, and Atherogenic Index of Plasma, suggesting a strong link between systemic inflammation and atherogenic dyslipidemia in type 2 diabetes mellitus.[11,12] Similar findings have been reported where inflammatory markers were closely associated with adverse lipid profiles and increased cardiovascular risk.[13] The lack of significant correlation between hs-CRP and blood pressure indicates that inflammatory status may be more influenced by metabolic abnormalities rather than hemodynamic factors.[14] The weak negative association with HDL-cholesterol supports previous evidence that HDL dysfunction rather than absolute HDL levels contributes to inflammation in diabetic patients.[15]

The present study showed in (Table III) that patients with hsCRP >3 mg/L had a significantly higher proportion of ischemic heart disease ($p = 0.009$), indicating that elevated inflammatory status is strongly linked with cardiovascular risk in type 2 diabetes mellitus, which is consistent with studies demonstrating hsCRP as an independent predictor of coronary artery disease.[16] The higher prevalence of ischemic heart disease among individuals with elevated hsCRP reflects the pro-atherogenic role of chronic inflammation in plaque formation and vascular dysfunction reported in diabetic populations.[17]

Multiple logistic regression analysis (Table IV) revealed that triglycerides were a significant independent predictor of elevated hsCRP, supporting previous research showing that hypertriglyceridemia contributes to systemic inflammation through increased production of inflammatory cytokines and endothelial activation.[18] Similarly, LDL-cholesterol was identified as an independent predictor of elevated hsCRP, aligning with evidence that LDL oxidation promotes inflammatory responses and accelerates atherosclerotic progression in patients with metabolic disorders.[19]

In contrast, total cholesterol and HDL-cholesterol did not show significant associations with elevated hsCRP in this study, which agrees with findings suggesting that composite lipid indices and triglyceride-rich lipoproteins may better reflect inflammatory cardiovascular risk than conventional lipid parameters alone.[20] Importantly, the Atherogenic Index of Plasma (AIP) remained a strong predictor of elevated hsCRP after adjustment for ischemic heart disease, with approximately nine-fold increased odds, supporting literature describing AIP as a powerful surrogate marker of cardiometabolic risk and inflammation.[12]

The present study demonstrated a positive linear relationship between hsCRP and Atherogenic Index of Plasma (AIP) (Figure 1) suggesting that increasing inflammatory status is associated with a more atherogenic lipid profile in type 2 diabetes mellitus, consistent with reports linking inflammation with adverse cardiometabolic indices.[12]

The upward trend between hsCRP and AIP supports previous findings that systemic inflammation promotes triglyceride-rich lipoprotein metabolism and contributes to atherosclerotic progression.[18]

Similar correlations between AIP and inflammatory biomarkers have been observed in diabetic populations, highlighting AIP as a strong surrogate marker of cardiovascular risk beyond traditional lipid parameters.[11]

The moderate linear association shown in this figure indicates that inflammatory activation may influence lipid remodeling and endothelial dysfunction, which has been reported in studies examining hsCRP-related vascular risk.[16]

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Patients with hsCRP > 3 mg/L showed a significantly higher mean Atherogenic Index of Plasma compared with those having hsCRP < 3 mg/L, suggesting that elevated inflammatory status is associated with increased atherogenic dyslipidemia, which is consistent with studies demonstrating AIP as a strong marker of cardiovascular risk in type 2 diabetes mellitus.[21] The significant difference in AIP between inflammatory groups supports previous evidence that systemic inflammation contributes to lipid remodeling and cardiometabolic risk, indicating that combined assessment of hsCRP and AIP may improve cardiovascular risk stratification.[20]

Limitations

- The cross-sectional nature of the study restricts causal inference between hsCRP, AIP, and ischemic heart disease, as temporal relationships between inflammation and lipid changes cannot be established.
- Single-time biochemical measurements may not reflect dynamic fluctuations of inflammatory and lipid markers, potentially underestimating long-term cardiometabolic variability.
- The study did not assess qualitative lipid characteristics such as small dense LDL or HDL functionality, which may better explain the inflammatory–atherogenic interaction observed.

Recommendations

- Future longitudinal cohort studies incorporating serial hsCRP and AIP measurements are recommended to clarify the temporal progression of inflammation-mediated atherogenesis in type 2 diabetes mellitus.
- Integration of advanced lipid biomarkers, such as apolipoprotein ratios or oxidized LDL, may provide deeper mechanistic insight into the inflammatory dyslipidemia observed in diabetic cardiovascular risk.
- Clinical risk stratification models should consider combining hsCRP with Atherogenic Index of Plasma to improve early identification of high-risk individuals beyond conventional lipid profile assessment.

Conclusion

The present study highlights a significant association between systemic inflammation and atherogenic lipid abnormalities in patients with type 2 diabetes mellitus, demonstrating that elevated hsCRP levels are linked with higher Atherogenic Index of Plasma and increased risk of ischemic heart disease. The findings suggest that inflammatory activation and dyslipidemia act synergistically in promoting cardiovascular risk, while traditional parameters such as blood pressure and disease duration show comparatively weaker relationships. Incorporating inflammatory biomarkers alongside composite lipid indices may enhance cardiovascular risk stratification and support more targeted preventive strategies in diabetic populations.

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Contribution of authors

SD-Conception, acquisition of data, data analysis, drafting & final approval.
MH-Design, interpretation of data, critical revision & final approval.
SC-Data analysis, drafting & final approval.
AM-Data analysis, interpretation of data & final approval.

Disclosure

The authors declared no conflict of interest.

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