Original Research Article

Lipid profile in type 2 diabetes mellitus: a case-controlled study

Babu Rajendran*, Seetha Rami Reddy Mallampati, Sheju Jonathan Jha J., Shameer Hakkim

Department of General Medicine, Vinayaka Missions Medical College, Vinayaka Mission Research Foundation- DU, Karaikal, Pondicherry, India

*Correspondence:
Dr. Babu Rajendran,
E-mail: rajivan777@gmail.com

ABSTRACT

Background: Atherosclerosis is caused by the combination of type 2 diabetes mellitus and dyslipidemia. Combination of DM and dyslipidemia is associated with increased mortality and morbidity. Hence, it is of utmost importance to know the nature of dyslipidemia in DM for its effective management. The major lipid abnormalities seen in DM are elevated triglyceride levels and lowered HDL-C levels.
Methods: A case-controlled study was initiated in Vinayaka Missions Medical college and hospital for a period of 2 year. Pre-prandial and post-prandial lipid profile was assessed in 50 cases of type 2 DM and was compared with age and sex matched healthy controls satisfying the inclusion and exclusion criteria.
Results: At the end of the study, the mean age±SD was 48.5±5.68 years. The mean HbA1c±SD of the study population was found to be 7.48±1.517. Looking at the lipid profile all cases in fasting state had elevated VLDL-C levels (mean 50.39±60.27), elevated TC (mean 169.70±39.917), elevated TGL (mean 146.04±60.140) and low LDL-C (mean 92.3±27.699) when compared to control group. In the postprandial state, there was a significant raise in TGL level (mean 188±68.59), raised TC (mean 180.74±38.46), decreased HDL-C (mean 38.761±9.028) compared to the fasting state.
Conclusions: Lipid profile of type 2 DM in pre-prandial 12 hour fasting state showed elevated TC, VLDL-C levels and low LDL-C and HDL-C levels. Where as in post prandial state TGL levels were markedly elevated with elevated TC and low HDL-C levels.

Keywords: Diabetic patients, Dyslipidaemia, Diabetes mellitus, HDL-C, Prandial lipid, VLDL-C level

INTRODUCTION

Diabetes Mellitus (DM) is a state of prolonged hyperglycemia due to underlying metabolic pathology. It is a group of common metabolic disorders that share the phenotype of hyperglycemia. Type 2 diabetes mellitus which is due to insulin resistance with relative insulin deficiency presents with frequent urination (polyuria), increased thirst (polydipsia) and increased hunger (polyphagia). The long-term complication includes CAD, stroke, kidney failure, non-healing ulcer, retinopathy. The complications develop when the disease is left untreated or inadequately and inefficiently managed.[1]

Being a chronic entity, in individual with diabetes mellitus, an estimated loss of 10 years in the life span is observed. It is also regarded as disease of the vasculature causing inflammatory changes, a two to four-fold rise in

the risk of coronary artery disease is seen. Diabetes mellitus is also regarded as the leading cause for renal impairment and non-traumatic blindness. When peripheral arteries are involved a 20-fold rise in the risk of limb amputation is observed. A grave combination of diabetes mellitus with dyslipidemia predisposes to vascular inflammation and there by atherosclerosis. Various studies have shown that the major lipid abnormality observed in diabetes mellitus includes elevated triglyceride levels and low HDL-C levels.

Insulin resistance and relative insulin deficiency is the major pathology behind type 2 diabetes and it is almost always associated with lipid disorder in the form of elevated triglyceride levels and low HDL-C levels.[1]

According to the Strong Heart study conducted in American Indian population, elevated LDL-C is the single most common cause and risk factor for coronary artery disease. It is also suggested that LDL-C directly proportional to the risk of coronary artery disease. It is also a named risk predictor for coronary artery disease. Diabetes mellitus has microvasculature and macrovascular complications which manifest as retinopathy, nephropathy, dermatopathy, coronary and cerebral artery disease, peripheral artery disease, etc. It is found that atherosclerosis is the major cause of mortality and morbidity in diabetes mellitus.[2]

According to American Heart Association, European society of cardiology, National Cholesterol Education Program, diabetes mellitus is regarded as a coronary heart disease equivalent. It is also suggested that to reduce the CHD risk, a prompt treatment for glycemic control, hypertension control and lipid management is suggested. Coronary artery disease is having equivalent risk compared to known diabetics. Even Americans Heart Association is mentioning that DM is equivalent to CAD. So, always for reducibly the CAD complications, we have to control the lipids and blood pressure.[3]

LDL cholesterol should be below 100mg/dL for CAD. Patients or CAD risk patients according for (ATP-III) and NCEP. If HDL less than 40mg/dL for men and less than 50mg/dL for women with TGL level more than 150mg/dL (both are risks for developing CAD/CHD).[4] These who are having diabetics or CAD target for LDL-C is less than 100mg/dL for DM type. A lower incidence of mortality and morbidity is observed when LDL-C is lowered adequately with treatment.

Higher LDL-C and lower HDL-C levels as contributors for atherogenicity. Prophylactic use of statins for high risk individuals have shown lower incidence of stroke and coronary artery disease. Also, high HDL-C is a predictor for protective effect from CAD or stroke or decreased atherogenic state.

Therapeutic Lifestyle Modification (TLC) is beneficial and it includes TLC diet (saturated fat <7% of calories,

cholesterol <200mg/day+high fibre diet), weight management, regular exercise/retraction of alcohol are the primary approach.

According to NCEP-ATP III guidelines (2001), LDL-CH <100mg/dL is considered optimal and 190mg/dL is very high. Desirable total-CH is <200mg/dL and ≥240mg/dL is considered high. HDH-CH <40mg/dL is considered low and ≥60mg/dl is considered high. A 9-12 hour fast is required to determine the lipoprotein levels. Coronary Heart Disease (CHD) risk equivalents includes clinical CHD, symptomatic carotid artery disease, peripheral artery disease and aortic artery aneurysm.

Risk factors that modify target LDL-CH levels are cigarette smoking, hypertension, low HDL-CH, family history of premature CHD (CHD in male first degree relative <55 years and CHD is first degree female relative <65years) men ≥45 years, women ≥55 years and type 2 diabetes mellitus. Risk categories includes CHD/CHD risk equivalents, 2+ risk factors and 0-1 risk factor.

Target LDL for CHD or CHD risk equivalents is <100mg/dl, ≥100mg/dl warrants therapeutic lifestyle changes (TLC) and ≥130mg/dl requires drug therapy. Goal LDL for 2+ risk factors are <130mg/dL, ≥130mg/dl requires TLC and ≥160mg/dl requires drug therapy. Goal LDL for 0-1 risk factors is <160mg/dl, ≥160 requires TLC and ≥190mg/dl requires drug therapy.

Clinical identification of metabolic syndrome in men should satisfy any 3 of the following: abdominal obesity-waist circumference >102cms, triglycerides >150mg/dl, HDL-CH <40mg/dl, BP≥130/≥85mmHg and fasting glucose ≥110mg/dl.

Clinical identification of metabolic syndrome in women should satisfy any 3 of the following: abdominal obesity-waist circumference >88cms, triglycerides >150mg/dl, HDL-CH <50mg/dl, BP≥130/≥85mmHg and fasting glucose ≥110mg/dl. Triglycerides <150mg/dl is considered normal and ≥500mg/dl is considered very high.[5]

METHODS

The study was carried out in a reputed institution in the South Eastern India, Vinayaka Missions Medical College, Vinayaka Mission research foundation. After ethical committee clearance of the institute and gaining informed and written consent, a total of 50 patients with type 2 diabetes mellitus were included and were compared with 50 age and sex matched healthy controls fulfilling the inclusion and exclusion criteria.

The aim was to correlate the severity of dyslipidemia in type 2 DM with the duration of the disease by assessing the fasting lipid profile of type 2 DM and controls and to compare the fasting lipid with the post prandial lipid load in type 2 DM.

The patients with type 2 diabetes mellitus, between the age of 31-80 years were included. Patients with Type 1 diabetes mellitus, forms of diabetes mellitus other than type 2, suffering from liver disease, thyroid disorders, nephrotic syndrome, alcoholic and those on medications that affect lipid metabolism such as statins, beta blockers, thiazides and oral contraceptive pills were excluded.

Data for the proposed study was collected in a pretested proforma, which included various parameters like age, sex, occupation, religion, income, etc. Detailed history and physical examination of all the cases and controls were done.

Fasting and postprandial lipid levels were estimated in all the cases and controls. Blood was collected from patients after an overnight (12 hour) fast and six hours postprandial (after a standard meal) for lipid profile measurements.

Statistical analysis was carried out using SPSS version 16 for windows. A p value <0.05 was considered as significant.

RESULTS

In the present study, the study group constituted cases from age 31-80 years. The majority of cases and controls were in the age group of 41-60 years with the mean age of 48.5±5.68 years (Figure 1).
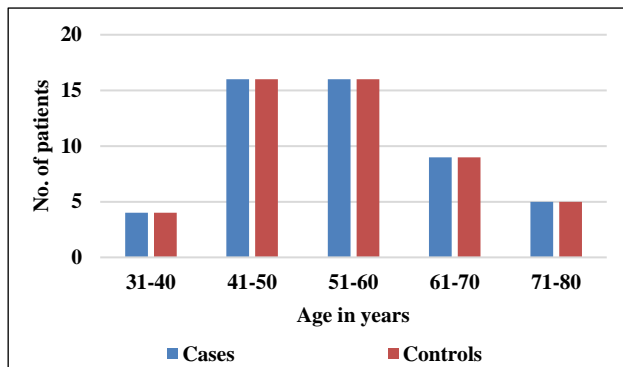

Figure 1: Age distribution of the cases and controls.

Male and female were equally distributed in this study (Table 1).

Table 1: Sex wise distribution of the cases and controls.

Sex	Male	Female
Cases	25	25
Control	25	25
Total	50	50

The mean HbA1C value among the cases was 7.48±1.517. There was no correlation between duration of diabetes and dyslipidemia (Table 2).

All the type 2 diabetes mellitus cases in the fasting state had a raised VLDL-C (mean 50.39±60.27), raised total cholesterol (mean 169.70±39.917) (Figure 2), raised TGL (mean 146.04±60.140) (Table 3), decreased LDL-C (mean 92.3±27.699) compared to the control group who had a VLDL-C (mean 32±22.372), total cholesterol (mean 168.02±34.65), TGL (mean 138.42±68.137), LDL-C (mean 105.02±36.432) in the normal range (Figure 3, Table 3).

Table 2: Duration of diabetes and the presence of dyslipdemia among the cases.

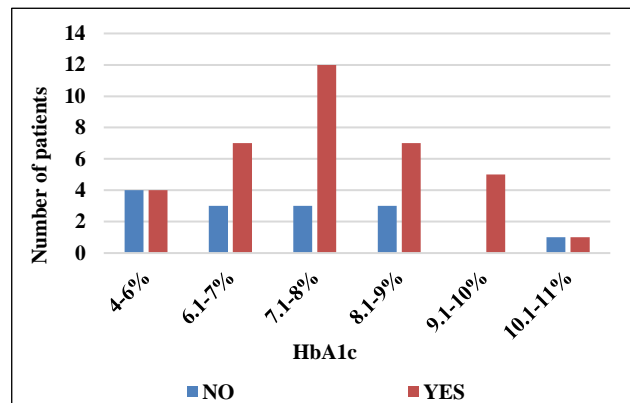| Duration of diabetes	No	Yes
Newly detected	1 (7.14%)	14 (38.88%)
1-5 years	7 (50%)	11 (30.55%)
6-10 years	3 (21.42%)	7 (19.44%)
11-15 years	2 (14.28%)	3 (8.33%)
>15 years	1 (7.14%)	1 (2.77%)
Total	14 (100%)	36 (100%)

Figure 2: Correlation between HbA1c value and dyslipidemia.

Table 3: Comparison of the mean fasting and post prandial triglyceride levels among the cases and controls.

Triglyceride (mg/dL)	Group	Mean	Standard deviation	N
Fasting	Case	146.04	60.14	50
	Control	138.4	68.137	50
	Total	142.22	64.138	100
Post prandial	Case	188.94	68.592	50
	Control	147.32	73.183	50
	Total	168.13	70.88	100

In the postprandial state, diabetes patients had a significant raise in TGL levels (mean 188±68.59), raised in total cholesterol (mean 180.74±38.46), decreased HDL-C (mean 38.761±9.028) (Figure 4) compared to the fasting state. There was significant increase in TGL (Table 3), total cholesterol and reduction in HDL-C in postprandial state compared to the fasting state (Figure 5, Table 3).
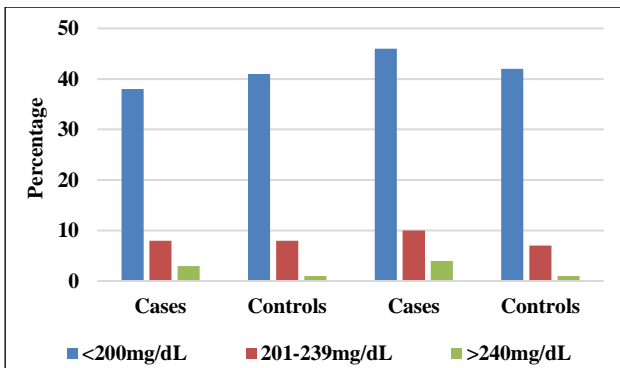
Figure 3: Fasting and post prandial total cholesterol levels among the cases and controls.
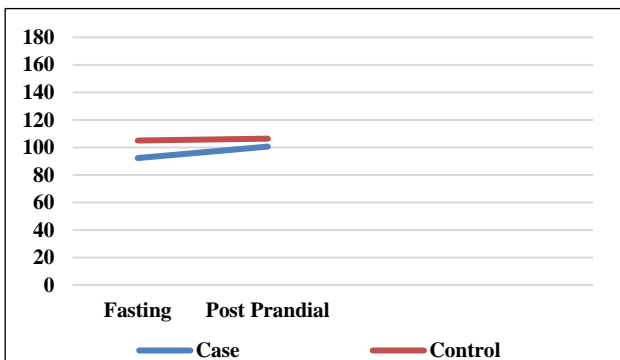

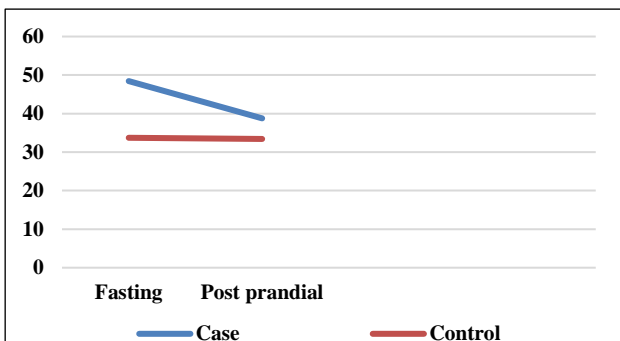**Figure 4: Comparison between mean fasting and post prandial LDL-C levels among cases and controls.**

Figure 5: Comparison of the mean fasting and post prandial HDL-C levels among the cases and controls.

DISCUSSION

In this study, pre-prandial 12 hour fasting and 6-hours postprandial lipid profile was done in 50 patients with type 2 diabetes mellitus and was compared with the fasting and postprandial lipid profile in 50 age and sex matched healthy controls, fulfilling the inclusion and exclusion criteria.

In this study, the study group constituted cases from age 31-80 years. The majority of cases and controls were in the age group of 41-60 years with a mean age of 57.02±12.43 years. In a similar study done by Addisu

YM et al, in South Africa, the mean age of the subjects was 53.8±12.2 years.[6] The results are consistent with a similar study done by Raj S et al, in the year 2005 at Trivandrum, India, wherein the mean age of the cases was 56.6±11.9 years and that of the controls was 53.5±12.7 years (Figure 1).[7]

In this study, 50% of the study group were males and 50% of the study group were females. The males and females were almost equally distributed with a male:female ratio of 1:1 (Table 1).

In this study, 72% of cases had dyslipidemia irrespective of duration of diabetes. It was found that there was no correlation between duration of diabetes and dyslipidemia as the p value 0.154 was not significant. Present study was consistent with the study done by Sumesh Raj et al (Table 2).[7]

In this study, 60% of the cases with dyslipidemia had poor glycemic control (HbA1C >7%) whereas 27% of the cases with dyslipidemia had good glycemic control (HbA1C <7%). This association has a p value of 0.738, which was statistically not significant. Hence, there was no correlation between HbA1c value and dyslipidemia. This differs from the study done by Haseeb Ahmad Khanin which HbA1C showed direct and significant correlation with TC, TG, LDL and inverse correlation with HDL (Figure 2).[8]

In this study, in the fasting state, 25% of cases had total cholesterol levels of >200mg/dL as compared with the controls where 18% of them had total cholesterol of >200mg/dL. This association has a p value of 0.133, which was statistically not significant. Hence, the pattern of distribution of patients in different cholesterol levels was found to be similar in both the cases and controls (Figure 3).

Similar observations were made in the studies done by Rajesh et al, however, in the study done by Raj S et al, it was found that diabetics had significantly higher levels of TC compared to the controls (p <0.05).[7]

In this study, the cases had a mean TC level of 169.70±39.917mg/dL in the fasting state and 180.74±38.76mg/dL in the postprandial state. The controls had a mean TC level of 168.02±34.65mg/dL in the fasting state and 165.06±39.27mg/dL in the postprandial state. This association has a p value of 0.854, which was statistically not significant.

Hence, there was no significant increase in the postprandial TC level in the cases compared to that of the controls.

Similar observations were made in the studies done by Sumesh Raj et al, 110 wherein the cases had a mean TC level of 209.45±40.27mg/dL in the fasting state and peak mean TC level of 232.45±53.13mg/dL in the postprandial

state. The controls had a mean TC level of 197.6±57.13mg/dL in the fasting state and peak mean TC level of 210.35±54.31mg/dL in the postprandial state.[7]

In this study, in the fasting state 31% of cases had LDL-C levels of <100mg/dL whereas 23% of controls had LDL-C of <100mg/dL. This association has a p value of 0.035, which was statistically significant. Thus, in the fasting state, the cases had a lower LDL-C levels compared to that of the controls (Figure 4).

This does not correlate with the study done by Raj S et al, and Raj S et al, which showed that LDL-C was higher in the diabetics than in the controls.[7]

In this study, the diabetics had a mean LDL-C level of 92.3±27.699mg/dL in the fasting state, which is within the normal range. In the Strong Heart, study done by Howard BV et al, it was shown that in American Indians, LDL cholesterol level was the most significant predictor of increased CHD despite an average LDL cholesterol level of approximately 115mg/dL in diabetics. In this study, LDL was a strong predictor of CHD at levels as low as 70mg/dL.[9]

In this study, the cases had a mean LDL-C level of 92.3±27.699mg/dL in the fasting state and 100.62±37.043mg/dL in the postprandial state. The controls had a mean LDL-C of 165.06±34.184mg/dL in the fasting state and 165.06±34.184mg/dL in the postprandial state. This association has a p value of 0.003, hence statistically significant.

Thus, in the postprandial state, the cases had a significant decrease in LDL-C level whereas the controls had a marginal increase in LDL-C level compared to that of the fasting state.

This correlates with a study done by Lund SS et al, which showed that in diabetics, LDL-C decreased significantly postprandially (p <0.005).[10]

In this study, in the fasting state, 37% of cases had total VLDL-C levels of >40mg/dL as compared with that of the control group whereas only 8% of the controls had VLDL-C levels of >40mg/dL. This association has p value of 0.000, which was statistically significant.

Thus, cases with diabetes were found to have elevated VLDL-C levels when compared with that of controls. This correlates with the study done by Rivellese AA et al.[11]

In this study, the cases had a mean VLDL-C level of 50.39±63.27mg/dL in the fasting state and 34.56±18.173mg/dL in the postprandial state. The controls had a mean VLDL-C level of 32±22.372mg/dL in the fasting state and 30.2±15.139mg/dL in the postprandial state. This association has a p value of 0.82, which was statistically not significant.

Hence, there was no significant increase in the postprandial VLDL-C levels in both the cases and controls. This correlates with the study done by Rivellese AA et al.[11]

In this study, in the fasting state, 58% of cases had total TG levels of >150mg/dL as compared with that of control group where 32% of them had TG levels of >150mg/dL. This association has a p value of 0.000, which was statistically significant (Table 3).

Thus, in the fasting state cases with diabetes were found to have elevated triglyceride levels when compared with that of the controls. This correlates with the studies done by Raj S et al, Rajesh et al, Rivellese AA et al.[7,11]

In this study, the cases had a mean TG level of 193.48±109.63mg/dL in the fasting state and 235.48±147.75mg/dL in the postprandial state. The controls had a mean TG level of 133.06±59.46mg/dL in the fasting state and 142.29±65.34mg/dL in the postprandial state. This association has a p value of 0.000. Hence, statistically significant.

Hence, there was a significant increase in the postprandial TG level in the cases compared to that of the controls.

Similar observations were made in the studies done by Raj S et al, wherein the cases had a mean TG level of 187.1±63.45mg/dL in the fasting state and peak mean TG level of 425.2±204.47mg/dL in the postprandial state. The controls had a mean TG level of 156.85±76.57mg/dL in the fasting state and peak mean TG level of 283.9±116.94mg/dL in the postprandial state. Similar observations were also made in the studies done by Raj S et al, (p<0.01) and Rivellese AA et al.[7,11]

HDL-C levels among the cases and controls: In this study, it was observed that in males 62.3% of the cases and controls had HDL-C levels of <35mg/dL in the fasting state. Similarly, in females, 80.9% of the cases and 89.4% of the controls had HDL-C levels of <45mg/dL in the fasting state. This association has a p value >0.05, which was not significant. Hence, there was no significant difference in the HDL-C levels in both the cases and controls in the fasting state (Figure 5).

This correlates with the study done by Raj S et al, which showed no significant difference in the HDL-C levels in the diabetics and controls.[7]

This does not correlate with the study done by Rajesh et al, which showed that diabetics had lower HDL-C levels compared to that of the controls. Though, the mean HDL-C level in diabetics in this study was low (34.46±10.92mg/dL), it was similar to that of the controls. Hence, the controls also had significant dyslipidemia in this study.[8] In this study, the cases had a mean HDL-C level of 48.44±17.721mg/dL in the fasting

state and 38.761±9.028mg/dL in the postprandial state. The controls had a mean HDL-C level of 33.72±11.021mg/dL in the fasting state and 33.42±10.779mg/dL in the postprandial state. This association has a p value of 0.020, which was statistically significant. Hence, there was a significant decrease in the postprandial HDL-C level in the cases compared to that of the controls.

Similar observations were made in the studies done by SV Madhu et al, in which the cases had a mean HDL-C level of 35.15±10.84mg/dL in the fasting state and 28.05±10.94mg/dL in the postprandial state. The controls had a mean HDL-C level of 42.9±14.11mg/dL in the fasting state and 37.15±13.52mg/dL in the postprandial state.[12]

CONCLUSION

A significant raise in triglyceride levels in the postprandial in diabetes patients was observed when compared to their fasting state. A decreased HDL-C levels were found in diabetes patients in both fasting and postprandial state as well, when compared to that of controls. An elevated level of VLDL-C was seen in the fasting state of diabetes patients. There was significant increase in total cholesterol level in fasting state of diabetes patients on comparing with the controls. There was significant reduction in the LDL-C levels in fasting state of diabetes patients.

ACKNOWLEDGEMENTS

REFERENCES

1. Havel RJ, Kane JP. Structure and metabolism of plasma lipoproteins. In: Scriver CR, Beaudet AL, Sly WS, eds. The Metabolic and Molecular basis of Inherited Disease, 8th ed. NY: Mcgraw-Hill; 2001;2:2705-2716.

2. Rader DJ, Hobbs HH. Disorders of lipoprotein metabolism. Harrisons Principles Inter Med. 2005;16(2):2286.

3. Brunzell JD, Hazzard WR, Motulsky AG, Bierman EL. Evidence for diabetes mellitus and genetic forms of hypertriglyceridemia as independent entities. Metab Clin Exp. 1975;24(10):1115-21.

4. Abrams JJ, Ginsberg H, Grundy SM. Metabolism of cholesterol and plasma triglycerides in nonketotic diabetes mellitus. Diab. 1982;31(10):903-10.

5. Grundy SM, Becker D, Clark LT, Cooper RS, Denke MA, Howard J, et al. National Cholesterol Education Program, National Heart, Lung and Blood Institute, National Institute of Health, NIH Publication No. 02-5212, 2002. Available at: https://www.nhlbi.nih.gov/files/docs/resources/heart /atp-3-cholesterol-full-report.pdf.

6. Mengesha AY. Lipid profile among diabetes patients in Gaborone, Botswana. South African Med J. 2006;96(2):147-8.

7. Raj S, Rajasekharan C, Jayakumar B. Postprandial hypertriglyceridaemia in type 2 diabetic subjects. Int J Diab Dev Ctries. 2006;26(4):161.

8. Khan HA, Sherwani SI. Significance of HbA1c testing in diagnosis and prognosis of Diabetic Patients. Biomark Insights. 2016;11:95-104.

9. Howard BV, Cowan LD, Go O, Welty TK, Robbins DC, Lee ET. Strong Heart Study Investigators. Adverse effects of diabetes on multiple cardiovascular disease risk factors in women: the Strong Heart Study. Diab Care. 1998;21(8):1258-65.

10. Lund SS, Petersen M, Frandsen M, Smidt UM, Parving HH, Vaag AA, et al. Sustained postprandial decrease in plasma levels of LDL cholesterol in patients with type-2 diabetes mellitus. Scandinavian J Clin lab Investigation. 2008;68(7):628-40.

11. Rivellese AA, Natale C, Di Marino L, Patti L, Iovine C, Coppola S, et al. Exogenous and endogenous postprandial lipid abnormalities in type 2 diabetic patients with optimal blood glucose control and optimal fasting triglyceride levels. J Clin Endocrinol Metab. 2004;89(5):2153-9.

12. Madhu SV, Mittal V. Postprandial Lipid Abnormalities inn Type 2 Diabetes Mellitus. Journal of Association of Physicians on India. December 2005;53:1043-6.