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"RELATIONSHIP BETWEEN GLYCATED HEMOGLOBIN, NON-HDL CHOLESTEROL, HS-CRP AND FRUCTOSAMINE IN DIABETIC AND HEALTHY INDIVIDUALS"

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Abstract

Introduction: Diabetes mellitus is a chronic metabolic disorder primarily characterized by elevated blood glucose levels. Many individuals with type 2 diabetes also develop dyslipidemia, marked by low HDL cholesterol and elevated levels of triglycerides (TG) and LDL cholesterol. The role of non-HDL cholesterol becomes even more crucial in these patients, as they often exhibit atherogenic dyslipidemia, with a combination of low HDL and high triglycerides, leading to an increased non-HDL cholesterol level compared to LDL cholesterol alone. Inflammation plays a key role in the development of coronary artery disease (CAD), with studies indicating that C-reactive protein (CRP) is actively involved in atherosclerosis. Furthermore, uncontrolled type 2 diabetes has been associated with increased CRP levels. Elevated fructosamine levels have also been linked to higher rates of CAD morbidity and mortality. This study aims to explore the relationship between glycated hemoglobin (HbA1c), non-HDL cholesterol, hs-CRP, and fructosamine in both type 2 diabetes patients and healthy controls.

Materials and Methods: A case-control study was conducted at Index Medical College, Indore, involving 210 participants. This group consisted of 105 individuals with type 2 diabetes and 105 age- and gender-matched healthy controls. The participants were assessed for fasting blood sugar (FBS), HbA1c, fasting lipid profile, non-HDL cholesterol, hs-CRP, and fructosamine levels. Data were analyzed using SPSS version 20.

Results: The findings indicated that type 2 diabetes patients had significantly higher levels of FBS and HbA1c compared to the control group ($p < 0.05$). Additionally, total cholesterol, LDL cholesterol, and triglycerides were also significantly elevated in the diabetic group ($p < 0.05$). Moreover, levels of non-HDL cholesterol, hs-CRP, and fructosamine were substantially higher in the diabetes patients ($p < 0.05$).

Conclusion: This study confirms that HbA1c is strongly associated with increased levels of non-HDL cholesterol, hs-CRP, and fructosamine in individuals with type 2 diabetes. These findings suggest that non-HDL cholesterol, hs-CRP, and fructosamine are more reliable indicators of diabetic dyslipidemia and cardiovascular risk than LDL cholesterol alone.

Keywords: Type 2 Diabetes Mellitus, Non-HDL Cholesterol, Glycated Hemoglobin (HbA1c), High-Sensitivity C-Reactive Protein (hs-CRP), Fructosamine, Dyslipidemia.

Introduction

Diabetes mellitus is a chronic metabolic disorder that occurs when the pancreas either does not produce enough insulin or when the body cannot effectively use the insulin it produces. This results in elevated blood glucose levels. Type 2 diabetes (T2DM) is primarily caused by the body's ineffective use of insulin, often exacerbated by factors such as obesity and lack of physical activity. According to the World Health Organization (WHO), 422 million adults worldwide were living with diabetes in 2014, a significant increase from 108 million in 1980. In 2012 alone, diabetes was responsible for 1.5 million deaths, with an additional 2.2 million deaths linked to the increased risk of coronary artery disease (CAD) and other complications arising from uncontrolled blood glucose levels[1].

In India, the International Diabetes Federation Atlas 2015 reported that approximately 69.2 million individuals were affected by diabetes[2].

Glycated hemoglobin (HbA1c) has become an essential biomarker for assessing long-term blood glucose control in individuals with diabetes, providing an average glucose level over the previous 8-12 weeks[3,4]. This test is preferred due to its convenience, as it can be conducted at any time of the day without the need for fasting. Beyond monitoring glycemic control, HbA1c is also increasingly used for diagnosing diabetes and screening individuals at high risk of developing the disease[5].

Non-high-density lipoprotein cholesterol (Non-HDL-C) is another critical marker in diabetic patients[6]. It is calculated by subtracting HDL cholesterol (HDL-C) from total cholesterol (TC)[7]. Non-HDL-C includes LDL cholesterol (LDL-C) and other potentially atherogenic lipoproteins such as VLDL, IDL, and Lp(a). In diabetic patients, who often exhibit atherogenic dyslipidemia characterized by low HDL-C and high triglycerides, non-HDL-C becomes a more accurate predictor of cardiovascular risk than LDL-C alone. Many diabetic individuals do not achieve the recommended levels for both non-HDL-C and LDL-C, placing them at an elevated risk for cardiovascular events[8].

Inflammation also plays a crucial role in the pathogenesis of CAD and its associated complications. C-reactive protein (CRP), an acute-phase reactant, is a key marker of inflammation[9]. Elevated levels of CRP have been associated with an increased risk of atherosclerosis, with uncontrolled T2DM contributing to elevated CRP levels[10,11,12]. The advent of high-sensitivity CRP (hs-CRP) testing allows for the detection of mild elevations of CRP, which are indicative of chronic low-grade inflammation[13].

Fructosamine, a marker for short-term glycemic control, reflects the average blood glucose levels over the previous 2-3 weeks[14]. It is especially useful in monitoring early responses to treatment and is a cost-effective, reliable, and minimally affected by conditions such as red blood cell disorders[15,16,17,18]. Elevated fructosamine levels have been linked to increased cardiovascular morbidity and mortality, both in individuals with diabetes and in those with normoglycemia[19,20,21,22].

Given the critical roles of HbA1c, non-HDL-C, hs-CRP, and fructosamine in the management of type 2 diabetes and cardiovascular risk, this study aims to explore the associations between these markers in individuals with T2DM and healthy controls. The findings of this study may provide valuable insights into better cardiovascular risk prediction and management in diabetic patients.

Materials and Methods

The present case-control study was conducted at the Department of Biochemistry, Index Medical College and Hospital, Indore, Madhya Pradesh, India from Dec.2022 to Dec 2023. A total of 210 participants were included in the study, consisting of 105 patients with type 2 diabetes mellitus (T2DM) and 105 age and gender-matched healthy controls, aged between 30 to 60 years. The study included newly diagnosed T2DM patients as well as individuals with known T2DM, either on or off treatment with oral hypoglycemic agents, insulin, or hypolipidemic drugs. Healthy controls were matched for age and gender to the T2DM patients.

Exclusion criteria for the study included individuals with type 1 diabetes mellitus, females on oral contraceptive pills, anemia, nephrotic syndrome, chronic renal failure, cirrhosis, liver diseases, pregnancy, thyroid disorders, hemoglobinopathies, recent myocardial infarction (MI), or those with acute illnesses. Additionally, patients who had undergone hs-CRP testing followed by the prescription of antibiotics, antivirals, or antimycotics within the preceding 7 days were excluded, as the use of these medications could indicate that infection was the underlying cause for the elevated hs-CRP levels.

The diagnosis of type 2 diabetes was confirmed based on the criteria outlined by the American Diabetes Association (ADA), specifically HbA1c levels ≥6.5% and fasting blood sugar (FBS) levels ≥126 mg/dl[23].

Estimation of fasting blood sugar and serum fasting lipid profile was done by Hexokinase[24,25,26] and other enzymatic methods respectively[27,28,29,30]. Using fully automated analyzer. Estimation of HbA1C by using Bio-Rad D-10 HbA1c program. Estimation of hs-CRP and fructosamine done by Particle enhanced immunoturbidimetric assay[31,32] and colorimetric test by reaction with nitroblue tetrazolium[33,34,35] respectively.

Statistical analysis was performed using the SPSS Software, version 20.0 for windows Continuous variables were expressed as mean, ± S.D and qualitative data were expressed in percentages. Independent T test was used to compare the parameters in case and control population. p-value < 0.05 was considered as significant.

Results

In this study a total 210 patients were evaluated. The overall distribution of patients is as shown in table 1.

Table 1: Distribution of patients by gender

Gender	Number of cases	Number of controls	Percentage (%)
Male	60	60	57.14
Female	45	45	42.86
Total	105	105	100

Table-2: Comparison of FBS, HbA1c, Lipid profile,Non-HDL-C, hs-CRP and fructosamine in cases and controls

Parameter	**Case(type 2 diabetes mellitus patients)**		**Control**		**p-value**
	MEAN	**S.D**	**MEAN**	**S.D**	
FBS (mg/dl)	161.62	45.14	104.88	13.33	<0.0001*
HbA1c (%)	8.31	1.79	5.78	0.39	<0.0001*
TC (mg/dl)	193.99	31.96	158.17	34.80	<0.0001*
LDL (mg/dl)	117.18	29.88	86.68	30.02	<0.0001*
HDL (mg/dl)	45.37	10.70	46.16	9.60	0.749
TG (mg/dl)	166.24	78.06	136.57	54.19	0.004*
NON-HDL(mg/dl)	148.62	30.43	112.01	32.58	<0.0001*
Hs-CRP (mg/L)	3.16	1.27	0.97	0.74	<0.0001*
Fructosamine (µmol/L)	390.83	122.31	258.88	31.71	<0.0001*

p value <0.05

Table 2 shows a comparison of various biochemical parameters, including serum fasting blood sugar (FBS), glycated hemoglobin (HbA1c), lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), non-HDL cholesterol, hs-CRP, and fructosamine between Type 2 diabetes patients and healthy controls.

The mean ± SD levels of FBS (161.62 ± 45.14 mg/dl) and HbA1c (8.31 ± 1.79%) were significantly higher in the Type 2 diabetes patients compared to the controls, who had a mean FBS of 104.88 ± 13.33 mg/dl and HbA1c of 5.78 ± 0.39% (p-value <0.05). Similarly, total cholesterol, LDL cholesterol, and triglyceride (TG) levels were significantly elevated in the diabetic patients compared to the controls (p-value <0.05).

However, no significant difference was observed in the HDL cholesterol levels between the two groups (p-value = 0.749). Non-HDL cholesterol levels were significantly higher in the Type 2 diabetes patients (148.62 ± 30.43 mg/dl) compared to controls (112.01 ± 32.58 mg/dl) with a p-value <0.05.

Additionally, the mean ± SD levels of hs-CRP (3.16 ± 1.27 mg/L) and fructosamine (390.83 ± 122.31 μmol/L) were also significantly higher in the Type 2 diabetes patients compared to controls (hs-CRP = 0.97 ± 0.74 mg/L and fructosamine = 258.88 ± 31.71 μmol/L), with p-values <0.05. These results suggest that type 2 diabetes is associated with altered lipid metabolism, elevated inflammatory markers, and poorer glycemic control compared to healthy individuals.

Discussion

The results of this study reveal significant differences between Type 2 diabetes mellitus (T2DM) patients and healthy controls in several key metabolic parameters, including fasting blood sugar (FBS), glycated hemoglobin (HbA1c), lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), non-HDL cholesterol, high-sensitivity C-reactive protein (hs-CRP), and fructosamine levels. These findings emphasize the altered metabolic state in individuals with T2DM, which is associated with an increased risk of cardiovascular complications and poor glycemic control.

Fasting Blood Sugar (FBS) and HbA1c: As expected, the levels of FBS and HbA1c were significantly elevated in T2DM patients compared to the healthy controls, with p-values of <0.05. These results are consistent with previous studies that show elevated blood glucose levels and poor long-term glycemic control in individuals with T2DM. FBS is a widely used marker for diagnosing and monitoring diabetes, and elevated HbA1c levels reflect poor glycemic control over the past two to three months[3,4,5].

Lipid Profile: In the current study, total cholesterol, LDL cholesterol, and triglyceride (TG) levels were significantly higher in the T2DM patients compared to the controls. This is in line with known dyslipidemia patterns seen in T2DM, where the presence of elevated LDL cholesterol and triglycerides, along with low HDL cholesterol, contributes to an increased risk of cardiovascular disease (CVD). A study by Buse et al. (2009) indicated that diabetic patients often exhibit atherogenic dyslipidemia, which is associated with an increased risk of atherosclerosis and coronary artery disease (CAD)[36]. Interestingly, HDL cholesterol levels did not show a significant difference between the two groups in this study (p-value = 0.749). While many studies report reduced HDL levels in T2DM patients, the lack of significant change in this study might be due to variations in the cohort or treatment effects. Studies have demonstrated that while HDL-C is protective against atherosclerosis, its function may be impaired in T2DM, which may not always reflect as a change in absolute levels[37].

Non-HDL Cholesterol: Non-HDL cholesterol levels were significantly elevated in T2DM patients, with a mean value of 148.62 ± 30.43 mg/dl compared to 112.01 ± 32.58 mg/dl in controls (p-value <0.05). Non-HDL-C includes all atherogenic lipoproteins, such as VLDL, IDL, and Lp(a), and has been identified as a stronger predictor of cardiovascular risk in diabetic individuals than LDL-C alone. This finding aligns with other studies suggesting that targeting non-HDL cholesterol in diabetes management may provide better outcomes for reducing cardiovascular risks [7,8].

High-Sensitivity C-Reactive Protein (hs-CRP): The mean hs-CRP levels were significantly higher in T2DM patients (3.16 ± 1.27 mg/L) compared to controls (0.97 ± 0.74 mg/L), with a p-value of <0.05. Elevated hs-CRP levels reflect a state of chronic low-grade inflammation, which is commonly seen in T2DM and is thought to contribute to the development of atherosclerosis and cardiovascular events. the findings were similar to the other studies conducted[9,10,11]. Elevated CRP levels are strongly associated with an increased risk of cardiovascular disease in individuals with diabetes. The increased

hs-CRP levels observed in our study further support the role of inflammation in the pathophysiology of cardiovascular complications in T2DM patients.

Fructosamine: Fructosamine levels were also significantly higher in T2DM patients (390.83 ± 122.31 μmol/L) compared to controls (258.88 ± 31.71 μmol/L), with a p-value of <0.05. Fructosamine provides a snapshot of glycemic control over the past 2-3 weeks and is useful for tracking short-term changes in blood glucose levels. Elevated fructosamine levels have been associated with increased cardiovascular morbidity and mortality in both diabetic and non-diabetic populations. In diabetic individuals, higher fructosamine levels can indicate inadequate glycemic control, which is a critical factor for the prevention of cardiovascular events. the findings were similar to the other studies conducted[38,39].

Conclusion: In conclusion, this study highlights the altered metabolic profile in T2DM patients, characterized by elevated blood glucose levels, dyslipidemia, increased inflammation, and poor glycemic control. These findings underscore the importance of monitoring multiple metabolic parameters, including HbA1c, lipid profile, hs-CRP, and fructosamine, to better assess the risk of cardiovascular complications in individuals with T2DM. Additionally, targeting non-HDL cholesterol and inflammation may provide better cardiovascular risk management in diabetic patients.

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