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Research Article

CORRELATION OF TYPE 2 DIABETES MELLITUS AND DYSLIPIDEMIA AMONG NEPALESE

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ABSTRACT

Objectives: More cardiovascular disease occurs in patients with either Type 1 diabetes mellitus (DM) or Type 2 DM (T2DM). Serum high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol profiles in T2DM is quite useful, as it may serve as a reliable monitor to judge the prognosis of the patients. The aim of the present study is to examine T2DM and dyslipidemia and their correlation in residents of Nepal. The detection of risk factors in the early stage of the disease will help the patients to improve and reduce the morbidity rate as LDL promotes cholesterol deposition in the arterial wall.

Methods: This case-control study was carried out in Lumbini Medical College, Palpa, Nepal, on total of 100 subjects, with 50 controls (non-diabetic cases) and 50 T2DM patients, to study their HDL and LDL profiles.

Results: The present study showed increased levels of fasting blood sugar (164.5 [51.17] than in control 95.4 [10.09]) and LDL cholesterol (121.4 [27.89] than in control 103.6 [30.67]) in T2DM subjects; conversely, serum HDL cholesterol (39.2 [7.96]) level was reduced significantly in T2DM patients (than in controls 44.0 [10.57]).

Conclusion: Thus, the findings of the present study imply a significant correlation between serum HDL and LDL cholesterols in T2DM subjects.

Keywords: Blood glucose, Cholesterol, High density lipoprotein, Low density lipoprotein, Non-insulin dependent diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both [1]. There are various genetic as well as environmental factors that can influence the occurrence of this disease [2,3]. DM is characterized by either the absence of insulin that is insulin dependent DM (Type 1 DM [T1DM]) and which is of insensitivity to the insulin i.e., non-insulin dependent DM (Type 2 DM [T2DM]). It is a complex disease where the carbohydrate and fat metabolism is impaired [4]. T2DM is associated with a marked increased risk of cardiovasculardiseases (CVD). Individuals with diabetes have an absolute risk ofmajor coronary events similar to that of non-diabetic individualswith established coronary heart disease (CHD) [5]. Low-density lipoproteins (LDL) cholesterol is the main lipid marker in cardiovascular risk estimation and the principle therapeutic target in diabetic subjects [6]. High-density lipoprotein (HDL) cholesterol is inversely correlated with cardiovascular events in all major epidemiological studies. Earlier reports have demonstrated that increased HDL cholesterol is associated with decreased cardiovascular risk in high-risk individuals such as patients with T2DM [7]. An abnormal lipid profile is more common in diabetics and gets aggravated with poor glycemic control. Thus, the analysis of lipid profile is needed to investigate how the lipid metabolism, especially HDL and LDL cholesterol, is affected by diabetes [8]. High levels of LDL cholesterol and low HDL cholesterol may be a consequence of obesity, increased calorie intake and a lack of muscular exercise in the patients with T2DM [4]. Insulin resistance is a multifaceted syndrome responsible for the future development of T2DM, obesity, hypertension, dyslipidemia and atherosclerotic CVD [9]. The cause of T2DM is defective production of insulin or defective action of insulin, a hormone that controls the metabolism of carbohydrates, proteins and lipids. T2DM is regarded as a long-term disease without variable clinical manifestation and progression of diseases. Chronic hyperglycemia can cause dyslipidemia, hypothyroidism and elevated thyroid stimulating hormone, CVD, renal diseases, neurological problems and recurrent infections [10]. T2DM is associated with a cluster of interrelated plasma lipid and lipoprotein (Lp) abnormalities that are all recognized as predictors for CHD. Elevated levels of Lp (a), a well-known independent predictor of CVD, has also been reported in diabetics [11]. DM induces a state of dyslipidemia with abnormalities in all Lp, namely, chylomicrons, very low density Lp, LDL, and HDL. The pattern of dyslipidemia, however, may vary among patients with T1DM and T2DM. Other studies have indicated that an increased triglyceride level is an independent risk factor and a predictor for the development of coronary artery disease (CAD), especially in T2DM. Frequent co-existence of hypertriglyceridemia and low HDL possesses a greater risk for CAD development [12]. Thus, there is a need to evaluate lipid profiles in T2DM population and determine the trends of the major lipid risk factors for CAD. Subsequently, this is an additional criterion for our physicians in making decisions about therapeutic and dietary measures in T2DM patients. Hence, the present study aims to give a better insight on the levels of HDL and LDL status and their correlation between these two parameters in T2DM subjects of Nepal.

METHODS

Experimental design

This case-control study was carried out in Lumbini Medical College, Palpa, Nepal, on a total of 100 subjects, with 50 controls as healthy non-diabetic cases (control group) and 50 T2DM patients (experimental group). The aim was to study the plasma HDL and LDL-cholesterol, among the experimental group and the control group. A total of 50 T2DM subjects were recruited for the study, among which 34 were males, and 16 were females, in the age group of 40-70 years (Table 1). All the experiments were carried out as per national guidelines and protocols, approved by Institutional Human Ethical Committee. Patients with

conditions that may affect the serum Lp concentrations, such as renal failure, hypertension, pregnancy, were excluded from the study. Other exclusion criteria were chronic alcoholism, drug addiction and familial disorders of Lp metabolism. Alternatively, a total of 50 healthy subjects without any history of DM, major illness or factors, which may alter the concentration of serum lipids, formed the control group. A total of 50 control subjects were recruited for the study, among which 27 were males, and 23 were females, in the age group of 40-70 years (Table 1).

Biochemical analyses

From the patients, venous blood sample were collected after overnight (12 hrs) fasting, in fluoride vacutainer and samples was centrifuged to obtain plasma for the determination of fasting blood sugar (FBS), serum HDL, serum LDL by using BS 300 fully automated chemistry analyzer (mindray) and the values were documented for statistical analysis.

Analysis of plasma glucose

Plasma glucose values were measured by following enzymatic photometric glucose oxidase-peroxidase (POD, KEE GAD Biogen), method using BS-300 fully auto chemistry analyzer (Guangdong, China) [13] with biological reference interval of 70-110 mg/dl for fasting plasma glucose.

Analysis of serum HDL and LDL cholesterol

Serum HDL and LDL were analyzed by enzymatic cholesterol oxidase-POD (Lifechem) immunoinhibition photometric method using BS-300 fully auto chemistry analyzer (Guangdong, China) [14] with biological reference of HDL cholesterol >40 mg/dl, LDL cholesterol <130 mg/dl.

Statistical analyses

Descriptive statistical analysis has been carried out in this present study. Results on continuous measurements are presented as mean (standard deviation) (min-max) and results on categorical measurements are presented in a number (%). Significance is assessed at $p<0.05$. Analysis of variance has been used to find the significance of study parameters between three or more groups of patients, Student's *t*-test (two-tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups inter-group analysis. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Pearson correlation of HDL and LDL cholesterol was computed both in control subjects and T2DM patients [15,16]. Significant figures: +suggestive significance ($p<0.05$, $p<0.10$), *moderately significant ($p<0.01$, $p\leq0.05$), **strongly significant ($p\leq0.01$). To carry out the statistical analysis, SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 were used for the analysis of the data.

RESULTS

The mean age of T2DM patients and the corresponding control group was 54.3 (8.48) (years) and 53.4 (7.95) (years) respectively, that showed a significance at $p=0.569$; whereas, the percentage of gender in studied population showed that control group consisted of 54% male and 46% female while, among T2DM patients 68% are male and 32% are female, showing a significance at $p=0.151$. Hence, the results suggest that the study comprised of equal distribution of age group and gender (Table 1).

The FBS and serum LDL cholesterol levels were significantly elevated in the case group (164.5 [51.17], 121.4 [27.89] respectively) with respect to the control group (95.4 [10.09], 103.6 [30.67] respectively), which implies a strong significance at $p<0.001$ and $p<0.003$ respectively (Fig. 1a and c). Whereas, HDL cholesterol levels are found to be lower in patients (39.2 [7.96]) than the control group (44.0 [10.57]), which also shows a moderate significance at $p=0.011$ (Fig. 1b).

A strong significance was observed between two groups with low, i.e., <40 mg/dl and moderate serum HDL cholesterol levels, i.e., 40-60 mg/dl ($p<0.001$). Significantly lower HDL cholesterol levels were seen in the case group than in controls (76% in controls versus

Table 1: Comparison of age and gender distribution of subjects studied

	N (%)	
	Controls	**Cases**
Age (in years)		
41-50	22 (44.0)	18 (36.0)
51-60	19 (38.0)	20 (40.0)
61-70	9 (18.0)	12 (24.0)
Total	50 (100.0)	50 (100.0)
Mean±SD	53.4±7.95	54.3±8.48
Gender		
Male	27 (54.0)	34 (68.0)
Female	23 (46.0)	16 (32.0)
Total	50 (100.0)	50 (100.0)

Samples are age matched with $p=0.569$. Samples are gender matched with $p=0.151$. SD: Standard deviation

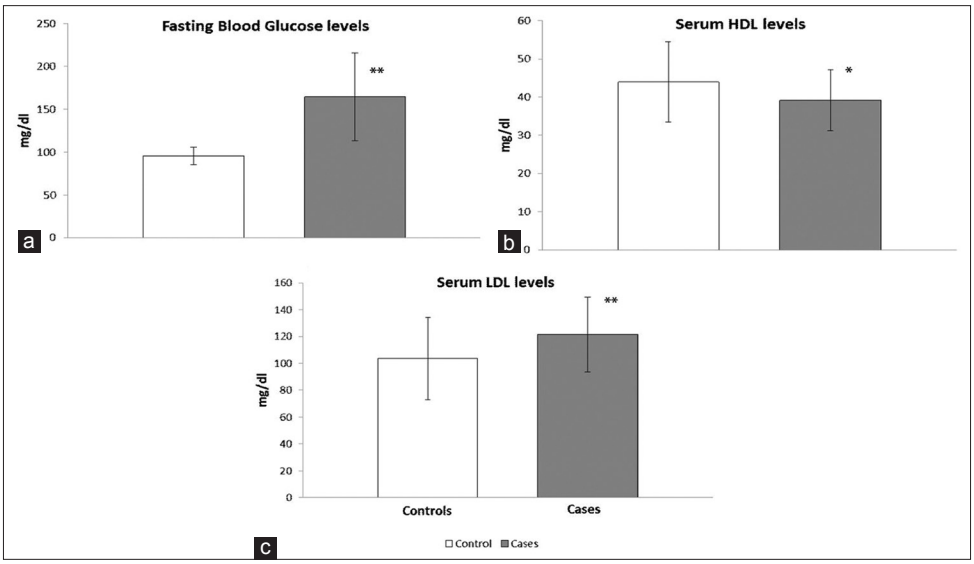

Fig. 1: Fasting blood sugar levels in control and cases. Each bar denotes mean±standard deviation respective groups. Mean values are significantly different at **p<0.001, *p<0.011

32% in T2DM patients, where HDL <40.0 mg/dl and 60% in controls versus 22% in patients, where HDL was in between 40 and 60 mg/dl). Whereas there was, no significance observed between control and case groups where HDL cholesterol levels where high, i.e., >60 mg/dl (p=0.362) (Table 2).

Serum LDL levels of T2DM patients also showed an increase in moderate, i.e., 130-159 mg/dl, and high serum LDL cholesterol levels, i.e., 160-189 mg/dl (Table 2). Whereas a significant difference was observed in LDL:HDL ratio was observed between control and T2DM (Fig. 2).

Fig. 3 shows a significant negative correlation between HDL and LDL cholesterol (r=−0.221) between the two groups.

DISCUSSION

T2DM is a chronic degenerative disease of epidemic proportion and is one of the major challenges to public health [17,18]. There are many experimental as well as clinical studies about the cause and occurrence of this disease, along with its correlation to other physiological functions in various species [19-21]. In this present investigation, the mean age of studied T2DM patients and control subjects were 54.3 (8.48) and 53.4 (7.95) respectively. Based on the findings of this study, there appears to be no sex predilection for T2DM that is in compliance with other publications that report no significant differences in the prevalence of T2DM between males and females [22,23].

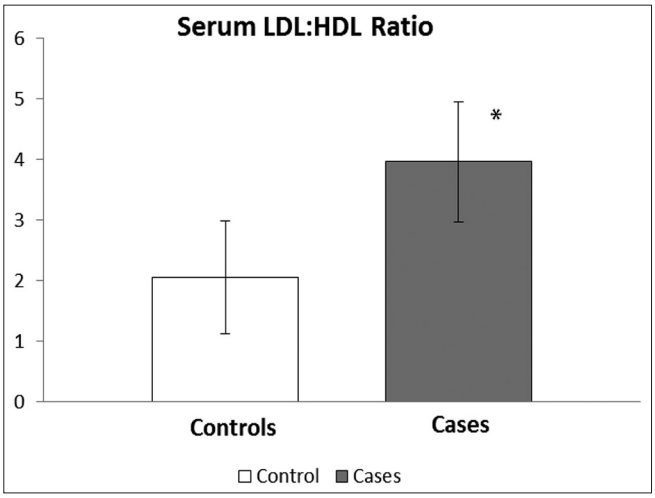

Fig. 2: Low density lipoprotein:High density lipoprotein cholesterol ratio in controls and Type 2 diabetes mellitus patients

DM comprises of a group of disorders that share a phenotype of hyperglycemia. The complications are an important cause of morbidity and mortality in the diabetic patients. In this report, the fasting blood glucose levels are found to be significantly (p<0.001) elevated in T2DM patients, when compared to their control counterparts, which is consistent with earlier reports by other researchers [24-26]. Similar finding is also reported in experiments with T2DM animal models [27,28].

HDL cholesterol was low in Type 2 patients when compared to control. The decrease was found to be moderately significant (p=0.011) in T2DM patients. Similar studies have been reported by Harno *et al.,* [29] in which they reported a reduction in HDL cholesterol in Type 2 diabetic patients due to the increased activity of hepatic lipase, which plays an important role in HDL metabolism. However, controversial studies also have been reported where no significant change in HDL cholesterol levels in diabetic patients were reported [17]. HDL cholesterol concentration is strongly and independently related to CAD, but the relationship is inverse a low HDL cholesterol being an important predictor of CHD and whereas high levels of HDL cholesterol is protecting against CHD. Hence, a possible explanation for these findings is the role played by HDL

Table 2: Different HDL and LDL levels in control subjects and T2DM patients

	n=50 (%)		p value
	Controls	Cases	
HDL			
Low (<40.0 mg/dl)	16 (32.0)	38 (76.0)	<0.001**
Borderline (40-60 mg/dl)	30 (60.0)	11 (22.0)	<0.001**
High (>60 mg/dl)	4 (8.0)	1 (2.0)	0.362
LDL			
Optimal (<100 mg/dl)	22 (44.0)	12 (24.0)	0.057
Normal (100-129 mg/dl)	18 (36.0)	19 (38.0)	1.000
Borderline high (130-159 mg/dl)	8 (16.0)	12 (24.0)	0.454
High (160-189 mg/dl)	2 (4.0)	7 (14.0)	0.160
Very high (≥190 mg/dl)	0	0	-

HDL: High density lipoprotein, LDL: Low density lipoprotein, T2DM: Type 2 diabetes mellitus

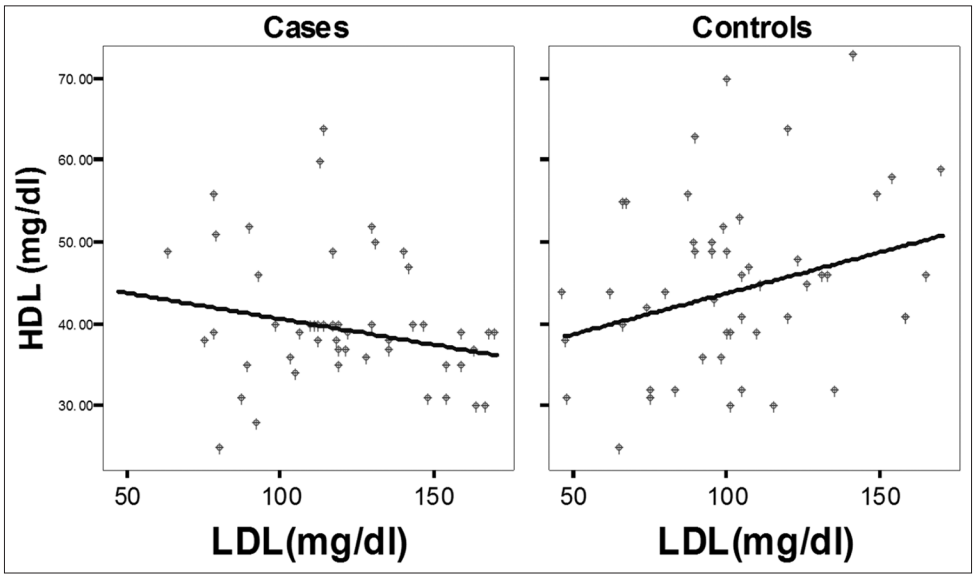

Fig. 3: Pearson correlation between high density lipoprotein and low density lipoprotein cholesterol

cholesterol in reverse cholesterol transport as an acceptor of cellular free cholesterol [30].

Dyslipidemia occurs frequently in T2DM; although, the most common dyslipidemic profile in T2DM is a hyper triglyceridemia and low HDL cholesterol levels. In this present study, LDL cholesterol is found to be elevated significantly ($p<0.003$) in Type 2 diabetic patients. However, there was a correlation between LDL cholesterol in Type 2 diabetic patients. The above findings are consistent with some observations by other workers [27,31]. Thus, the results obtained from the present study have confirmed the previous observations of increased LDL and decreased HDL cholesterol levels in diabetic patients [32]. Some reports also suggested that differences in LDL receptor genes in T2DM patients also results in abnormal lipid metabolism [33].

Though, metabolic reasons for lower HDL levels have not been fully documented, decreased synthesis of HDL has been found in some studies [34-37]. Schmitt *et al.* suggested that LDL uptake by fibroblasts may be impaired in Type 2 diabetics. This may lead to an increase in LDL cholesterol levels and decrease in HDL cholesterol levels and an increase in the LDL:HDL ratio in Type 2 diabetics. In our study, LDL:HDL ratio differs significantly between control and diabetics. Similar results have also been forwarded by Singla *et al.* [40]. This is quite similar to our study showing a negative correlation between LDL and HDL cholesterol ($r=-0.221$) in diabetics.

CONCLUSION

Estimation of serum HDL cholesterol and LDL cholesterol in T2DM is quite reliable and valid as it may serve as a useful monitor for the prognosis of dyslipidemia and risk to CVD in patients. The results of the present study suggest that FBS and serum LDL cholesterol levels were elevated in T2DM subjects, whereas, serum HDL cholesterol level was reduced statistically, resulting in increased LDL: HDL ratio in patients. Thus, a significant negative correlation was observed between serum HDL and LDL cholesterol levels in diabetic subjects.

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