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Original Research Article

Gender based variation of lipid abnormalities in type-2 diabetes mellitus patients

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ABSTRACT

Background: Dyslipidemia has a varying pattern among the male and female patients of type 2 diabetes mellitus (DM).
Methods: This study was conducted in the out-patient department (OPD) of department of medicine at GMERS, Patan, Gujarat from July 2020 to December 2020 for a period of six months. Fasting blood sugar, hemoglobin A1c (FBS, HbA1c) lipid profile triacylglycerol-triglyceride, total cholesterol, low density lipoprotein cholesterol and high-density lipoprotein cholesterol (TG, TC, LDL-C, and HDLC) were measured. Statistical analyses were performed with the SPSS software program.
Results: A total number of 200 type 2 DM patients (100 males and 100 females) attending to GMERS OPD were recruited in this study. Blood sugar was higher than normal in both male and female (FBS=142.44±36.21, 146.40±41.49 respectively). TG level was also higher in two groups of study subjects with female level slightly more than male (164.99±67.1and 138.21±70 respectively) with no significant difference between the groups (p>0.05).Total cholesterol and LDL-C level was within normal physiological level in both groups, where-as these levels were higher in female in comparison to male (TC=198.07±40.82 and 169.5±36.13 respectively, LDLC=118±34 and 99±27, respectively), showing significant difference between the groups (p=0.014). HDL-C was not below normal in both male (41±5.4) and female (43.99±4.31); however, HDL-C was slightly higher in female than male and the difference was significant (p=0.0129).
Conclusions: Dyslipidemia was noticed in a greater proportion of female diabetic patients than male diabetic patients

Keywords: Type 2 DM, Dyslipidemia, LDL, FBS, TG, LDL-C, HDL-C, Non-HDL

INTRODUCTION

Going by estimates 194 million people had diabetes in the year 2003 and about two-thirds of them lived in developing countries.[1] Lack of insulin or relatively low insulin level affects the metabolism of carbohydrate, protein, fat, water and electrolyte balance resulting in diabetes.[2] The most common form of the DM is type 2 DM, constituting approximately 90% of all affected individuals and is caused by relatively impaired insulin secretion and peripheral insulin resistance. As age progresses the prevalence of type-2 DM increases thus in developing countries, most diabetics are in the age bracket of 45 to 65 years, while in developed countries the largest number is found in those aged 65 years and above. The major risk factors for type-2 DM are obesity and sedentary lifestyle.

A state of dyslipidemia is induced by DM with abnormalities in all lipoproteins, namely, chylomicrons, very low-density lipoproteins (VLDL), LDL, and HDL. There might be variation in the pattern of dyslipidemia, among patients with type 1, type 2, or other types of DM.[3] Other studies have indicated that increased TG levels are an independent risk factor and a predictor for development of coronary artery disease (CAD), especially in type 2 diabetics.[4] Concomitant hypertriglyceridemia and low HDL poses a greater risk for CAD development.[5] Evaluation of lipid profiles in type 2 DM population and determining the major lipid risk factors for coronary artery disease is required. Dyslipidemia is elevation of plasma cholesterol, TG or both or a low HDL level that contributes to the development of atherosclerosis of which causes may be primary or secondary and diagnosed by measuring plasma levels of total cholesterol, TG and individual lipoproteins. Studies are needed to look at the differences in dyslipidemia of females and males. Women have notably different lipid profiles than men regardless of menopausal status.

Many epidemiological studies have found a sex difference in lipoprotein distribution among diabetics. The objective of the present study was to observe gender difference of the lipid abnormalities in type-2 DM patients.

METHODS

This observational study was conducted at GMERS medical college and hospital Patan, from July 2020 to December 2020, over a period of six months. Patients from the OPD of general medicine of GMERS medical college and hospital Patan were included in this study with their informed consent, on the basis of inclusion and exclusion criteria. Patients with systemic diseases, with hepatic, renal, endocrine disorders, who already had history of CAD or cerebrovascular accident (CVA) or were diagnosed as having CAD or CVA on enrolment, history of drug treatment for hyperlipidemia, pregnant women, alcoholics, and smokers were excluded from the study. Information was obtained about demographic characteristics and medical history of all patients concerning their age, sex, history and duration of DM, hypertension, smoking, medications and co-morbidities. All subjects underwent physical examination, including measurements of height, weight, and blood pressure (sitting position after at least 10 min rest).

All procedures were approved by the committee on human research and ethics of GMERS medical college and hospital, Patan.

Patients' heights were measured in centimeters with shoes off and weights were measured in kilograms in indoor clothing. Body mass index (BMI) was calculated using the formula BMI= weight (kg)/ height^2 (m).

Laboratory data

After taking written consent, blood was drawn using standard venipuncture techniques and serum was separated from blood cells as soon as possible. The whole blood was used for glycated hemoglobin. Fasting blood samples (12-14 hours) were analyzed for FBS, serum triglycerides, LDL-C, HDL-C and total cholesterol by using automated chemistry analyzer (Abbott c 4000 system) and VLDL-C were estimated by Fried Ewald's formula.[6] Current American diabetes association definitions were used to label patients as type 2 diabetics.[7] Diabetic dyslipidemia was characterized based on National cholesterol education program (NCEP) adult treatment panel (ATP III) guideline as below:[8] Hypercholesterolemia: >200 mg/dl, high TG concentrations: >150 mg/dl, Low-HDL-c concentrations: <40 mg/dl, Increased LDL-c concentrations: >100 mg/dl and Non high-density lipoprotein cholesterol (Non-HDL-c) concentrations: >130 mg/dl

The percentage of patients who had none, one, two, or all three of these lipoproteins not at goal levels was also determined.

Statistical analyses

Statistical analyses were performed with the SPSS software program (SPSS version 21.0). Analysis of variance was used to determine differences in patient characteristics and analysis of covariance was used to test for differences in mean lipid levels. The chi-square (X2) test was used to test for differences in proportions.

RESULTS

A total 200 patients with T2 DM were recruited for the study comprising of 100 males and 100 females to assess the alteration in lipid profile. The distribution of patients according to age groups is illustrated in Table 1 which revealed that there was highly significant difference in the prevalence of DM type 2 among different age groups.

Table 1: Prevalence of DM type 2 among different age groups.

Age groups (Years)	Male patients	Female patients	P value
	N	N	
Mean ± SD	55.04±8.42	55.64±8.59	0.4214
≤40	8	5	0.774
41 to 50	26	23	
51 to 60	33	40	
>60	33	32	
Total	100	100	

The mean BMI of the patients was evaluated and it was seen that the mean BMI was 25.56±2.83. The mean BMI of males was 25.44±2.85 while that of females was 25.60±2.82, and the difference was not statistically

significant as shown in Table 2. Categorization of patients as per the Asian BMI criteria revealed that BMI distribution was comparable between the 2 populations.

Table 1: BMI of patients.

BMI (kg/m^2)	Total	Male patients	Female patients	P value
	N	N	N	
Mean ± SD	25.56± 2.83	25.44± 2.85	25.60± 2.82	0.4214
Normal	29	15	14	0.4136
Overweight	127	64	63	0.9281
Obese	44	21	23	0.7418

The systolic blood pressure (SBP) of the male subjects (129.27±7.54) and the female subjects (130.36±6.55) were not statistically different. The same could be said of the diastolic blood pressure (DBP).

Table 3: SBP and DBP of patients.

Gender	SBP		DBP	
	Mean	SD	Mean	SD
Male	129.27	7.54	80.53	3.49
Female	130.36	6.55	81.22	3.27
Grand total	129.82	7.09	80.88	3.40

The duration of diabetes was evaluated and the data was as shown in Table 4. The duration of diabetes was nearly comparable in both the groups.

Table 4: Duration of diabetes.

Duration of diabetes	Total (%)	Male (%)	Female (%)	P value
Mean ± SD	15.93± 9.14	15.64± 9.24	16.22± 9.03	0.4098
≤5	17	17	17	
>5- ≤10	17	19	15	
>10- ≤ 15	12.50	14	11	
>15- ≤20	19.50	15	24	
>20- ≤ 25	14.50	16	13	
>25	19.50	19	20	

Thus, the various parameters were impartial between the two groups and the differences observed were reliable differences due to gender between the 2 groups.

The mean FBS was higher than normal 144.42 SD±38.99 and mean HbA1c was 7.03 SD±0.99.

The control of sugar in the patients was evaluated show in Table 3. It was observed that 61% males and 65% females had FBS >126 mg/dl and 42% males and 43% females had HbA1c levels ≥7%.

Table 5: Mean FBS and HbA1c of the patients.

Blood sugar	Total		Male patients		Female patients		P value
	Mean	SD	Mean	SD	Mean	SD	
FBS	144.42	38.99	142.44	36.21	146.40	41.49	0.0887
HbA1c	7.03	0.99	7.00	0.92	7.07	1.05	0.0951

Table 6: Classification of patients based on FBS and HbA1c levels.

Variables	Total		Male		Female	
	N	%	N	%	N	%
FBS levels						
≤100	23	11.50	14	14	9	9
101-126	51	25.50	25	25	26	26
>126	126	63	61	61	65	65
HbA1c categorization						
<6	6	3	3	3	3	3
≥6- <7	109	54.50	55	55	54	54
≥7- <8	46	23	23	23	23	23
≥8- 9	33	16.50	17	17	16	16
≥9	6	3	2	2	4	4

The prevalence of different types of dyslipidemia in all of patients and in males and females are shown in Table 7.

For serum lipid reference level, NCEP, ATP III guideline was referred. According to NCEP-ATP III guideline, hypercholesterolemia is defined as TC >200 mg/dl, high LDL-c when value is >100 mg/dl, hypertriglyceridemia as TG >150 mg/dl and low HDL-c when value is <40 mg/dl. Dyslipidemia was defined by the presence of one or more than one abnormal serum lipid concentration. In our study, total cholesterol was more than 200 mg/dl in 65 (32.5%) and HDL-c were less than 40 mg/dl in 58 (29%) of all patients. LDL level higher than 100 mg/dl were present in 123 (61.5%), while 85 (42.5%) of all patients had triglyceride level higher than 150 mg/dl.

Table 7: Prevalence of dyslipidemia in studied diabetic patients.

Lipid type	Total (%)	Female (%)	Male (%)	P value
TC	32.5	47	18	0.0000
TG	42.5	55	30	0.0001
LDL	61.5	71	52	0.0018
HDL	29	14	44	-0.0000

Table 8: Lipid profile in males and females.

Lipid profile (mg/dl)	Male	Female	P value
	Mean ± SD	Mean ± SD	
TC	169.5±36.13	198.07±40.82	0.1132
TG	138±70	164±67.1	0.3373
HDL	41±5.4	43.99±4.31	0.0129
DLDL	99±27	118±34	0.0114
Non-HDL	128.7±35.32	154.08±40.13	0.1029

Table 8 shows the mean ± SD values of lipid profiles (mg/dl) of males and females. The results in Table 8 revealed that diabetic females had higher level of TC (198.07 mg/dl vs. 169.5 mg/dl) and higher level of HDL-c (43.99 mg/dl vs. 41 mg/dl) ($p<0.05$) compared to matched male patients, whereas LDL-c and TG were significantly increased in females (118 mg/dl, 71%; 164.40 mg/dl, 55%) in comparison to males (99 mg/dl, 52%; 138 mg/dl, 30%) respectively ($p<0.05$). In this study females had higher mean non-HDL 154 mg/dl as compared to males mean non- HDL 129 mg/dl.

Blood sugar was higher than normal in both male and female (FBS=142.44±36.21 mg/dl, 146.40±41.49 mg/dl respectively. Though the value of FBS is more in female than in male, no significant difference between the groups was found ($p>0.05$) (Table 5). TG level was also higher in two groups of study subjects with female level is slightly more than male (164±67.1 mg/dl and 138±70 mg/dl respectively) with no significant difference between the groups ($p>0.05$). Total cholesterol and LDLC level were higher in female in comparison to male (TC=198.07±40.82 mg/dl and 169.5±36.13 mg/dl respectively, LDLC=118±34 mg/dl and 99±27 mg/dl respectively), showing significant difference between the groups ($p=0.0114$) (Table 8).

DISCUSSION

A greater risk of morbidity and mortality from cardiovascular disease is coupled with type 2 DM. One major step towards reducing the risk of cardiovascular disease associated with diabetes is detection and treatment of dyslipidemia in diabetes. The pathogenesis of heart disease in diabetes is many-sided, but serum lipids are frequently abnormal and likely to add to the risk of coronary artery disease.[9] DM type 2 is typically associated with a dyslipidemia characterized by hypertriglyceridemia and low HDL levels, while the levels of total cholesterol and LDL may or may not differ significantly from those in the non-diabetics.[10-11] In this study, 71% female and 52 percent male diabetics were having high LDL-C and low HDL-C was seen in 44 percent males and 14 percent females. These results are in agreement with the results given by other studies done in south-east Asian region.[12] Similar proportion of patients were found to have high LDL, in a study conducted by Taskinen et al in which they determined the lipid level differences and hypertension effect in black and white population with type 2 diabetes. In a native Pakistani study done recently by Firdous and Zafarullah the percentage of diabetic patients affected by high LDL cholesterol was 32% where as our study shows 61.5%. Khalid et al found high LDL in 30 percent of patients. Statistically significant levels of high-risk LDL were reported among urban dwellers in an Iranian study by Sadeghi and coworkers.[13-14] Naheed and Khan observed similar trends in another Pakistani study.[15] In our study the distribution of low HDL-C in male and female was 44% and 14% respectively. Our findings are in accordance with Firdous and Zafarullah and also Mooradian who found out 60% of the diabetic population suffering from high-risk HDL levels, more so in men as compared to female on a percentage basis. In a meta-analysis done by Wei et al about 45% of American subjects had high-risk category HDL, although these studies were not done specifically on diabetic patients.[16]

Regarding triglyceride (TG) concentrations, in patients total 42.5% had high TG levels, 30% male had high-risk TG levels and 55% female patients had high-risk, TG levels. In another native study done by Firdous and Zafarullah 38% of diabetic subjects were found to have high- risk category TG levels. This was restated in another native study done by Cleeman and Grundy.[17] In the Palestinian study mentioned above and also in the Iranian IHPP study, 35 to 40% of the diabetic population was found to have high risk category hypertriglyceridemia. In the study hypertriglyceridemia is prominent in female diabetics because high TG level was present in 55 females and male diabetics with high TG were 30. Hypercholesteremia was eminent in female diabetics because 47 female diabetics had high TC level where as 18 male diabetics had high TC level.

Fontbonne et al in a prospective cohort study found out that elevated plasma levels of TG in diabetic patients was positively and significantly correlated with CAD events and CAD mortality.[18] Hypertriglyceridemia may possibly be the best lipid predictor of CVD in type 2 diabetic patients.[18] Recent studies have demonstrated that in diabetic patients TG levels is a risk factor for CVD independent of HDL-C level and despite glycemic control.[19,20] Mean levels of total cholesterol and LDL-C in those with type 2 diabetes may not differ significantly from those in non-diabetic subjects. Type 2 diabetic patients have an oddly high number of small, dense LDL-C particles.[21-23] Additionally, patients with small, dense

LDL-C will also typically have lower HDL-C and elevated TG blood levels, which may further increase risk of atherosclerosis.[21] A restraint to our study was the inaccessibility to differentiate the LDL-C subclasses. The prevalence of small and dense LDL-C may clinically show itself as an increased level of non-HDL cholesterol plasma level which shows a stronger association with CVD and mortality than LDL-C.[24,25] Non-HDL-C includes all lipoprotein particles that contain apo-B and are potentially atherogenic, including LDL-C, Lp (a), intermediate density lipoprotein (IDL-C), and very low density lipoprotein (VLDL-C).[26] In this study females had higher mean non HDL 154 mg/dl as compared to males mean non HDL 129 mg/dl.

Essentially, most of our female diabetic had high TG levels and combination of high LDL which is the most common pattern of dyslipidemia found in the study. The second most common pattern of dyslipidemia was unfavorable levels of three lipoprotein (LDL-C, TC, HDL-C) which was found in female diabetics.

Limitations

The study contains small sample size. Further, studies will be needed with large sample size and including multiple centers to better validate the conclusion

CONCLUSION

The present study shows that the derangement in the lipid profile in patients of type 2 DM is more adverse in females as compared to male patients. Thus, the relevance of the present study lies in recognizing increased risk of dyslipidemia in female type 2 diabetic patients and hence keep an eye on of the lipid profile of newly diagnosed female type 2 diabetic patients, so that early intervention is possible. While this study shows there are gender differences in lipid profile in patients with type 2 DM. These differences may in part explain the difference in the incidence of CHD between the sexes hence this study advances knowledge and understanding in the field. Further studies are required to corroborate these findings.

An approach with gender in insight is recommended in planning interventions (counseling and treatment) to reduce the risk of cardiovascular disease.

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