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THE USEFULNESS OF TOTAL CHOLESTEROL AND HIGH DENSITY LIPOPROTEIN - CHOLESTEROL RATIO IN INTERPRETING LIPID PROFILE RESULTS OF DIABETES MELLITUS PATIENTS

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ABSTRACT

Objective: To determine the usefulness of total cholesterol/high-density lipoprotein cholesterol and/or high-density lipoprotein cholesterol/total cholesterol ratios in the interpretation of lipid profile result in clinical practice.

Methods: This is a prospective case-control study involving 109 diabetics, 98 diabetic hypertensives, 102 hypertensives and 120 control subjects. Serum lipid profile and plasma glucose were determined using appropriate methods.

Results: The mean ages of the different study groups were similar. Body mass indices of diabetics with or without hypertension were significantly higher than that of the controls. The difference in the mean total cholesterol of each group was not statistically significant when compared with the controls. A significant difference existed in the mean LDL when the different study groups were compared with the controls. There was a significant difference in the mean TG of DM and DM/hypertension patients compared with that of controls. However, the mean TG of hypertensive patients was not statistically different with that of the controls. The mean HDL was lower in each group of patients compared to that of the controls however the difference was not statistically significant. The mean TC/HDL ratios were significantly higher in all groups of patients when compared to that of the controls while HDL/TC ratios were significantly lower in all categories of patients when compared to that of the controls.

Conclusion: The ratios identified more dyslipidaemia than either of the lipid profile components. Therefore, the use of TC/HDL and or HDL/ TC ratios should be encouraged in screening for dyslipidaemia in diabetic patients with or without hypertension in clinical practice.

Key Words: Total Cholesterol/HDL ratio, Diabetes mellitus, Hypertension, Nigeria. *(Accepted 30 July 2008)*

INTRODUCTION

People with diabetes have a risk of cardiovascular disease (CVD) two to five times that of non-diabetic individuals [1-3]. Cardiovascular disease accounts for 66%[3] and 75%[4] of deaths in diabetic patients in Europe and USA respectively. Fatal CVD events occurred 70 times more frequent among diabetic patients in the UK[5]. Cardiovascular disease was the highest cause of hospital admission in Benghazi[6] and Jeddah[7] and second cause of admission and death in Nigerian diabetic patients[8,9]. One of the most important risk factors of CVD in diabetic patients is dyslipidaemia[10]. Miller reported that low HDL-C is the commonest lipoprotein abnormality in diabetic patients with CVD and is predictive of CVD events, even when total cholesterol levels are normal[11]. Usually the predominant small, dense LDL particles, which are more susceptible to oxidation, and the decrease in HDL-C found in DM patients are not typically associated with marked increase in plasma total cholesterol and LDL concentrations[10,12].

In health, plasma HDL-C is found to be higher in Africans[13,14]. Although reduced HDL-C levels have been associated with most CVD risk factors, it is not significantly reduced in diabetes[15] and hypertensive[16] patients in Nigeria. Notwithstanding, CVD is increasingly becoming one of the most important causes of admission and death in Nigerian diabetes mellitus patients today[8,9]. This variation in plasma HDL-C concentration in health and diseases in Africans, and its role in reverse cholesterol transport in particular, brings in the importance of TC/HDL-C ratio. The TC/HDL-C ratio explained a greater proportion of interpopulation variation in CVD mortality than did either TC or HDL-C alone[17]. Higher TC/HDL-C ratio has been found to be the variable most predictive of the presence of CVD and it has been demonstrated that a decreased as small as a unit in the TC/HDL-C ratio accounted for a 53% reduction in the risk of CVD[18,19].

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The TC/HDL-C ratio has therefore been strongly suggested for routine use in screening to identify patients with hyperlipidaemia as it is identified as the most efficient predictor of CVD at all ages. There have been many publications regarding hyperlipidaemia in DM patients but generally, there is paucity of information on TC/HDL-C ratio in interpreting lipid profiles in our environment in general and in DM patients in particular. We therefore, carried out this study to ascertain the usefulness of the ratio in interpreting lipid profiles in clinical practice.

MATERIALS AND METHODS

The subjects in this study were 109 diabetes mellitus patients, 98 diabetics with hypertension, 102 hypertensive patients, and 120 subjects who were neither diabetic nor hypertensive, who served as controls. Informed consent was obtained after briefing the subjects about the study. All the patients were diagnosed and managed in the Out-patient Department of University of Maiduguri Teaching Hospital (UMTH), between January and December 2005. Serum lipid analysis was performed in the chemical pathology department. The controls were hospital workers, and those who came for general medical checkup. Excluded were subjects who were acutely ill, those who had surgery within three weeks, patients who take alcohol and/or smoke cigarettes or females on oral contraceptives, because these conditions cause serum lipid variation[20].

In all the subjects, age, sex, weight (Kg), height (M) and blood pressure were recorded and Body Mass Index (BMI) calculated as Wt (Kg)/Ht (m^2). Ten ml of venous blood was drawn asceptically from the antecubital fossa of every subject after an overnight fast (10-14hrs). Eight ml was dispensed into a plain container and spun at 3000rpm for 10 minutes after clotting and serum separated from cells. The remaining 2ml was dispensed into a fluoride oxalate container, spun at 3000rpm for 10 minutes and the plasma separated from cells. Analytes determined in the serum were total cholesterol, triglycerides, and high-density lipoprotein-cholesterol,[21-23] while low-density lipoprotein cholesterol was calculated using the Friedwald formula[24]. Fasting plasma glucose was determined in the plasma by glucose oxidase method[25]. Data obtained from the study were analyzed using EPI-info version 6.03. The mean$\pm$SD values were calculated for all the variables. Their observed differences in maen$\pm$SD values then analyzed for statistical significance using the Student's t-test and $p<0.05$ was considered statistically significant. Deviations from the hospital reference values for the lipid profiles were noted and percentages calculated.

For the TC/HDL-C ratio, we used the range obtained from results of control subjects in this study since reference values for these parameters were not available. We therefore determined the numbers and percentages of the values whose results were higher than the upper limit of the range obtained from the control values. An observed difference of the percentages of those considered to have dyslipidaemia using the TC/HDL-C ratio as compared with those from the individual parameters of lipid profile were also noted.

RESULTS

Table 1 shows mean $\pm$ SD values of each parameter of lipid profile, TC/HDL-C and HDL-C/TC ratio. There was no statistically significant difference between the mean $\pm$ SD ages of each group of patients when compared with that of the control. The mean $\pm$ SD body mass index (BMI) of diabetics with or without hypertension were significantly higher than the control group. However, the observed difference in BMI between the hypertensive patients and the controls was not statistically significant ($p > 0.05$). The mean $\pm$ SD fasting plasma glucose of the diabetics with or without hypertension was statistically significant compared with that of the controls ($p<0.05$) while that of the hypertensive patients and controls was not statistically different ($p>0.05$). No statistically significant difference was observed between the mean$\pm$SD of fasting plasma glucose in diabetes with and without hypertension ($p>0.05$). The difference in mean $\pm$ SD total cholesterol of each group when compared with that of the controls was also not statistically significant (>0.05). A significant difference exists in the mean $\pm$ SD LDL-C when each group was compared with the controls. The mean $\pm$ SD HDL-C was however lower in each group of patients when compared to that of the controls but the difference was not statistically significant. There was a statistically significant difference in the mean $\pm$ SD TGs of DM and DM/Hypertension patients when compared to that of the controls. The observed difference in the mean $\pm$ SD TGs of hypertensive patients was not statistically different compared to that of the controls. The mean $\pm$ SD TC/HDL-C ratios were significantly higher in all groups of patients when compared to that of the controls. While HDL-C/TC ratio was significantly, lower in all categories of patients when compared to that of the controls.

Table 2 shows the number (percentage) of subjects considered dyslipidaemic in each group by the components of lipid profile alone as well as ratios. In this study, dyslipidaemia was considered when TC =6.2mmol/L, TGs =4.5mmol/L, LDL =4.1mmol/L, HDL <0.9mmol/L [26,27], and when the TC/HDL-C ratio is =4.5 and HDL/TC >0.45 [28-32]. The TC/HDL-C ratio diagnosed dyslipidaemia significantly more in each

group of patients than did each of the components of lipid profile alone. Similarly, HDL-C/TC ratio also diagnosed significantly more dyslipidaemia than did each of the lipid profile components. However, when the two ratios were compared, there was no observed significant difference between them.

Table 1: Mean ± SD distributions of study variables in different groups of patients and controls.

Variable	DM (n=109)	DM/HTN (n=98)	HTN (n=102)	Control
Age (yrs)	50.3± 11.2	50.8± 14.5	49.6± 14.8	51.3± 9.1
BMI (Kg/M^2)	27.2± 5.9	27.3± 6.7	26.4± 8.2	25.8± 7.2
FPG (mmol/L)	7.1± 3.6	8.6± 3.9	5.1± 1.2	4.0± 0.6
TC (mmol/L)	5.2± 1.4	5.3± 1.0	5.4± 1.5	4.5± 1.2
LDL (mmol/L)	3.5± 2.3	3.5± 1.2	3.3± 1.3	2.2± 0.8
HDL (mmol/L)	1.3± 0.6	1.2± 0.6	1.4± 0.5	1.5± 0.7
TGs (mmol/L)	2.6± 1.3	2.5± 0.8	1.3± 0.7	1.4± 1.3
TC/HDL	4.8± 2.2	5.1± 0.3	4.0± 1.4	3.4± 0.9
HDL-C/TC	0.27± 0.11	0.23± 0.11	0.28± 0.10	0.32± 0.12

Key: DM= Diabetes Mellitus HTN = Hypertension

Table 2: The percentage of subjects with dyslipidaemia in the different study groups.

Variables	DM (%)	DM/HTN (%)	HTN (%)	Control (%)
TC	48(44.0)	46(46.9)	51(50.0)	3(2.5)
LDL	34(31.2)	35(36.7)	32(31.4)	3(2.5)
HDL	27(24.8)	35(35.7)	21(20.6)	2(1.7)
TGs	27(24.8)	31(31.6)	12(11.8)	3(2.5)
TC/HDL-C	57(52.3)	54(55.1)	58(56.9)	5(4.2)
HDL-C/TC	59(54.1)	51(52.0)	57(55.9)	4(3.3)
Total Number of Subjects	**109**	**98**	**102**	**120**

Key: DM= Diabetes Mellitus HTN = Hypertension

DISCUSSION

In this study, most of the subjects were in the economically productive ages. This is in keeping with previous reports from the same hospital[9,33]. This implies the grave consequences of diabetes on the economy of the country. Being part of the metabolic syndrome (Syndrome X), [34] screening for lipid abnormalities in diabetics needs to be at diagnosis as the development of and damage by dyslipidaemia starts even before the diagnosis is made[33]. This study demonstrates that diabetes patients with or without hypertension had higher BMI compared with those with hypertension only and the controls. This supports the association between diabetes And obesity as an integral component of the metabolicsyndrome[33]. A study in Nigeria[35] had demonstrated that weight reduction leads to improved glycaemic control in diabetic patients. Emphasis on weight reduction and consistent exercise will be a more useful strategy in these patients[36,37]. The presence of hypertension in diabetes may make glycaemic control more difficult as demonstrated by higher mean fasting plasma glucose in our cohort.

The presence of co-morbidity may imply an additional economic burden on these subjects, which might ultimately affect control. A similar finding in other studies in Nigeria[15,33] did not reveal any significant difference in the

total cholesterol in diabetics with and without hypertension. This could be due to the presence of the small dense LDL-C described as the quality of dyslipidaemia in diabetes patients[10,38,39]. However, total cholesterol was significantly higher in the hypertensive patients compared with controls.

The TG levels in diabetics with or without hypertension was significantly higher than that of the controls and is similar to previous reports[15,33]. The insulin-resistant state impairs the normal suppression of fatty acids released from adipose tissue in the postprandial state[39]. Consequently, the flux of FFAs to the liver increases and overproduction of VLDL from these substrates occurs. However, the TG levels in the hypertensive patients were not significantly higher than that of the controls. The similarities between the findings in this study and the one in Ilorin [16] may not be environment-dependent.

HDL-C has been found to be higher in healthy children and adults in Africa[13,14] as well as diabetics[15] and hypertensives[16] in Nigeria. Consequently, the lower HDL-C usually found in diabetes mellitus did not occur in this study. This indicates the importance of the TC/HDL-C ratio especially in Nigerian diabetes, which suggested more dyslipidaemia in the present study than did any of the components of the lipid profile alone. In this study, the mean ± SD TC/HDL-C ratio determined was 3.4± 0.9 with a range of 2.5-4.3. This is in keeping with other values found in previous studies [28-32]. By this result since the TC/HDL-C ratio has not been in widespread use, we might have been under-diagnosing dyslipidaemia in these patients and subsequently acting too little too late in managing this important cardiovascular risk factor. The results of this study and the increasing prevalence of CVD in Nigerians[8,9,40] should therefore lead to a more detail interpretation of lipid profile results of diabetes patients in this environment.

The TC/HDL-C ratio, a preferred screening tool for CVD, is an important predictor of CVD among middle-aged men[17]. Similarly, since this ratio diagnoses more dyslipidaemia than any other component of lipid profile it implies that the ratio predicts more CVD in our patients. Hence, diabetes mellitus patients who are also obese and have increased TC/HDL-C ratio have triple risk of CVD in the future regardless of their total cholesterol or HDL-C values. The mean ± SD HDL-C/TC of the controls in this study was 0.32± 0.12 with a range of 0.20-0.44. This is also similar to reports from within [37] and outside [36] Nigeria. The HDL-C/TC ratio in this study also agrees with Taylor's report [32] which emphasized that the ratios of the different fractions of lipoproteins could be more useful predictors of coronary heart disease than the level of individual component of lipid profile. This is similarly observed in the present study where the ratios suggested more dyslipidaemia, a coronary heart disease risk factor, than did either of the components of lipid profile. Considering the substantial risk for developing CVD in patients with diabetes, a greater emphasis should be placed on the holistic interpretation of lipid profile in order to reduce the economic and medical burden associated with this condition.

CONCLUSION

The use of TC/HDL-C and/or HDL-C/TC ratios should be adapted in screening for dyslipidaemias in diabetic patients with or without hypertension since the ratio predicts more future CVD than did either TC or HDL-C alone.

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