Original Article

TRENDS OF LIPID ABNORMALITIES IN PAKISTANI TYPE-2 DIABETES MELLITUS PATIENTS: A TERTIARY CARE CENTRE DATA

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ABSTRACT

Objective: To ascertain trends of lipid abnormalities in Pakistani Type-2 Diabetes Mellitus patients.

Methodology: Fasting lipid profiles of 328 outpatient adult type 2 diabetes mellitus patients visiting the Aga Khan University Hospital, from January 2005 to January 2006 were prospectively reviewed and abstracted on a pre-specified proforma. Demographic features, different patterns of dyslipidemia in accordance with specified risk categories, and the proportion of patients with none, one, two, or three lipid values outside clinical targets were noted. The influence of sex on dyslipidemia pattern was also assessed

Results: Our patients had higher average HbA1c levels and higher total cholesterol, LDL and lower HDL levels. The triglycerides levels in our female patients were higher. The percentage of our patients with a high-, borderline-, or low-risk LDL cholesterol were 54, 29, and 16%, respectively (P = 0.51). On a percentage basis, 73% were in the high-risk HDL cholesterol group, 18% were in the borderline-risk group and 9% in the low-risk group, respectively (P< 0.0001). Regarding triglyceride concentrations, 16% had high-risk triglyceride levels, 34% were in the borderline-risk category, whereas 50% had a low-risk triglyceride levels (P< 0.0001). Patient proportion with None, One, Two, or Three Values outside clinical targets on percentage basis were 2, 16, 48, and 34%, respectively (P< 0.0001). Women were found to have greater odds of having LDL cholesterol above the target level i.e. >100mg/dl.

Conclusion: Combination of high LDL and a low HDL cholesterol level was the commonest pattern of dyslipidemia found. Second was unfavorable levels of all three lipoproteins combined and the third was an isolated increase in LDL cholesterol. A greater proportion of women were found dyslipidemic.

KEY WORDS: Dyslipidemia patterns, High LDL, Type 2 DM dyslipidemia.

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INTRODUCTION

Diabetes mellitus induces a state of dyslipidemia with abnormalities in all lipoproteins, namely, chylomicrons, very low density lipoproteins (VLDL), low density lipoproteins (LDL), and high density lipoproteins (HDL). The pattern of dyslipidemia, however, may vary among patients with type 1, type 2, or other types of diabetes mellitus.[1] Also other studies

have indicated that increased triglyceride (TG) levels is an independent risk factor and a predictor for development of coronary artery disease (CAD), especially in type 2 diabetics.[2] Frequent co-existence of hypertriglyceridemia and low HDL poses a greater risk for CAD development.[3] Thus there is a need to evaluate lipid profiles in our type 2 diabetes mellitus population and determine the trends of the major lipid risk factors for CAD. Subsequently, this will supplement our physicians in making decisions about therapeutic and dietary measures in diabetic population.

The objective of this study was to evaluate patient characteristics and their lipid profiles to assess specific lipid patterns in type 2 diabetes mellitus Pakistani patients and to see if these patterns conform or differ with the trends of lipid abnormalities already known internationally.

METHODOLOGY

This study was conducted at the Aga Khan University Hospital, under supervision of Dr. Sajid Dhakam, from January 2005 to January 2006, over a period of one year. Convenient sampling method was used and data assessed in a prospective manner. A total of 328 randomly selected patients from Diabetes Clinics were included in this study with their informed consent, on the basis of inclusion and exclusion criteria. Patients on statins or fibrates were not included. Fasting blood samples (12-14 hours) were analyzed for serum triglycerides and total cholesterol, using automated chemistry analyzer. HDL-C was determined by precipitation method and LDL-C and VLDL-C were estimated by Friedewald's formula.[4]

Current American Diabetes Association definitions and ATP III guide lines were used to label patients as type 2 diabetics and to classify lipoprotein concentrations into different cardiovascular disease risk categories respectively.[5,6] The values used to define low-, borderline-, and high-risk LDL cholesterol were <100, 100-129, >130 mg/dl, respectively. For triglycerides, the cutoff points were <200, 200-399, and >400 mg/dl. High-, borderline-, and low-risk categories for HDL concentrations were defined according to sex. For men, the cutoff points were <35, 35-45, and >45 mg/dl, respectively. For women, the cutoff points were <45, 45-55, and >55 mg/dl, respectively. Because American Diabetic Association guidelines recommend an LDL of <100 mg/dl, a triglyceride levels of <200 mg/dl, and an HDL cholesterol level of >45 mg/dl in men and >55 mg/dl in women,[5,6] the percentage of patients who had none, one, two, or all three of these lipoprotein not at goal levels were also determined.

Statistical analyses were performed with the SPSS software program. 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. Multiple logistical regressions adjusted for patient characteristics and method of treatment for hyperglycemia were used to determine the influence of sex on the risk of having and LDL cholesterol, HDL cholesterol, or triglyceride levels outside of the desirable clinical targets.

RESULTS

A total of 328 patients were identified during the study. The mean age was 54±0.6 with 141 (43%) subjects were males. Small but statistically significant differences were detected in some patient characteristics at their first clinic visit (Table-I). Our patients had higher average HbA1c levels. Overall, our patients, both men and women, had significantly higher total cholesterol, LDL and lower HDL levels. The triglycerides levels, total cholesterol, LDL were significantly higher and HDL at lower level in our female patients as compared to their male counterparts.

Patterns of Serum Lipids by Risk Category: The percentage of our patients with a high-, borderline-, or low-risk LDL cholesterol were 54, 29, and 16%, respectively (P = 0.51). More of our women patients (61%) than men (46%) had LDL cholesterol in the high-risk category and a significant difference in the distribution by risk

Table-I: Characteristics and fasting lipid profiles of our patients with type 2 diabetes

	Both	*Men*	*Women*
n	328	141	187
Age (years)	54 ± 0.6	54 ± 0.9	54 ± 0.9
Diabetes duration (years)	5.9 ± 0.4	5.6 ± 0.6	6.1 ± 0.6
Body Mass Index (kg/m)	33 ± 0.4	32 ± 0.6	34 ± 0.6*
HbA1c (%)	8.6 ± 0.1	8.5 ± 0.2	8.7 ± 0.2
Fasting plasma glucose	204 ± 4.3	191 ± 6.3	213 ± 5.8*
Percentage on each therapy			
Diet	24.1	17.7	28.3
Sulfonylureas	41.2	43.9	39.0
Sulfonylurea and insulin	3.4	2.8	3.7
Insulin	31.4	35.5	28.3
Lipids			
Total cholesterol	213 ± 3.1	198 ± 4.0	225 ± 4.5‡
LDL cholesterol	136 ± 2.3	129 ± 3.2	143 ± 3.2‡
HDL cholesterol	37 ± 0.6Ø	34 ± 0.9	39 ± 0.9‡
Triglycerides	266 ± 15Ø	234 ± 16	291 ±24‡

Data are n, means ± SEM, or %. LDL cholesterol values are data from 278 patients. *P< 0.01, comparison of women vs. men within the whole group (ANOVA); 1P< 0.01;‡p<0.01,women vs. men (ANCOVA, adjusted for age, duration of disease, fasting plasma glucose, HbA1c, and BMI);ØP<0.001.

class were also detected between men and women (P < 0.026, chi- square sex comparison). Differences in the proportion of patients in each HDL cholesterol risk category were clearly evident. On a percentage basis, 73% were in the high-risk HDL cholesterol group, 18% were in the borderline-risk group and 9% in the low-risk group, respectively (P< 0.0001). The distribution of HDL cholesterol level by risk category was less favorable among women than men, as evident by the fact that 76% of men and 69% of women, respectively, were in the high-risk HDL group (P < 0.0001). Regarding Triglyceride (TG) concentrations, in our patients, 16% had high-risk TG levels, 34% were in the borderline-risk category, whereas 50% had a low-risk TG levels (P< 0.0001). In our male patients 13%, 32%, and 55% had high-risk, borderline-risk, and low-risk TG levels, respectively, whereas the distribution in women patients was 17%, 36%, and 47%, respectively (P <0.01, chi-square sex comparison).

Proportion With None, One, Two or Three Values Outside Clinical Targets: For subjects with a TG level of < 400 mg/dl (because higher values did not permit valid LDL calculation), the proportion of patients who had none, one, two, or three lipid (LDL, HDL, and TG) values outside of clinical targets were determined. Therefore, this analysis considered those patients who had an LDL level of >100 mg/dl (patients with borderline- and high-risk LDL), those with HDL levels <45 mg/dl in men and < 55 mg/dl in women (patients with borderline- and high-risk HDL), and TG levels of 200- 399 mg/dl (Table-II). In our 278 patients, on a percentage basis, the values were 2, 16, 48, and 34%, respectively (P< 0.0001). A combination of an LDL level above target with HDL below target levels was observed in about 50% of the patients which made this the most frequently observed pattern of dyslipidemia. The second most prevalent pattern was a dyslipidemia consisting of all three lipoproteins (LDL, HDL, and TG), which was observed in 34% of the patients (Table-II).

Influence of Sex: Multiple logistical regression analyses were performed to examine the influence of sex on the probabilities of having serum lipids that were outside of recommended clinical targets after adjusting for other variables (Table-III). On the basis of sex, women were found to have greater odds of having LDL cholesterol above the target level i.e. >100mg/dl as compared to men but almost similar probabili-

Table-II: Patients with none, one, two, and three lipid values not at clinical targets

Number not at target	*Both*	*Men*	*Women*
None out of target	5 (1.8)	3 (1.1)	2(0.7)
One out of target	45 (16.2)	26 (9.4)	19(6.8)
LDL cholesterol >100mg/dl ±	21 (7.6)	13 (4.7)	8 (2.9)
HDL cholesterol below target (mg/dl)¶	22 (7.9)	13 (4.7)	9 (3.2)
Triglyceride 200-399 mg/dl	2 (0.7)	— —	2 (0.7)
Two out of target	134 (48.2)	59 (21.2)	75(27.0)
LDL cholesterol >100mg/dl + HDL cholesterol below target	117 (42.1)	49 (17.6)	68 (24.5)
LDL cholesterol >100mg/dl + Triglyceride 200-399 mg/dl	—	—	—
HDL cholesterol below target + Triglyceride 200-399 mg/dl	17 (6.1)	10 (3.6)	7 (2.5)
Three out of target	94 (33.8)	35 (12.6)	59(21.2)

Data are n (%). *Data only for those patients for whom LDL cholesterol could be calculated (i.e TG <400mg/dl); ± patients in borderline- and high-risk LDL cholesterol categories; ¶ HDL cholesterol < 45mg/dl in men and <55mg/dl in women (patients in borderline- and high-risk HDL cholesterol categories).

ties of having HDL cholesterol below the target and triglyceride levels outside clinical targets.

DISCUSSION

Diabetes mellitus is associated with a greater risk of morbidity and mortality from cardiovascular disease. Detection and treatment of dyslipidemia in diabetes is one major step towards reducing the risk of cardiovascular disease associated with diabetes.[7] Patients in our large urban outpatient diabetes clinics are primarily with type 2 diabetes and represent a group at high risk for cardiovascular disease. Therefore, efforts to reduce the risk of heart disease through evaluation of risk factors and introduction of preventive and therapeutic measures into a comprehensive treatment program must be a primary focus when caring for the diabetic patients.

The pathogenesis of heart disease in diabetes is complex, but serum lipids are frequently abnormal and likely to contribute to the risk of coronary artery disease. Diabetes mellitus type 2 is typically associated with a dyslipidaemia characterized by hypertriglyceridaemia and low HDL levels, while the levels of total cholesterol and LDL may or may not differ significantly from those in the non-diabetics.[8]

In our study, when applying current American Diabetic Association guidelines to classify lipoprotein concentrations, the proportion of patients who had an LDL level that was within low-, borderline-, and high-risk categories was almost similar for our male and female patient i.e. 54, 29, and 16% respectively, except that more women than men were in the high-risk LDL category. These results are in conformity with the results given by Moradian AD et al.[9] and also coincide with other studies done in south-east Asian region.[10] Similar proportion of patients were found to have high LDL, in a study conducted by Taskinen MR et al.,[11] 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 Samar Firdous et al.,[12] the percentage of diabetic patients affected by high LDL cholesterol was 32%. In one Palestinian study done by Hannan F. et al.,[13] who did a comparison of the metabolic syndrome and reported high LDL in 35% of urban dwellers. A similar frequency of high LDL was also reported by Mooradian AD et al.,[14] in their study on plasma lipids and diabetes mellitus in an adult community. In another study done by Khalid AM and coworkers,[15] LDL was found

Table-III: Multiple logistical regression analyses examining the influence of sex on the probability of dyslipidemia in type 2 diabetes

		P
Probability of LDL cholesterol >100mg/dl Women versus men	2.31 (1.12-4.74)	0.023
Probability of HDL cholesterol below target‡ Women versus men	1.56 (0.68-3.60)	0.29
Probability of Triglycerides >200mg/dl Women versus men	1.10 (0.68-1.80)	0.69

Data are odd ratios (95% CIs). Analyses adjusted for sex, mode of hyperglycemic therapy at presentation, patient age, duration of disease, HbA1c, fasting plasma glucose, BMI, and blood pressures; ‡ defined as value of <45mg/dl in men and < 55 mg/dl in women.

high in 30 percent of patients. In an Iranian study by Masoumeh Sadeghi and coworkers statistically significant levels of high-risk LDL was reported among urban dwellers.[16] Similar trends were found in another Pakistani study done by Talat Naheed et al.[17] In the San Antonio Heart Study 50% of the patients with type 2 diabetes were found to be in the high-risk LDL cholesterol category.[18] In a Turkish study by Alaettin Avsar et al, 45% of the patients were found to have high LDL cholesterol levels.[19]

In our study, the distribution of unfavorable HDL by risk category is higher in both men and women and the sex comparisons for HDL risk categories were statistically significant, especially for women with a high-risk HDL profile. In our study, the percentage of patients in high-, borderline-, and low-risk HDL category were 73, 18, and 9%, respectively. Similar results have been reported by Samar Firdous et al.,[12] and also by Mooradian AD et al.,[14] who found out 60% of the diabetic population suffering from high risk HDL levels, more so in women as compared to men on a percentage basis. In a metaanalysis done by James I. Cleeman et al.,[20] about 45% of American subjects had high-risk category HDL, albeit these studies was not done specifically on diabetic patients. In another study The West of Scotland Coronary Prevention Study[21] about 50% of the patients were found to have high-risk HDL. In a subgroup analysis of the famous 4S Study,[7] high-risk HDL was found in 48% of the patients. Keeping in view the above comparisons, and given the recent finding of the beneficial effect of increasing HDL cholesterol level,[12] our data also indicate that elevated HDL, along with lowering LDL should be an important target for intervention as described in other studies.[22] In the Iranian IHPP-study,[16] significantly low levels of HDL were reported in type 2 diabetics. In San Antonio Heart Study 30% of patients with type 2 diabetes were reported to have low HDL levels.[18] In the Turkish study mentioned above low HDL levels were found in 30% of diabetic patients.[19]

Regarding triglyceride (TG) concentrations, in our patients, 16% had high-risk TG levels, 34% were in the borderline-risk category, whereas 50% had a low-risk TG levels. In our male patients 13%, 32%, and 55% had high-risk, borderline-risk, and low-risk TG levels, respectively, whereas the distribution in women patients was 17%, 36%, and 47%, respectively. In the study done by Alaettin Avsar et al.,[19] overall 25% of the diabetics were found to have high-risk HDL levels. In another native study done by Samar Firdous et al.,[12] 38% of diabetic subjects were found to have high- risk category TG levels. This was reiterated in another native study done by Khan SR et al.[22] In the Palestinian study mentioned above[13] and also in the Iranian IHPP study,[16] 35 to 40% of the diabetic population was found to have high risk category hypertriglyceridemia.

In our study diabetic women were found to have more elevation of LDL as compared to men but the trends were similar to previous studies[23] with regards HDL below or TG levels above the target levels. No other major sex differences were noted. Previous studies have also shown

that the impact of diabetes on the relative risk for developing CHD is greater for women than men, as diabetes eliminates the "female advantage". This increased risk in diabetic women is due to lower HDL levels (<50 mg/dL) and raised TG levels.[24] Other native studies[25,26] have shown similar trends.

In essence, most of our patients with triglyceride levels of < 400 mg/dl had a combination of high LDL and a low HDL level, which is the most common pattern of dyslipidemia found in our study. The second most common pattern of dyslipidemia was unfavorable levels of all three lipoproteins (LDL, HDL and TG) combined. Moreover, overall 50% of our patients had a TG level of >200 mg/dl, suggesting that reduction in triglycerides levels is also an important target for therapy in our diabetic population.

CONCLUSION

Most of our patients had a combination of high LDL and a low HDL cholesterol level, which is the most common pattern of dyslipidemia found in our study. The second most common pattern of dyslipidemia was unfavorable levels of all three lipoproteins (LDL cholesterol, HDL cholesterol and triglycerides) combined. The third most common pattern found was an isolated increase in LDL cholesterol. Overall, a greater proportion of women were found dyslipidemic as compared to men.

At present time there is good body of evidence[6] with inferences from pathophysiological information and extrapolation from different studies[7,21] which strongly supports the treatment of dyslipidemia where it exists in diabetes. The treatment regimen should optimize glycemic control and use diet and life style modification, as well as drug therapy directed to the specific lipoprotein disorder that is present. This will eventually help in the reduction of morbidity and mortality associated with cardiovascular diseases in diabetes mellitus.

LIMITATIONS OF THE STUDY

This study has several limitations. Because this analysis was based on clinic population, data from other centers are required to determine whether our findings can be generalized to other diabetic care settings. Every effort was made to exclude the use of medications that can effect lipid levels that the patients might have been taking at the time of their initial visits but still in our environment we cannot negate totally the spurious use of the drugs affecting the lipid levels and also the use of homeopathic medications. Another catch was that the data on the physical activity of the patients was not available. Also the data on the socioeconomic status of the patients was not available, to check for its influence on the dyslipidemic state of our patients. Finally, a similar group of patients from our health system without diabetes was not available to allow comparison with subjects in this study. And therefore, a complete profile of cardiovascular disease risk could not be obtained; however, data like our study will be necessary for the development of a future comprehensive cardiovascular disease risk reduction program.

REFERENCES

1. Chahil TJ, Ginsberg HN. Diabetic dyslipidemia. Endocrinol Metab Clin North Am 2006;35:491–510.
2. Ahmad J, Hameed B, Das G, Siddiqui MA, Ahmad I. Postprandial hypertriglyceridemia and carotid intima – media thickness in north Indian type 2 diabetic subjects. Diabetes Res Clin Pract 2005;69:142-50.
3. Dodani S. Distribution and determinants of coronary artery disease in an urban Pakistani setting. Ethn Dis 2005;15:429-35.
4. Friedwald WT, Levy RI, Frederickson DS. Estimation of LDL cholesterolin plasma without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
5. American Diabetes Association: Consensus statement on detection and management of lipid disorder in diabetes. Diabetes Care 1996;19(Suppl no.I):S96-S102.
6. Expert Panel On Detection, Evaluation, and Treatment of high blood cholesterol in adults; Summary of the third report of NCEP (Adult Treatment Panel III). JAMA 2001;285: 2486 -2497. Updated 2004.
7. Pyorala K, Pederson TR, Kjekshus J, Faergeman O, Olosson AG, Thorgeirsson G. The Scandinavian Simvastatin Survival Study (4S): Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary artery disease, a subgroup analysis. Diabetes Care 1997;20:614-620.

8. Nesto RW. Beyond low-density lipoprotein: addressing the atherogenic lipid triad in type 2 diabetes mellitus and the metabolic syndrome. Am J Cardiovasc Drugs 2005;5:379-87.
9. Mooradian AD. Low serum high-density lipoprotein cholesterol in obese subjects with normal serum triglycerides: the role of insulin resistance and inflammatory cytokines. Diabetes Obes Metab 2007;9:441–443.
10. Ahmad J, Hameed B, Das G, Siddiqui MA. Postprandial hypertriglyceridemia and carotid intima – media thickness in north Indian type 2 diabetic subjects. Diabetes Res Clin Pract 2005;69:142-50.
11. Taskinen MR. Diabetic dyslipidaemia: From basic research to clinical practice. Diabetologia 2003;46:733-749.
12. Firdous S, Zafarullah M. Comparison of patterns of lipid profile in type-2 diabetics and non-diabetics. Ann King Edward Med Coll. 2007;13(1): 84-87.
13. Hannan F, Abdullatif H, Nahida H. The metabolic syndrome in west bank population, an urban-rural comparison. Diabetes Care 2001;24:275-279.
14. Mooradian AD. The effect of select nutrients on serum high-density lipoprotein cholesterol and apolipoprotein. A-I levels. Endocr Rev 2006; 27: 2–16.
15. Khalil AM, Rehman S. Prevalence of diabetic dyslipidemia in 120 patients of type 2 Diabetes Mellitus. J Med Sci 2005; 13(2):128-31.
16. Sadeghi M, Raza H. Serum lipid distribution and prevalence of Dyslipidemia in urban and rural communities in Iran - IHHP study. Pak J Cardiol 2004;15(2): 88-94.
17. Naheed T, Khan A. Dyslipidemias in type II Diabetes Mellitus patients in a teaching hospital of Lahore, Pakistan. Pak J Med Sci 2003;19(4):283-6.
18. Wei M, Mitchell BD, Haffner SM. Effects of cigarette smoking, diabetes, high cholesterol, and hypertension on all-cause mortality and cardiovascular disease mortality in Mexican Americans: The San Antonio Heart Study. Am J Epidemiol 1996;144:1058-1065.
19. Alaettin A, Abdullah D, Murat S. The predictive and discriminative value of serum lipoproteins in atherosclerotic coronary artery disease. Pak Heart J 1998;31:23-30.
20. Cleeman JI, Grundy SM. Implication of recent clinical trials for the NCEP, ATP III guidelines. Circulation 2004;110:227-239.
21. Ford I, Murray H. Long term follow up of the West of Scotland Coronary Prevention study. New Eng J Med 2007;357:1477-1486.
22. Khan SR, Ayub N. Triglyceride profile in dyslipidemia of Type 2 Diabetes Mellitus. J Coll Physicians Surg Pak 2008;18(5):270-3.
23. Gardener CD, Fortmann SP, Krauss RM. Association of small LDL particles with the incidence of CAD in men and women. JAMA 1996;276:875-881.
24. Nakhjavani M, Esteghamati AR. Dyslipidaemia in type 2 diabetes mellitus: more atherogenic lipid profile in women. Acta Med Iran 2006;44:111-8.
25. Habib SS, Aslam M. Gender differences in Lipids and Lipoprotein (A) profiles in healthy individuals and patients with type 2 Diabetes Mellitus. Pak J Physiol 2005;(1-2):2-6.
26. Jawed S, Sultan A, Fiaz. Effect of Diabetes Mellitus on Liporpotein Triglyceride and Cholesterol Concentrations Related to Sex. Ann King Edward Med Coll 2000;2(6):126-30.

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