https://africanjournalofbiomedicalresearch.com/index.php/AJBR
Afr. J. Biomed. Res. Vol. 27(4s) (November 2024); 1381-1388
Research Article

A Study To Compare Health Status High-Sensitivity C-Reactive Protein And Lipid Profile In Patients With Adult-Onset Type2 Diabetes Mellitus

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Abstract-
The most significant and challenging health issue of the modern era is diabetes mellitus and its complications. Inflammation plays a crucial role in the development and progression of diabetes. Type 2 Diabetes Mellitus patients (T2DM) are at significant risk of developing cardiovascular diseases. High-sensitive CRP (hsCRP) has become a reliable indicator of low-grade inflammation. Since very little is known regarding the relationship between hs-CRP and T2DM, the goal of this study was to evaluate hs-CRP levels and lipid profile and to study their relationship to cardiovascular problems in Type 2 Diabetes Mellitus patients.
Material and Methods:
The current study was carried out at Rajeev gandhi College and Hospital in Bhopal. The study group consisted of 60 healthy controls and 60 Type 2 Diabetes Mellitus patients who had been diagnosed following WHO criteria. Serum hs-CRP concentrations as well as the lipid profile (total cholesterol, HDL, and TG) were assessed. Descriptive Statistics Calculator(https://www.calculatorsoup.com/calculators/statistics/descriptivestatistics.php) and https:// www. so csci statistics.com/tests/studentttest/default2.aspx was used to analyze the data.
Results:
In comparison to controls, individuals with Type 2 Diabetes Mellitus had significantly higher levels of hsCRP, with a mean value of 2.74 +1.20 (p 3 mg/L, with a high risk of developing CVD whereas 32 (53%) of them had an intermediate risk of developing CVD with serum hs-CRP values between 1-3 mg/L. Conclusion: The present study showed that patients with T2DM had considerably higher levels of hs-CRP and lipid parameters than the controls. Furthermore, it was indicated that in patients T2DM patients with higher hs-CRP levels >3 mg/L there was a significant association between BMI, serum LDL-C, total cholesterol, and triglycerides. These results imply that hs- CRP may serve as a helpful tool for assessing atherosclerosis risk and cardiovascular complications in T2DM patients.

Keywords-hs-CRP, lipid profile, type 2 diabetes mellitus, cardiovascular disease.

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Received: 26-10-2024 *Accepted: 12-11-2024*

DOI: https://doi.org/10.53555/AJBR.v27i4S.3809

Introduction

Diabetes, specifically type 2 diabetes mellitus (T2DM), is one of the most challenging health problems in the 21st century. Its prevalence is increasing worldwide, it was 150 million in 2000, 171 million in 2007, and expected to reach 366 million in 2030[1,2] . In India the estimated prevalence was 41 million in 2006 and is expected to reach 70 million by the year 2025[1,2] The cause of higher prevalence of CAD in T2DM is multifactorial which includes factors like physical inactivity, obesity, smoking, hypertension and dyslipidemia[3] .

A group of metabolic disorders known as diabetes characterized by hyperglycemia results from deficiencies in insulin secretion, action, or both [4]. According to the World Health Organization's most recent data from 2016, an estimated 422 million adults worldwide have diabetes mellitus. By the end of 2040, this figure is expected to rise to 642 million [5]. Due to its concurrent microvascular sequelae, including neuropathy, nephropathy, and retinopathy as well as macrovascular problems, such as cardiovascular illnesses resulting in myocardial infarction and stroke, chronic hyperglycemia is accompanied by a high mortality and morbidity rate [6, 7]. The exact etiopathogenesis of diabetes is still up for debate, despite significant progress in understanding its etiology. Reactive oxygen species, immunological responses, and inflammatory factors have all emerged as the main pathogenic effects of diabetes. The role of low-grade inflammation in the etiology of type 2 diabetes has drawn more and more attention [8].The three primary proinflammatory cytokines—tumor necrosis factor- alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6(IL-6)—can, however, be produced and released by adipose tissue[9]. These cytokines, which are atherosclerotic risk factors, encourage the release of acute-phase proteins. Several metabolic processes related to insulin resistance, comprising reactive oxygen species, lipoprotein lipase activity, and adipocyte function, involve pro-inflammatory cytokines and acute phase reactants [10]. C-reactive protein (CRP) is an acute-phase protein that is elevated in inflammatory disorders such as diabetes, cancer, and coronary heart disease as well as infections. A particularly sensitive variant of CRP is called high sensitivity CRP (hs-CRP). It has become the "golden biomarker" for malignancies and even inflammatory diseases [9, 11]. It is detected using highly sensitive assays, which are capable of detecting CRP levels with a sensitivity range of 0.01 mg/L to 10 mg/L. In the absence of noticeable inflammation, these assays can therefore detect even lowgrade inflammation. High sensitivity CRP levels quickly increase to more than 10 mg/L in acute situations. According to the American Heart Association, it is known that high sensitivity CRP levels > 1 mg/L are linked to a low risk of cardiovascular disease, whereas levels 1-3 mg/L is linked to moderate risk and > 3 mg/L to high risk [12-14]. Cytokines also influence the liver, resulting in the typical dyslipidemia of type 2 diabetes mellitus [15]. The relationship between cardiovascular illnesses and hs-CRP has been examined in a number of researches. On the other hand, very little research has been conducted to study the relationship between hs-CRP and T2DM-related cardiovascular problems. Therefore, the purpose of the current study was to evaluate hs-CRP levels and lipid profiles in patients with T2DMand to study their relationship to cardiovascular problems in Type 2 Diabetes Mellitus patients.

Material and Methods

This hospital-based observational and comparative study was conducted between march 2023 and march 2024. The study was conducted in the Rajeev gandhi College, bhopal and included 60 T2DM patients and 60 age- and sex-matched healthy controls. The Biochemical investigations were carried out in the Department of pathology, Rajeev Gandhi college and Hospitals Bhopal.

Inclusion criteria

Patients diagnosed with Adult-onset type2 diabetes mellitus who were above 30 years but under 60 years of age and met the WHO criteria (Fasting plasma glucose levels equal to or greater than 126 mg/dl and HbA1c > 6.4 Prediabetes were included in the study[16].

Exclusion criteria

Patients taking anti-inflammatory medicines that are known to lower CRP levels, statins, and thiazolidinediones (TZDs) were excluded from the study. The study also excluded individuals with heart disease, acute febrile illness, kidney, liver, and malignant disorders, chronic illnesses, symptomless infections, type 1 diabetes, gestational diabetes, alcoholics, pancreatitis, other endocrinal disorders, individuals receiving diuretic therapy, and individuals taking aminoglycosides[16]. The patient's informed consent was obtained.

Sample collection

After 12 hours of fasting venous blood sample of all the participants was taken from ante-cubital vein under aseptic conditions. The sample was dispensed in fluoride vials for analysis of plasma glucose levels, in EDTA vials for HbA1c, and plain vials for lipid profile and hs-CRP. After 1 hour, serum was separated by centrifugation at 3,000 rpm for 10 minutes. Plasma

glucose levels were determined using the GOD-POD method [17], HbA1c was calculated using the High-Performance Liquid Chromatography technique [18], serum cholesterol was determined using the cholesterol oxidase peroxides method [19], serum TGs were determined using the Glycerol oxidase-Trinder method[20], and high-density lipoprotein (HDL) levels were determined using modified polyethylene glycol precipitation method[21]. The Fridelwald equation was used to compute LDL [22] Immunoturbidometric analysis of serum hs-CRP was performed using a COBAS501 fully automated analyzer of Roche Diagnostics [23],[24].

Statistical analysis

Descriptive Statistics Calculator (https://www.calculatorsoup.com/calculators/statistics/descriptivestatistics.php) and https://www.socscistatistics.com/tests/studentttest/default2.aspx was used to evaluate the data outcomes. For the distribution of diabetes cases and controls by age and BMI, descriptive data (frequency and percentage) were obtained. For both the cases and the healthy controls, the mean and SD were calculated. Using an independent t- test, the mean values of continuous variables were compared. Significance was assessed at a 5% level of significance. The association between hs-CRP and various other factors was analyzed using Pearson's correlation coefficient test. One-way Anova was used to compare the means of different groups of T2DM patients categorized on the basis of their hs-CRP levels as low, intermediate and high risks of cardiovascular disease. The interpretation of results was done on the following basis:

- p-value <0.05 – Significant (S)
- p-value <0.01- Highly significant (HS)
- p-value > 0.05 – Not significant (NS)

Results

Table 1 Distribution of Type II Diabetic Mellitus Patients According to Age

AGE GROUP(YEARS)	NUMBER OF CASE (N=60)	PERCENTAGE
30-40	10	16.7
41-50	19	31.7
51-60	31	51.7

Table 2 Distribution of healthy controls according to age

AGE	NUMBER OF CASES	PERCENTAGE
30-40	14	23.3
41-50	23	38.3
51-60	23	38.3

Table 3 Distribution of the study population according to BMI

BMI	DIABETIC CASES		CONTROLS	
(kg/m2)	(N=60)	%	(N=60)	%
Below 18	1	1.7	5	8.3
18-24.99	21	35.0	31	51.7
25-29.99	28	46.7	20	33.3
30 and above	10	16.7	4	6.7
mean	25.7		23.4	
SD	4.1		4.0	

Table 3 shows that 31 (51.7%) of the controls and 20 (33.3%) of the patients both had normal BMIs. 28 cases (48.7%) were found to be overweight (BMI 25–29.99), compared to 21 controls (35%) who fall into this category. 10 (16.7%) of the diabetic patients were obese with a BMI of 30 or higher, compared to 4 (6.7%) controls.

Table 4 Comparison of glycemic parameters between type II diabetic mellitus patients and healthy controls

PARAMETERS		FBS	PPBS	HbA1c
DIABETIC CASES	Mean	166	268	8.7
	SD	23.1	28.5	1.2
CONTROLS	Mean	88.9	119.0	5.4
	SD	5.8	5.9	0.3
p-Value		< .00001	< .00001	< .00001

FPG, PPBS and HbA1c levels in diabetes patients were substantially higher than in controls. .The difference was highly significant with p-value<0.001

Table 5
Comparison of lipid profile between type II diabetic mellitus patients and healthy controls

PARAMETERS		TOTAL CHOLESTEROL (mg/dl)	TRIGLYCERIDE (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
DIABETIC CASES	Mean	205.6	210.0	43.9	119.3	42.0
	SD	28.5	29.5	5.1	26.7	5.9
CONTROLS	Mean	166.8	143.9	48.2	84.8	28.8
	SD	15.2	18.7	4.1	15.6	3.7
p-Value		< .00001	< .00001	< .00001	< .00001	< .00001

According to the above table, cases with Type 2 diabetes mellitus had considerably higher serum total cholesterol, LDL, VLDL, and TG levels as compared to controls.

Table 6
Comparison of hs-CRP between type II diabetic mellitus patients and healthy controls

PARAMETERS		hs-CRP(mg/L)
DIABETIC CASES	Mean	2.74
	SD	1.20
CONTROLS	Mean	1.11
	SD	0.33
p-Value		< .00001

The hs-CRP levels in patients with Type 2 Diabetes Mellitus are significantly higher than those in controls, with a mean value of 2.74 + 1.20 mg/L versus 1.11 + 0.33 mg/L ($p < 0.001$), according to the above- mentioned table.

Table 7
Categorization of type 2 diabetic mellitus patients and healthy controls according to levels of hs-CRP protein

PARAMETERS		<0.9 mg/L, N(%) Low Risk	1.0-2.9 mg/L, N(%) Intermediate Risk	≥3.0mg/L,N(%) High Risk
DIABETIC CASES	Mean	6	32	22
	%	10	53	37
CONTROLS	Mean	11	49	0
	%	18	82	0

In accordance with the above table, 6 (10%) of the 60 diabetes cases and 11 (18%) of the 60 controls have a low risk of developing cardiovascular disease (CVD), 32 (53%) of the cases and controls have an intermediate risk, and 22 (37%) of the cases have a high risk. Bat intermediate and high risk total leval average 90%.and controls leval patients high risk laval 0%.

Table 8
Comparison of BMI and different parameters of lipid profile among three groups of hs-CRP

PARAMETERS		BMI	TC	TG	HDL	LDL	VLDL
<0.9 mg/L, N(%) Low Risk	Mean	21.3	176.8	173.1	43.9	98.3	34.6
	SD	3.5	24.8	24.1	4.6	24.1	4.8
1.0-2.9 mg/L, N(%) Intermediate Risk	Mean	24.7	191.7	196.8	46.2	106.2	39.4
	SD	4.2	16.3	18.3	4.4	15.5	3.7
≥ 3.0mg/L,N(%) High Risk	Mean	28.3	232.7	239.3	40.6	144.2	47.9
	SD	2.5	21.3	16.1	4.6	21.7	3.2

According to Table 8, which elaborates the data for the BMI and lipid profile parameters in the three groups, it was observed that values of BMI, TC, LDL, and TG were considerably greater in patients with hs- CRP levels >3 mg/L than in those with hs-CRP levels 1-3 mg/L, which was higher than those with hs-CRP levels

Table 9
Distribution of patients with T2DM on the basis of their ldl levels in three groups of hs-CRP

PARAMETERS		<0.9 mg/L, N(%) Low Risk	1.0-2.9 mg/L, N(%) Intermediate Risk	≥ 3.0mg/L,N(%)High Risk
LDL<100mg/dl	Mean	4	10	1
	%	6.7	16.7	1.7
LDL>100mg/dl	Mean	2	22	21
	%	3.3	36.7	35.0

The above table shows that 22(36.7 %) cases with Serum LDL levels >100mg/dl have their hs-CRP levels between the range of 1-3mg/L(Intermediate risk) whereas 21(35 %) of the cases have their hs-CRP levels >3 mg/L. 10(16.7%)out of 60 cases who have their LDL levels

Discussion

Inflammation and insulin resistance have been linked in several studies to the pathophysiology of T2DM and the development of atherosclerotic plaques [25]. Reactive oxygen species, activated PKC, and activated glycation products are some of the potential pathways for the formation of atherosclerotic plaques. [26-28] . According to numerous research, inflammation causes an increase in hs-CRP levels, and hs-CRP concentration is related to future cardiovascular risk [28] .The pentameric protein known as hsCRP, an inflammatory marker, is produced by hepatic cells under the influence of cytokines [29]. Previous research showed that high levels of serum hs-CRP are present in diabetes patients [30], which activates inflammatory pathways and advances CVD [31].

Therefore, the current study attempted to evaluate hs-CRP with glycemic parameters and lipid profile in patients with Type 2 Diabetes Mellitus. It also compared the levels of hs-CRP and lipid profile in patients with Type 2 Diabetes mellitus with that of healthy controls. We also investigated whether type 2 DM patients' hs- CRP levels are related to CVDs[32].

The distribution of Type 2 Diabetes Mellitus patients by age is shown in Table 1. Out of 60 patients, 10 (or 16.7%) were found to be between the age group of 30 and 40 years. 31 (51.7%) of the cases were in the age group of 51–60 years, while 19 (31.7%) of the cases were in the 41–50 years age group. The distribution of healthy controls is shown in Table 2. Out of 60 controls, 14 (23.3%) belonged to the 30–40 year age range, while 23 (38.3%) each belonged to the 41–50 year and 51–60 year age ranges.

The distribution of the study population by BMI is shown in Table 3. In this study, 21 (35%) patients out of 60 had normal range BMIs between 18 and 24.99, while the majority 28(46.7%) cases were overweight with BMIs between 25 and 29.99 and 10(16.7%) cases of diabetes patients were obese (BMI 30 and above). Our results are consistent with those of Williams et al., who demonstrated that obesity was independently connected to hs-CRP and that a rise in hs- CRP is related to a rise in BMI[33]. Similar to this, other study showed in their study that patients with poor glucose tolerance had significantly higher levels of high sensitivity CRP[34,35]. According to this study, patients with T2DM had significantly higher levels of glycemic markers than healthy controls, with a pvalue of 0.001. In the current investigation, we also noticed that patients with T2DM had significantly higher levels of hs-CRP, with a mean value of 2.74 ± 1.20mg/L compared to controls, who had a mean value of 1.11 ± 0.33mg/L ($p<0.001$) [Table 6]. It is noteworthy that persistent hyperglycemia encourages the release of different inflammatory cytokines (IL 6; TNF) and causes the liver to secrete acute phase reactants, which in turn causes hs-CRP to rise along with fasting plasma glucose levels to rise[36].

Our results are consistent with those of Laaksonan et al.8, who in their prospective analysis hypothesised that a high hsCRP level is linked to a higher risk of acquiring type 2 diabetes. According to Festa et al., higher hs-CRP levels have been linked to obesity, insulin resistance, and glucose intolerance, indicating that inflammation may also play a role in the development of type 2 diabetes[37,38].

Additionally in this study, compared to controls, patients with Type 2 DM exhibited higher levels of Total Cholesterol, LDL, VLDL, and TG. In diabetic cases, the mean serum cholesterol level was 205.6 ± 28.5 mg/dl, compared to 166.8± 15.2 mg/dl in control groups. The mean level of serum LDL in diabetic patients was 119.3 ±26.7 mg/dl, compared to 84.8 ± 15.6 mg/dl in controls. When compared to controls, who had a mean value of 28.8 ± 3.7mg/dl, diabetic cases' mean serum VLDL levels were higher at 42.0 ±5.9 mg/dl. The results of TG likewise showed a similar pattern, with mean values of 143.9 ± 18.7 mg/dl in individuals without diabetes and 210 ± 29.5 mg/dl in patients with diabetes. [Table 5].

The onset and progression of atherosclerosis are correlated with LDL-C, triglycerides, and total cholesterol [39]. Low-density lipoprotein cholesterol serves as the body's transporter of cholesterol and other lipids (LDL-C). Once oxidised, LDL-C is known as tiny dense LDL, which can cause a localised, low-grade

inflammatory response that results in the production of cytokines. When monocytes phagocytose oxidised LDL, they turn them into foam cells with a lipid core, which is the first step in the creation of atherosclerotic plaque. Additionally, the release of IL-6 by adipose tissue can be triggered by the excessive loading of triglycerides in adipose tissue seen in obesity [39]. On the other hand, because HDL-C is involved in reverse cholesterol transfer, having high levels of serum HDL-C is linked to a lower risk of developing atherosclerotic disease. Therefore, it is thought that HDL-C particles are anti-atherogenic and inhibit the pathways of thrombosis, inflammatory response, and LDL-C oxidation [40]

Study participants were divided into three groups as shown in Table 7. Eight of the cases (n=60) had low risk hsCRP values of less than 0.99 mg/L, forty had intermediate risk, and twenty-two had high risk of MI with hs-CRP values > 3mg/L.

We also discovered that patients with hs-CRP levels >3 mg/L had values for BMI, TC, LDL, and TG that were significantly higher than those with hs-CRP levels 1-2.99 mg/L, and even higher than those with hs- CRP levels 1 mg/L. [Table 8]. The serum level of LDL has been advised to be kept below 100 mg/dl in Type 2 Diabetes as it has been established as an independent marker of CVS risk. In this study we observed that 22(33.37 %) cases with Serum LDL levels >100mg/dl have their hs-CRP levels between the range of 1-3mg/L(Intermediate risk) whereas 21(35.0 %) of the cases have their hs-CRP levels >3 mg/L. 10 (16.17%) out of 60 cases have their LDL levels

Conclusion

According to the study data, patients with T2DM had significantly higher levels of both hs-CRP and lipids than the controls. Additionally, it confirms that there was a significant association between BMI, serum LDL-C, total cholesterol, and triglycerides in people with higher hs-CRP levels >3 mg/L (high-risk patients), indicating that people with T2DM may have low-grade systemic inflammation. These findings suggest that hs- CRP may be useful for atherosclerosis risk assessment and screening in patients with T2DM. Atherosclerosis is considered a type of arteriosclerosis.hs-CRP has the potential to serve as a marker of future risk of cardiovascular disease as a categorical variable. Therefore, screening of T2DM for serum hs-CRP levels and lipid profile at an earlier stage may be done to identify those patients who are at a higher risk of developing atherosclerosis or cardiovascular events in the future. In atherosclerosis, fat, cholesterol, and other substances build up on the walls of the arteries, called plaque. This plaque can narrow the arteries and restrict blood flow.

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