DIABETIC DYSLIPIDEMIA AMONG DIABETIC PATIENTS ATTENDING SPECIALIZED CLINICS IN DAR ES SALAAM

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Abstract

Background: Diabetes mellitus is a major healthcare problem globally, and by 2030 there will be approximately 360 million patients world – over. Diabetes mellitus is associated with dyslipidemia involving quantitative and qualitative changes in lipoproteins. Correcting lipid abnormalities reduces the risks of coronary heart diseases (CHD) among diabetics. The prevalence of diabetic dyslipidemia and its association with glycemic control are all largely undetermined in Dar es Salaam.

Objective: to determine the prevalence of diabetic dyslipidemia and its association with glycemic control among diabetes mellitus patients in Dar es Salaam.

Methodology: A descriptive cross – sectional study was conducted between November 2006 and January 2007. Diabetic patients aged 18 years and above were recruited by simple random sampling technique from diabetic clinics in the city of Dar es Salaam. After enrolment each subject was interviewed using a structured questionnaire before undergoing a full physical examination. Fasting lipid profiles and glycosylated hemoglobin were measured using Konelab ™ (© 2003 Thermo Electron Corporation) machine. Chi – squared test, Student's t – test and multiple logistic regression were used for data analysis. A p – value of < 0.05 was taken to represent a statistically significant difference between variables.

Results: The prevalence of dyslipidemia was 95%. The commonest lipid derangement was hypertriglyceridemia with serum triglyceride level ranging from 1.00 – 3.26 mmol/L (mean 2.22 ± 0.69). Dyslipidemia was mostly asymptomatic with only few presenting with angina, peripheral vascular disease and corneal arcus. In a multivariate analysis, poor glycemic control as determined by measurement of glycosylated hemoglobin was independently associated with dyslipidemia.

Conclusion and Recommendation: The prevalence of dyslipidemia among diabetes mellitus patients attending diabetic clinics in government hospitals in Dar es Salaam is alarmingly high. Since risk factors for heart diseases among diabetics are known to be additive and even multiplicative, mild degrees of dyslipidemia may increase CHD risk. Controlling dyslipidemia should be given equal emphasis as controlling hyperglycemia in managing diabetes mellitus.

Key words: Dyslipidemia, Dar es Salaam

Introduction

Diabetes mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism.[1] It is a major global public health problem and it has been projected that, by 2030 there will be approximately 360 million patients world – over, with about two thirds of them living in the developing world.[2,3] Type 2 diabetes is the most predominant form, affecting 70% – 90% of all patients.[3, 4] The prevalence of diabetes in Africa is increasing with the aging of the population and changes in lifestyle associated with urbanization and westernization.[4, 5, 6] Diabetic patients are at an increased risk of cardiovascular, peripheral vascular and cerebrovascular disease partly due to the accompanying dyslipidemia.[7, 8, 9]

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Dyslipidemia is a disorder in the levels of plasma lipoproteins and is classified into hypo- and hyperlipidemia referring to decreased and elevated plasma lipoproteins respectively.[1, 6, 10] Lipoproteins are complexes of lipids and proteins that are essential for the transport of cholesterol, triglycerides, and fat-soluble vitamins.[10, 11] Classification of lipoproteins has been made according to their densities into: Very Low Density Lipoproteins (VLDL) which carry endogenously synthesized cholesterol and triglycerides; Low Density Lipoproteins (LDL) which are the principal vehicles for cholesterol transport and are taken up by LDL receptors on hepatocytes and peripheral cells for cellular use and High Density Lipoproteins (HDL) which mediate the reverse transport of cholesterol from peripheral tissues to the liver.[10, 11] Hyperlipidemia is the commonest dyslipidemia which is in turn classified into 'primary hyperlipidemia', which cannot be linked to an identifiable disease and 'secondary hyperlipidemia' which is associated with some underlying conditions, most importantly, type 2 diabetes mellitus.[11] In addition to type 2 diabetes mellitus, secondary hyperlipidemia occurs also in conditions like hypothyroidism, obstructive liver disease, nephrotic syndrome and obesity.[11] Hyperlipidemia is usually asymptomatic, being noticed for the first time during routine check-up or after an attack of myocardial infarction or stroke [10]. The hypolipidemias are very rare but, when they occur, they present with spectacular clinical features.[10]

According to the Centers for Disease Control and Prevention (CDC), 97% of diabetic adults have one or more lipid abnormalities.[10] Dyslipidemia in type 2 diabetes mellitus is typically characterized by elevated plasma levels of triglycerides, particularly the triglyceride-rich VLDL and decreased HDL cholesterol levels.[11] Furthermore, diabetic patients typically have a preponderance of smaller, denser, oxidized LDL particles although the concentration of the actual LDL cholesterol may not be significantly different from that of the non diabetic individuals.[12, 13] Elevation of levels of oxidized LDL particles may increase atherogenicity, even if the absolute concentration of LDL cholesterol is not elevated [12, 13]. When this characteristic lipid profile triad is seen in type 2 diabetes mellitus, i.e. elevated VLDL, decreased HDL and elevated oxidized LDL, it is known as 'diabetic dyslipidemia' and confers a significant risk for cardiovascular diseases.[12] Previous studies have documented on racial differences in the prevalence of diabetic dyslipidemia.[1] A study done in the U.S. to determine the pattern of diabetic dyslipidemia among African-Americans showed that African-Americans have generally lower LDL-C and higher HDL-C levels when compared to their Caucasian counterparts.[14] Diabetic dyslipidemia is more common in females than males.[14] For reasons that are not fully understood, women without diabetes are partially protected from atherosclerosis in their pre-menopausal years; however, they lose much of this protection

when they develop diabetes.[11]

Despite the presence of abundant epidemiological evidence pointing to the rising disease burden attributable to diabetes mellitus in Tanzania, the prevalence of dyslipidemia among diabetic patients and its association with glycemic control are not yet clearly determined. The objective of this study therefore was to determine the prevalence of diabetic dyslipidemia and describe its association with glycemic control among diabetic patients attending specialized diabetes clinics in Dar es Salaam.

Methodology

A hospital – based, descriptive, cross – sectional study was conducted in Dar es Salaam from November 2006 to January 2007. Patients with well established prior diagnosis of diabetes mellitus and who were attending specialized diabetes clinics at Muhimbili National Hospital; the biggest referral and University Teaching Hospital in the country as well as at all three municipal hospitals in the City of Dar es Salaam, were invited to participate in the study. Patients were consecutively recruited through a simple random sampling technique until the required sample size was achieved. Fully informed written or verbal consent was sought from each participant. Subjects included into the study were those aged 18 years and above; receiving treatment for diabetes mellitus and residing in Dar es Salaam for at least 3 years. Excluded subjects were those who refused to consent; pregnant; known HIV on treatment and patients with well established renal disease.

Definition of Terms

Dyslipidemia was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and the American Heart Association,[15] as derangement in any of the lipid components: low density lipoprotein cholesterol (LDL-C) > 2.6mmol/L (100mg/dL); high density lipoprotein cholesterol (HDL-C) < 1.1mmol/L (40mg/dL) for men and <1.38mmol/L (50mmol/dL) for women; triglycerides (TGs) > 1.7mmol/L (150mg/dL) and Total cholesterol (TC) > 5.2mmol/L.

Poor diabetes control was defined as a level of glycosylated hemoglobin > 7% [16]. Body Mass Index (Kg/M^2) was classified as 'normal' (BMI 18.50 – 24.99); 'underweight' (BMI < 18.50); 'overweight' (BMI 25.00 – 29.99) or obese (BMI > 30.00).[17]

Clinical work – up

After enrolment, patients were interviewed using structured questionnaires after which, physical examination was performed to detect clinical features of dyslipidemia which included: symptoms of angina, symptoms of peripheral vascular disease and the presence of corneal arcus. A bathroom scale was used to measure weight in kilograms and height was measured in meters by a tape measure.

Laboratory work – up

About 4 ml of venous blood was taken from each subject for lipid profile and glycosylated hemoglobin assays. Total Cholesterol (TC), HDL-C, Triglycerides, and Glycosylated hemoglobin were measured by Konelab™ machine (© 2003 Thermo Electron Corporation). LDL-C was calculated indirectly from TC, HDL-C and TGs according to the Friedewald formula (Friedewald et al., 1972): LDL-C = [TC – HDL-C – (TGs/2.2)] (mmol/L).

Data analysis

Data was double checked for correctness before being entered into a computer software Epi info version 6. Chi – Squared test was used to test for association between categorical variables and student's t-test was used for continuous variables. Multiple logistic regression was used to determine the predictors of the dependent variables. A p-value < 0.05 was taken to be statistically significant.

Ethical Considerations

Ethical clearance was obtained from Muhimbili University of Health and Allied Sciences Research and Ethics Committee.

Results

One hundred and fifty diabetic patients were recruited into the study from a total of 1824 who attended diabetes clinics during the study period. Table 1 shows the clinical characteristics of the diabetic patients. Age ranged from 18 to 77; with a mean of 52.4 + 11.5. Fifty five percent of the participants (83/150) were females. The mean duration of diabetes was 6.5 + 5.4 years (range 1 to 30) with about 80% of the patients having lived with diabetes for duration not more than 10 years. Two thirds of the patients 100/150 (66.6%) were either over – weight or obese.

Twenty five patients (17 %) were past or current smokers and 39% (59/150) had hypertension. Of the 150 diabetic patients, 34 (23 %) were on insulin, 114 (76.0%) on oral hypoglycemic agents while 2 (1 %) patients were on diet only. Table 2 shows the frequency distribution of the different subclasses of dyslipidemia among diabetic patients by sex. Diabetic dyslipidemia was found in 142/150 (95 %) patients. Of the 67 male diabetic patients, dyslipidemia was present in 65 (97%) of them, while in the 83 female patients, dyslipidemia was present in 77 (93 %) patients and the difference was not statistically significant (p=0.3).

Only one of the 150 diabetic patients had a prior record of lipid profile and had dyslipidemia. She had elevated total serum cholesterol (5.6 mmol/L) as well as triglycerides (2.16 mmol/L). She was not on any treatment for dyslipidemia. In all other participants, lipid profiles were established for the first time during the study. The main dyslipidemia was elevated serum triglyceride, present in 142/150 (95 %)

patients. The serum triglyceride level ranged from 1.00 – 3.26 mmol/L (mean 2.22 ± 0.69). Elevated LDL-C dyslipidemia was present in 49/150 (33 %) patients and the serum level ranged from 0.00 – 4.46 mmol/L (mean 3.42 ± 1.02). Low HDL-C dyslipidemia was found in 53/150 (35 %) patients, with serum level ranging from 0.7 – 2.24 mmol/L (mean 1.11 ± 0.01). Hypercholesterolaemia was encountered in 31/150 (21 %). Total serum cholesterol level ranged from 3.2 – 6.9mmo/L (mean 4.91 ± 0.62).

Table 3 shows clinical characteristics of patients with diabetic dyslipidemia. Of the 142 patients with diabetic dyslipidemia, 58 (41 %) were hypertensive and 25 (17 %) were past or current smokers. Dyslipidemia was present in all categories of diabetes treatment: Of the 34 patients on insulin, 30 (88.2%) had dyslipidemia while of the 114 patients on oral hypoglycemic agents, 110 (96.5%) had dyslipidemia and the two patients on diet only had dyslipidemia as well. There was no statistically significant difference regarding the type of treatment and the presence of dyslipidemia (x^2 3.65; df =2; p <0.25). The clinical features of dyslipidemia included; history of angina in 11% (17/150); history of peripheral vascular disease in 2% (3/150) and corneal arcus in 21% (31/150) while the majority (66%) were asymptomatic. None of the patients had tendon xanthomas.

Table 1: Clinical Characteristics of diabetic patients attending diabetes clinics in Dar es Salaam (n = 150)

Variable	Number	% of Total
Age (years)		
< 20	1	0.7
20 – 30	7	4.7
31 – 40	17	1.3
41 – 50	31	20.7
51 – 60	59	39.3
61 – 70	30	20.0
70+	5	3.3
Sex		
Males	67	44.7
Females	83	55.3
Duration of Diabetes (years)		
1 – 10	125	83.3
11 – 20	19	12.7
21 – 30	6	4.0
BMI (Kg/m^2)		
< 18.50	7	4.7
18.50 – 24.99	43	28.7
25.00 – 29.99	59	39.3
30+	41	27.3
Past or current smoker	25	16.7
Hypertensive	59	39.3
Type of treatment		
Insulin	34	22.7
Oral hypoglycemics	114	76
Diet	2	1.3

Table 2: Distribution of subclasses of Dyslipidemia among Diabetic Patients by sex (n = 150)

Dyslipidemia	Males (n=67)	Females(n = 83)	Total(%)	P value
Overall	65(97.0%)	77(92.8%)	142 (95)	0.30
ETC	10(14.9%)	21(25.3%)	31 (21)	0.18
ELDL – C	20(29.9%)	29(34.9%)	49 (33)	0.62
LHDL –C	28(41.8%)	25(30.1%)	53 (35)	0.19
ETG	65(97.0%)	77(92.8%)	142 (95)	0.30

NB: = ETC = elevated total cholesterol; ELDL – C = elevated low density lipoprotein – cholesterol; LHDL – C = low high density lipoprotein – cholesterol; ETG = elevated triglycerides

Almost all patients (147/150; 98 %) were on their normal physical activities and about 95% of them, (139/150) had dyslipidemia. The three patients who admitted to having no any physical activities (sedentary life style) had dyslipidemia as well. All 142 patients with diabetic dyslipidemia were not on any form of treatment for their dyslipidemia.

Table 4 shows a multivariate analysis of factors which are likely to be associated with diabetic dyslipidemia. The mean level of glycosylated hemoglobin among the dyslipidemic patients was higher (6.926 ± 2.610%) compared to that of non-dyslipidemic patients (4.538 ± 1.265%), p = 0.01. Even after adjusting for hypertension, smoking, physical activity, duration of diabetes, age and Body Mass Index, the level of glycosylated hemoglobin remained independently associated with the development of diabetic dyslipidemia (p = 0.036).

Table 3: Clinical characteristics of Patients with Diabetic Dyslipidemia in Dar es Salaam (n = 142)

Variable	Number of Patients	%
Hypertension	58	40.8
Smoking	25	16.7
Type of Treatment of Diabetes		
Insulin	30	21.1
Oral Hypoglycemic Agents	110	77.5
Diet Only	2	1.4
Angina	17	11.3
*PVD	3	2.1
Corneal Arcus	31	21.8

* = Peripheral Vascular Disease

Table 4: Multivariate Analysis of factors likely to be associated with Dyslipidemia among Diabetic Patients in Dar es Salaam (n = 150)

Variable	Regression Coefficient, β	P value
Glycosylated Hemoglobin	0.618	0.036
Physical Inactivity	7.345	0.957
Smoking	8.044	0.862
Hypertension	1.277	0.277
Duration of Diabetes	0.229	0.215
Age	0.015	0.686
BMI	5.067	0.361

Discussion

The prevalence of diabetic dyslipidemia among diabetic patients in this study was 95 % and the commonest type was elevated triglyceride level, which occurred in all patients. Derangement in other lipid subclasses also was encountered with low HDL–C level as the second commonest form of dyslipidemia occurring in 35 % of the diabetic patients.

The high prevalence of dyslipidemia among diabetic patients in this study is close to that reported by Fagot-Campagna *et al* in the U.S., which was 97%.[10] This prevalence as well as ours appears to be higher than that found by Isezuo *et al* when they were determining the demographic and clinical correlates of metabolic syndrome in native African type 2 diabetics, in which the prevalence of dyslipidemia was 72%[18]. This difference could be explained by the higher cut-off values used by Isezuo *et al.* Many other studies have reported elevated triglycerides and depressed HDL-C levels as being the most common forms of dyslipidemia among diabetic patients.[1,6,8,11]

In this study, dyslipidemia occurred equally in both sexes. This contradicts findings by some studies done in the Middle East. For example, Abdul Rahman Al Nuaim *et al* in a study among the Saudi diabetic patients found that females were more dyslipidemic than males.[19] M. Nakhjavani *et al* in Iran reported that all types of dyslipidemia were significantly more prevalent in females.[20] This could probably be explained by the racial and cultural differences between the populations studied.

Only one of the 150 patients in this study had a prior record of lipid profile. She had elevated total cholesterol and triglycerides. She however, was not on any treatment for dyslipidemia. This shows that diabetic patients in Dar es Salaam are not routinely screened for dyslipidemia. Likewise, none of the 142 dyslipidemic patient was on any form of treatment for dyslipidemia. These findings are similar to those observed in some developed countries. A study by Jacobs MJ *et al* in the U.S. found that only about 28 % of diabetic dyslipidemia patients were on treatment and that only 3% were controlled to target levels.[21]

From this study, poor glycaemic control was associated with development of abnormal lipid profiles (dyslipidemia). These findings are similar to those by A. Caixas et al in which normalization of blood glucose was associated with improvement in the levels of lipids, particularly LDL-C,[22] and they are also similar to findings by Stern MP *et al*, that the prevalence of dyslipidemia rose with worsening glycemic control.[23] However, in a study by Stern MP *et al*, it was found that glycemic control alone did not suffice to control lipid profile and that a significant number of dyslipidemia patients will need direct lipid management.[23]

The type of diet, smoking, physical activity, hypertension, duration of diabetes, age and the body mass index (BMI) all have an influence on the development of dyslipidemia. In our study, poor glycemic control was independently associated with the development of dyslipidemia even after adjusting for the above predictors in multivariate analysis. The lack of association between these predictors and dyslipidemia in this study can be explained by the fact that, there were very few patients without dyslipidemia; 8/150 (5.3%).

Finally, as expected the majority of dyslipidemic patients were asymptomatic which stresses the importance of routinely screening diabetic patients for dyslipidemia without waiting for development of symptoms.

Conclusion

1. The prevalence of dyslipidemia among diabetic patients in Dar es Salaam is high
2. The commonest dyslipidemias are elevated triglyceride and depressed HDC – C levels.
3. There is gross lack of awareness and proper management of dyslipidemic diabetic patients.

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