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Biochemical Profile in Type 2 Diabetes Mellitus with Special Reference to Dyslipidemia: A Retrospective Study

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ABSTRACT

Aim: This study is intended to determine the biochemical profile in type 2 diabetes mellitus with special reference to dyslipidemia. Methods: This study was conducted in 100 human subjects, out of which 50 were normal healthy individuals (control group) and 50 were with type 2 diabetes mellitus. The plasma glucose, serum total Cholesterol, Triglycerides, HDL-Cholesterol, Uric acid, Urea, creatinine, Total bilirubin, Serum Glutamate-Oxaloacetate Transaminases (SGOT/AST) and Serum Glutamate-Pyruvate Transaminases (SGPT/ALT) was estimated by using semi-automated enzymatic analyzer (Micro lab-300, Merck, Mumbai, India). The serum LDL- Cholesterol and VLDL-Cholesterol were estimated by Friedwald's Formula. Results: The fasting blood sugar, post-prandial blood sugar, total cholesterol, triglycerides and VLDL-cholesterol were statistically significant ($P < 0.001$) as compared to control group while VLDL-cholesterol was statistically significant ($P < 0.01$) as compared to control group. The uric acid was statistically significant ($P < 0.05$) as compared to control group but the HDL-cholesterol, serum creatinine, urea total bilirubin, direct bilirubin, SGOT and SGPT were not statistically significant as compared to control group. Conclusion: The high prevalence of dyslipidemia in t2DM patients plays a major role in the development of cardiovascular diseases. The optimal care of diabetic patients should include routine monitoring of blood sugar and serum lipid profile. Aggressive lifestyle changes, such as weight reduction and physical exercise should be initiated first followed by medication with lipid lowering drugs. The optimum treatment with antidiabetic drugs to obtain fair glycaemic control should go hand-in-hand with lipid-lowering drugs.

Keywords: Type 2 diabetes mellitus**,** dyslipidemia, liver function test, kidney function test.

INTRODUCTION

Diabetes Mellitus is a serious health hazard all over the world [1]. In the South East Asian region of which India is a part, there were 72 million adults with diabetes mellitus in 2013 and it is expected to rise to more than 123 million by 2035 [2]. India, the largest country in this region, has 65.1 million individuals with diabetes mellitus and it is second only to the China in the world [3]. The frequency of diabetes mellitus is increasing many folds in South Asian population due to the high degree of genetic predisposition and high susceptibility to environmental factors, characterized by a high BMI, high upper body adiposity, a high body fat percentage and a high level of insulin resistance [4]. All forms of diabetes are characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism [5].

The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels [6]. As diabetes is a metabolic disorder, people with diabetes are in a risk of other associated complications. Several changes that occur are due to high rise in blood sugar levels

and hence diabetes is associated with long-term complications that affect almost every part of the body. Diabetes is associated with significantly accelerated rates of several debilitating micro-vascular complications such as nephropathy, retinopathy, neuropathy and macro-vascular complications such as atherosclerosis and stroke [7]. The term "dyslipidemia" is increasingly popular to describe abnormal changes in lipid profile, replacing the old term "hyperlipidemia". Dyslipidemia encompasses changes in high density lipoprotein cholesterol (HDL-C), the size and density of Low density lipoprotein cholesterol (LDL- C), very low density lipoprotein cholesterol (VLDL-C) and triglyceride (TG) level. The term diabetic dyslipidemia comprises a triad of raised triglycerides, reduced HDL-C and excess of small, dense LDL particles [8]. The lipid abnormalities are prevalent in diabetes mellitus because insulin resistance or deficiency affects key enzymes and pathways in lipid metabolism [9].

The present study was carried out to find the serum lipid profile, liver function test, uric acid and kidney function test in type 2 diabetes mellitus subjects in view of the hypothesis that early detection and treatment of biochemical abnormalities can minimize the risk for micro-vascular and macro-vascular complications associated with type 2 diabetes mellitus. It is a retrospective study based on the available biochemical data of type-2 diabetic patients visiting the Biochemistry department for biochemical investigations, after prescription and medication from OPD and IPD of the Regional Ayurveda Research Institute for Drug Development Gwalior, (M.P.). Blood sugar, lipid profile, liver function test, uric acid and kidney function test were performed to assess the biochemical profile of the subjects.

Material and Methods:

Subjects: This retrospective study was carried out in the Biochemistry and Pathology laboratory of Regional Ayurveda Research Institute for Drug Development Gwalior, (M.P.) India. Cases reported for type 2 diabetes mellitus were selected for this study. The study was conducted in 100 human subjects out of which 50 were normal healthy individuals (control group) and 50 were with type 2 diabetes mellitus. All the patients were on medication with oral Ayurvedic drugs. The patients reported with other ailments and metabolic disorders were excluded from the study. The individual information about clinical symptoms, weight, height and diagnosis by the hospital physicians were well documented in medical records of the hospital. All necessary permission were taken prior and during this study.

Sample collection and preparation: 5 ml of blood sample was withdrawn from the antecubital vein following overnight fasting .The blood sample was collected in plain vacutainers and was incubated at 37°C for 30 minutes in the same. After incubation, clot was removed and remaining sample was taken in centrifuged test tube. Samples were centrifuged at 3000 rpm for 10 to 20 minutes. Supernatant collected in clean and dry test tube for analysis of biochemical test.

Estimation of Biochemical parameters: The plasma glucose, serum total Cholesterol, Triglycerides, HDL-Cholesterol, Uric acid, Urea, creatinine, Total bilirubin, Serum Glutamate-Oxaloacetate Transaminases (SGOT/AST) and Serum Glutamate-Pyruvate Transaminases (SGPT/ALT) were estimated by GOD/POD method, oxidase/peroxidase method, glycerol phosphate oxidase/peroxidase method, direct detergent method, Uricase Peroxide enzymatic method, Glutamate dehydrogenase – Urease method, Jaffe's method, Acid- Diazo method, dynamic extended stability (modified IFCC) method and dynamic extended stability (modified IFCC) method respectively using semi-automated enzymatic analyzer (Micro lab-300, Merck, Mumbai, India). The serum LDL- Cholesterol and VLDL-Cholesterol were estimated by Friedwald's Formula: LDL-Cholesterol = TG- (HDL-C + VLDL-C) and VLDL- Cholesterol = TG/5.

Statistical analysis: The data obtained was analyzed for significance between the type 2 diabetes mellitus patients and control groups by using the Statistical Package for the Social Sciences, version 23.0 (SPSS software).

Results: The fasting blood sugar, post-prandial blood sugar, total cholesterol, triglycerides and VLDL-cholesterol were statistically significant ($P < 0.001$) as compared to control group while VLDL-cholesterol was statistically significant ($P < 0.01$) as compared to control group. The uric acid was statistically significant ($P < 0.05$) as compared to control group but the HDL-cholesterol, serum

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creatinine, urea total bilirubin, direct bilirubin, SGOT and SGPT were not statistically significant as compared to control group shown in table 1. The comparative changes of blood sugar, lipid profile, liver function test, uric acid and kidney function test were shown in figure 1, 2, 3 and 4 respectively.

Table 1: Showing the comparative changes of the biochemical profile of T2DM patients and control subjects

Group	Control subjects	T2DM patients
	Mean ± SD	**Mean ± SD**
Fasting Blood Sugar (mg/dl)	80.27 ± 7.8	253.48 ± 111.27***
Post Prandial Blood Sugar (mg/dl)	119.41 ± 27.14	350.11 ± 129.74***
Total cholesterol (mg/dl)	177.1 ± 40.7	220 ± 67.5***
Triglycerides (mg/dl)	120.99 ± 57.1	197.6 ± 94.3***
HDL- Cholesterol (mg/dl)	32.79 ± 10.3	34.77 ± 12.5 ^{NS}
LDL- Cholesterol (mg/dl)	120.09 ± 36.86	146.07 ± 63.19**
VLDL- Cholesterol (mg/dl)	24.18 ± 11.42	39.52 ± 18.84***
Uric acid (mg/dl)	4.16 ± 1.68	3.47 ± 1.49*
Creatinine (mg/dl)	0.80 ± 0.58	0.85 ± 0.38 ^{NS}
Urea (mg/dl)	26.92 ± 10.74	28.68 ± 10.16 ^{NS}
Total Bilirubin (mg/dl)	0.93 ± 0.7	0.88 ± 0.4 ^{NS}
Direct Bilirubin (mg/dl)	0.38 ± 0.4	0.49 ± 0.3 ^{NS}
SGOT (IU/L)	37.1 ± 10.6	36.5 ± 11.5 ^{NS}
SGPT (IU/L)	34.3 ± 18.8	36.3 ± 22.8 ^{NS}

*Statistically significant ($P < 0.05$) as compared to control group

**Statistically significant ($P < 0.01$) as compared to control group

***Statistically significant ($P < 0.001$) as compared to control group

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Figure 1: Showing the comparative changes of fasting and post-prandial blood sugar of T2DM patients and control subjects

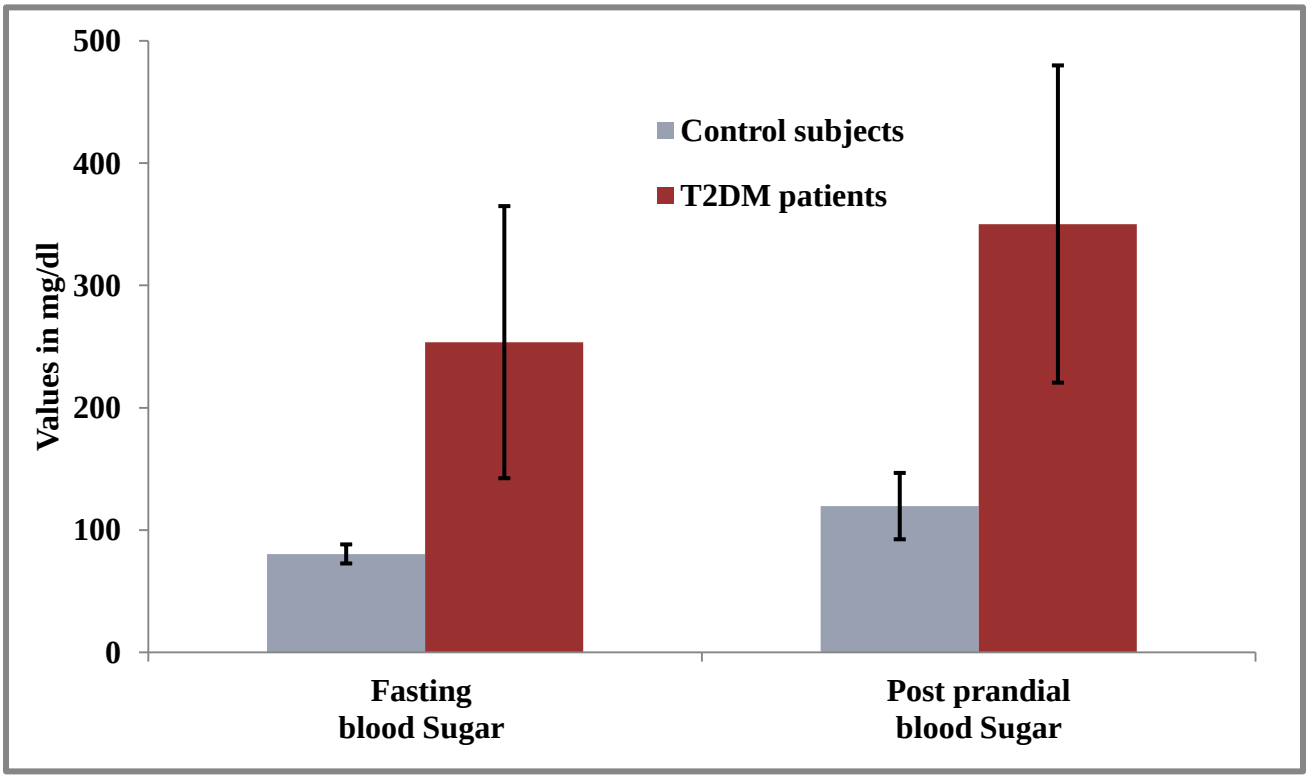

Figure 2: Showing the comparative changes of lipid profile of T2DM patients and control subjects

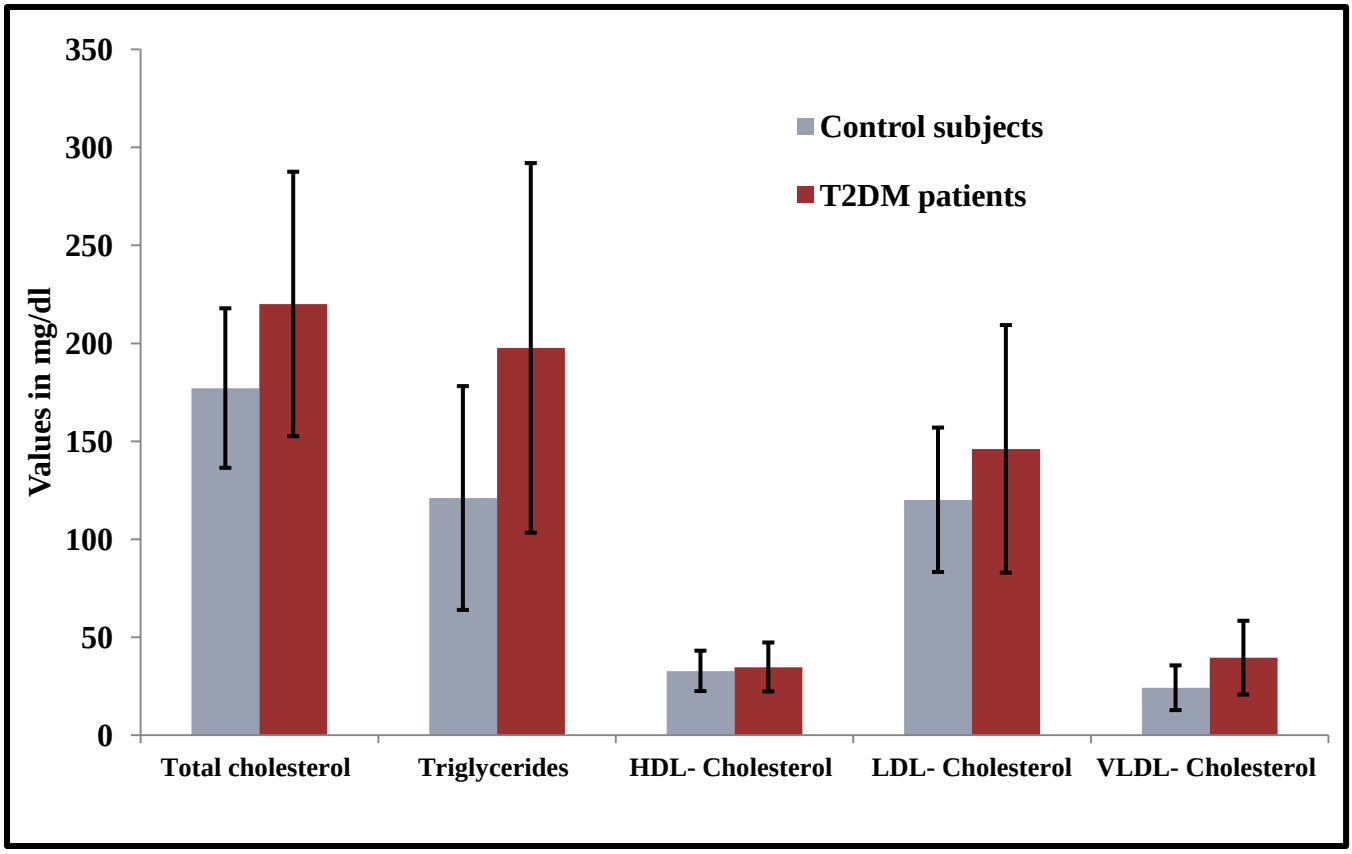

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Figure 3: Showing the comparative changes of liver function test of T2DM patients and control subjects

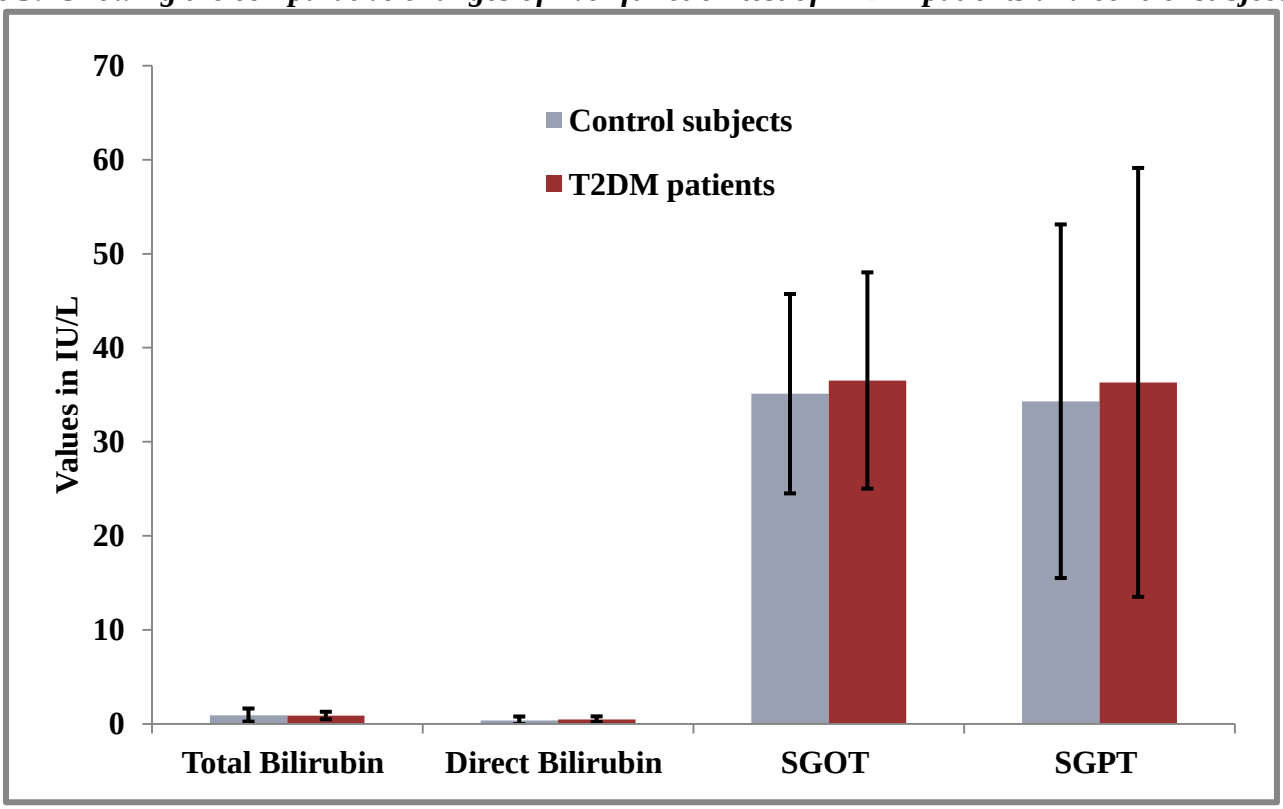
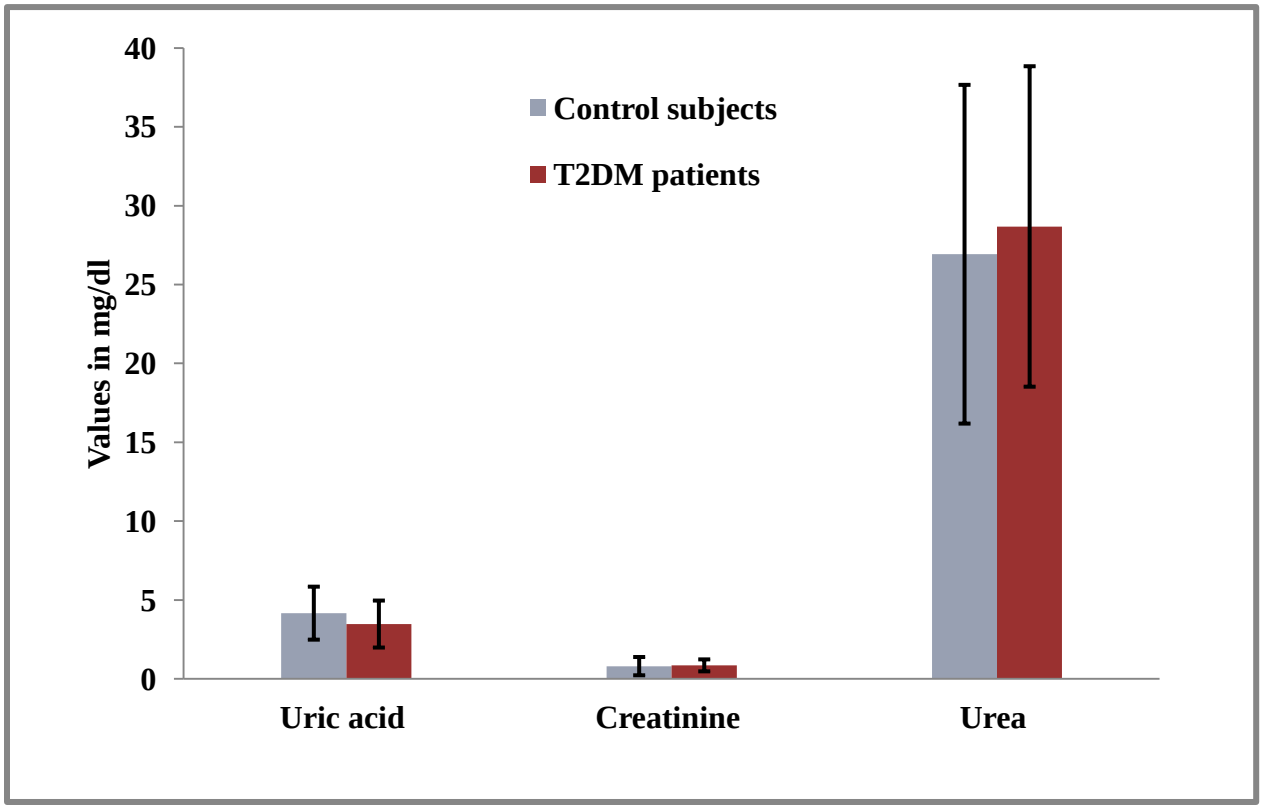


Figure 4: Showing the comparative changes of uric acid and kidney function test of T2DM patients and control subjects



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Discussion: Diabetes mellitus is a complex disorder affecting the metabolism of carbohydrate, protein and lipids. Hyperglycemia is known to play a pathogenic role due to the excess formation of glucose-derived end products. Results of the blood sugar profile suggest that all individuals of diabetic groups were hyperglycemic. It was also observed that some patients have controlled FBS, but their PPBS were uncontrolled. Therefore, the range of FBS in some patients looks nearly normal or controlled; while in few patients it was uncontrolled.

The relation between diabetes mellitus and serum lipid profile had been much discussed during the past decades [10-13]. Both lipid profile and diabetes have been shown to be the important predictors for metabolic disturbances including dyslipidemia, hypertension, cardiovascular diseases, hyperinsulinemia etc [14]. Over 70% of patients with diabetes mellitus had one or more types of dyslipidemia. Similarly, our results reveal high prevalence of hypercholesterolemia, hypertriglyceridemia and high LDL-C levels, which are well known risk factors for cardiovascular diseases among patients. These patients were on high-risk without complications but already had significant dyslipidemia, which enhances the risk of cardiovascular events, certainly required therapeutic intervention.

In diabetes many factors may affect blood lipid levels, because of interrelationship between carbohydrates and lipid metabolism. Therefore, any disorder in carbohydrate metabolism leads to disorder in lipid metabolism and vice versa. Insulin resistance is a primary defects in the majority of diabetes mellitus patients. In non - diabetic individuals insulin resistance in combination with hyperglycaemia has a strong predictive value for future development for diabetes [15]. Several studies showed that insulin affects the liver apolipoprotein production and regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein, which causes dyslipidemia in diabetes mellitus. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase [16]. Abbate and Brunzell reported that the increase in triglycerides in poorly controlled patients was related to the decrease of activities of adipose tissue and muscle lipoprotein lipase activity [17].

A study by Packard et al., reported that reduced HDL-C as a powerful predicator for premature coronary heart diseases [18]. Goldberg reported that hyperglycaemia progressively increases the transfer of cholesterol esters from HDL-C to VLDL-C particles, hence, denser LDL particles acquire a large proportion of these HDL esters, further diminishing the HDL-C level [14]. In addition, HDL-C is a substrate for hepatic lipase which converts it into smaller particles, which are readily cleared from the plasma. As with the triglycerides, improvement in glycemic control leads to an increase in the levels of HDL-C and suggest the evidence for a role for poor glycaemia in decreasing the level of this lipoproteins [15]. Poor insulinization results in increased lipolysis in adipocytes. The resulting increase in fatty acid transport to the liver, which is a common abnormality in diabetes, may cause an increase in VLDL-C. Insulin directly degrades the Apo B (which is the major protein of VLDL particles) and thus insulin may increase secretion of Apo B (and then VLDL) [19].

The level of total cholesterol is usually normal or near normal if glycemic control is adequate and worsening of control raises the level [20]. Therefore, improving glycemic control can substantially reduce the risk of cardiovascular events in diabetic patients. As the occurrence of dyslipidemia depends on factors such as insulin action on peripheral tissues and liver, apoprotein production and regulation of lipoprotein lipase, the duration of diabetes seems to play only a minor role in modifying these factors.

Liver dysfunction is a known association with diabetes. The different liver abnormalities in diabetes cover the entire spectrum from asymptomatic transamnitis to cirrhosis. However, we have not found any significant difference in the selected liver function test, while many authors have reported prevalence of abnormal liver function in patients with type 2 diabetes mellitus.

Gonem et al., tried to assess the prevalence of abnormal liver function tests in patients with diabetes mellitus [21]. Salmela et al., studied the prevalence of abnormal LFTs and their relationship to clinical findings in 175 unselected diabetic outpatients in

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Finland. Fifty-seven percent of the 175 diabetic outpatients (100 subjects) had at least one abnormal LFT; 27% (48 subjects) had at least two abnormal tests [22]. It is also hypothesized that elevation in alanine aminotransferase (ALT), a gluconeogenic enzyme whose gene transcription is suppressed by insulin, could indicate impairment in insulin signalling rather than purely hepatocyte injury [23]. Ohlson et al., found elevated ALT in non- diabetic Swedish men to be a risk factor for type 2 diabetes, independent of obesity, body fat distribution, plasma glucose, lipid, aspartate aminotransferase (AST), bilirubin concentrations and family history of diabetes [24].

Our study demonstrated significant difference in the uric acid content while kidney function i.e. urea and creatinine showed no significant difference. Levels of uric acid increased in serum of diabetic group as compared to control and this effect was also more profound in male than in female diabetics. In correlation studies, urea showed strong positive correlation with creatinine which is in agreement with the previous studies.

When blood sugar is high, it can put too much stress on kidneys causing serious damage to the blood vessels, leading to kidney disease. Generally, urea and creatinine are the parameters to diagnose functioning of the kidney [25]. Changes in serum creatinine concentration more reliably reflect changes in glomerular filtration rate (GFR) than do changes in serum urea concentrations. Urea formation is influenced by a number of factors such as liver function, protein intake and rate of protein catabolism [26]. If levels of creatinine rise, then kidneys may be malfunctioning.

Dyslipidemia management in people with diabetes mellitus, just like in any other individual, starts with a thorough evaluation that aims to identify secondary causes that might contribute to the abnormal lipid profile [27]. Lifestyle changes, including increased physical activity and dietary modifications, are the cornerstones of management. The highest priority for diabetic individuals who have poor glycemic control should be to achieve near normal blood glucose levels, in the expectation that this approach will also improve dyslipidemia.

Our study clearly shows that lipid fractions are abnormal in diabetes mellitus. Liver function test and renal function test are found normal in diabetic patients as compared to control. Realizing that most of the diabetics have a high probability of developing cardiovascular and cerebrovascular disease, it is essential that an individual who is diabetic should take care of dyslipidemia. Our study clearly suggests the dominance of hyperlipidemia over increased prevalence of dyslipidemia. Prospective and longitudinal studies are needed at the time of diagnose to estimate true population prevalence of dyslipidemia in patients with diabetes mellitus.

Conclusion: In the present study, the biochemical profile i.e. blood sugar, lipid profile, renal function test, liver function test etc. of patients with type 2 diabetes mellitus along with control were performed. Results suggest a high prevalence of dyslipidemia, which might be playing a major role in the development of cardiovascular diseases among diabetic patients. The optimal care of diabetic patients should include routine monitoring of blood sugar and serum lipid profile. Aggressive lifestyle changes, such as weight reduction and physical exercise should be initiated first followed by medication with lipid lowering drugs. The optimum treatment with antidiabetic drugs to obtain fair glycaemic control should go hand-in-hand with lipid-lowering drugs.

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