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TOTAL CHOLESTEROL AND HDL RATIO IN NORMOGLYCEMIC OFFSPRING OF PATIENT WITH T2DM ON GRADED EXERCISE

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ABSTRACT

Objectives: The primary causes of Type 2 Diabetes Mellitus (T2DM) are largely unknown but increase in Total Cholesterol and HDL ratio (TC and HDL ratio) has been reported to be a risk factor for the T2DM through the alteration of Lipid Profile (LP). However, it is uncertain if exercise could influence the occurrence of T2DM in offspring of diabetic parents by altering the lipid profile. Therefore this study was designed to assess the effect of exercise on TC and HDL ratio in offspring of T2DM parents compared with offspring of non-diabetic parents. **Design:** This study involved selection of 42offspring of T2DM parents attending University College Hospital, Ibadan and 53 offspring of non-diabetic parents who are undergraduate students of the University of Ibadan, Nigeria.. Participants were randomly assigned into four groups; 27 Normal-weight Offspring of Non-Diabetic Parents (NONDP), 21 Normal-weight Offspring of Diabetic Parents (NODP), 26 Overweight Offspring of Non-Diabetic Parents (OONDP) and 21 Overweight Offspring of Diabetic Parents (OODP). Each participant followed a protocol of graded exercise using the tummy trimmer everyday spending 30-45 minutes daily for 24 weeks. Blood samples were obtained after an overnight fasting for determination of lipid profile levels at baseline, six week, 12 weeks, 18 weeks and 24 weeks, respectively.The LP determined from the fasting lipid Profile was measured spectrophotometrically using standard laboratory kits supplied by BIOLABO, France. Data were analyzed using descriptive statistic and student t test with significance at $p<0.05$. **Results:** After exercise, there were reductions in total cholesterol (mg/dL). There is reduction from 5.45±1.14 to 3.33±0.30 ($p<0.05$) in OODP from 3.85± 0.42 to 3.26±0.33(p=NS) in NODP from 4.01±0.31 to 3.07±0.16($p<0.05$) in OONDP from 4.72±0.40 to 3.94±0.30($p<0.05$) in NONDP. There were significant changes in TC and HDL ratio between baseline and at 24 weeks. **Conclusions:** Graded exercise reduced TC and HDL ratio in all the groups. The clinical importance of graded exercise in prevention of diabetes mellitus along with reducing lipid concentrations, among offspring of diabetic parents looks promising.

KEYWORDS: Graded exercise, Diabetic parents' offspring, TC and HDL ratio.

INTRODUCTION

Diabetes mellitus, commonly known as diabetes, is a disorder of intermediary carbohydrate, protein and lipid metabolism. It is characterized by hyperglycemia glucosuria, polydipsia, polyphagia and weight loss. It is usually associated with secondary alterations in glucose, fat and protein metabolism, leading to many biochemical disorders. It is characterized by peripheral insulin resistance, impaired regulation of hepatic glucose production with declining β-cell function which can eventually lead to β-cell failure.[1]

Type 2 Diabetes Mellitus (Type 2DM) is characterized by a combination of peripheral insulin resistance and inadequate insulin secretion by pancreatic beta cells.[2]

Insulin resistance has been attributed to elevated levels of free fatty acids and pro-inflammatory cytokines in plasma, leading to reduced glucose transport into muscle cells, elevated hepatic glucose production, and pronounced break down of fat.[2]

Studies have found that obesity and diabetes are connected. Individuals who are obese are at high risk of developing T2DM, particularly if a close family member is affected with T2DM. Researchers have not yet

discovered a specific gene that causes obesity although, several genes are considered to play a role.[3] There appears to be a connection between abdominal fats and diabetes, hence any factor that will reduce abdominal fat will likely reduce diabetes.[3]

Epidemic of diabetes, affecting about 3-5% of Western populations, is one of the main threats to human health in the 21st century.[3] Changes in the human environment, behavior, and lifestyle have resulted in a dramatic increase in the incidence and prevalence of diabetes in people with genetic susceptibility to diabetes. The global number of people with diabetes was 151 million in 2000, and now increased to 221 million in 2010 (an increase of 46%) both in developed and developing countries.[4]

Chronic hyperglycemia leads to many long-term complications in the eyes, kidneys, nerves, heart, and blood vessels. Individuals with pre-diabetes, undiagnosed type 2diabetes and long-lasting type 2 diabetes are at high risk of all complications of macrovascular disease, coronary heart disease (CHD), stroke, and peripheral vascular disease.[5] More than 70% of patients with type 2 diabetes die of cardiovascular causes.[5] Therefore, the epidemic of type 2 diabetes will be followed by an epidemic of diabetes-related cardiovascular disease (CVD).

Exercise has been known to ameliorate the effect of diabetes by improving insulin sensitivity and reduced the lipid level. The aim of this to work is to study the effect of exercise on Total cholesterol and HDL in normoglycemic offspring of patients with type 2DM.

METHODS

Experimental interventional study was carried out in which blood sample was collected from offspring of patients with type 2 diabetes mellitus and normoglycemic offspring of non-diabetic parents. The parents of the test group were attending the medical out-patient clinic (MOP) of the University College Hospital (UCH), Ibadan and Catholic Hospital Oluyoro, Oke-Ofa, Ibadan, South Western, Nigeria. The normoglycemic offspring of non-diabetic parents aged 25 years and above were randomly selected from general population of Ibadan Community, Ibadan in South-Western Nigeria, and undergraduate students of University of Ibadan. These are normoglycemic offspring of non-diabetic with normal weight that served as control subjects.

The participants were divided into four groups as follows:
A – Overweight / Obese offspring of DM parents (OODP).
B – Normal weight / Normal Body Mass Index (BMI) offspring of DM parents (NODP).
C – Overweight / Obese offspring of non-diabetic parents (OONDP).
D – Normal BMI / weight offspring of non-diabetic parents (NONDP).
The study was approved by the University of Ibadan Teaching Hospital Ethical Committee (UI/UCH joint IRB) and Catholic Hospital Ethical Committee prior to its implementation.

The parameters measured include: Total Cholesterol (TC) and High Density Lipoprotein (HDL)

10ml of venous blood specimen was obtained from antecubetal vein of each subject into plain bottles. Separation of serum at centrifugal force of 30,000rpm was carried out at IMRAT (Institute of Medical Research and Training) of the College of Medicine, University of Ibadan. The serum so obtained was stored at temperature not exceeding – 40^{o}c for lipid profile estimation, each in a refrigerator at UCH Pharmacology Department until used for the determination of biochemical profile.

This is by venous blood sampling and by measurement of anthropometric variables. This is repeated as follows: Baseline measurement and after 6, 12, 18 and 24 weeks.

Total cholesterol level was measured spectrophotometrically using standard laboratory supplied by BIOLABO, France. Cholesterol esters in the presence of cholesterol esterase cholesterol and free fatty acids. The cholesterol formed reacts with oxygen in the presence of cholesterol oxidase to form cholesten-4-one-3 and hydrogen peroxide. The hydrogen peroxide formed reacts with phenol and 4-amino-antipyrine in the presence of peroxidase to give aminoneimine (pinkish in colour) and water. The intensity of the pink/red colour formed is proportional to the cholesterol concentration. The procedure employed was as follows as described by LinLi et al, 2014.

The cholesterol concentration was determined as follows.

$$\text{Total cholesterol concentration (mg/dl)} = \frac{\text{Absorbance } \textit{sample} \text{ X Standard concentration}}{\text{Absorbance } \textit{standard}}$$

HDL cholesterol level was measured spectrophotometrically using standard lab kits supplied by BIOLABO, France. Low density lipoproteins (LDL) contained in serum are precipated by addition of phosphotungstic acid and magnesium chloride. High density lipoproteins (LDL) which remains in the supernatant (obtained after centrifugation) react with the cholesterol reagent and proportionally with the cholesterol standard as described by LinLi et al, 2014.[6]

HDL cholesterol concentration (mg/dl) = $\frac{\text{Absorbance } \textit{sample} \text{ X Standard concentration}}{\text{Absorbance } \textit{standard}}$

Heights of participants were taken using standard hospital-adult vertical rule with sliding arms which had been recalibrated and certified by a Biomedical Engineering technician prior to use. The study subject stood erect, upright and bare-footed. Those who had extra clothes such as coats and sweater removed them while Omron equipment measurements were being taken.

Body mass index (BMI) reading, Total body fat, visceral fat values for the subject were read off as displayed on the screen of Omron equipment. The BMI values were used to group subject into four categories. Underweight - BMI<18.5KG/M^2 Normal weight – BMI = 18.5 to 24.9kg/m^2 Overweight – BMI = 25-29.9kg/m^2 Obese – BMI =>30.0kg.m^2 (NIH calculator, 2011)[7] Omron fat estimator(Yunmai smart scale)[8] was used to measure the BMI. The subject stood uprightly bare-footed put on light clothing. The subject held his stretched hands forward as if he was riding a motor-bike.

Tummy trimmer, a portable lightweight equipment (European Home Choice Company, Lagos<Nigeria) was selected for the study. It is an in-door aerobic equipment. It is compact and can fit right in the subject's brief case.

During each phase of exercise the Tummy trimmer, is held at the two handles and the sole of the two feet are put inside the pedal rest while the subject assumes different positions (in IV phase). In phase I, the subject will then pull the tummy trimmer's spring towards himself or herself either while lying flat or sitting up on the floor or carpeted hard surface.

In phase II, subject sits up with leg straight, leans his or her body backwards until completely lying back with head on floor. He/she returns to sitting position in harmonic fashion. The subject was advised to start slowly and work up to repetition as she/he feels comfortable with harmoniously.

In phase III, the subject was advised to lie flat on floor, extend his/her legs straight up in the air. He will be keeping his/her back on the floor and raise lower legs without bending them. The subject was advised to sit erect with legs straight horizontally, he/she raises handle to tummy height using arms only.

Finally, in phase IV, subject was advised to lie flat on the floor while he/she bends knees up to his/her chest. He/she makes a circular motion push feet up and then round towards the floor again. The different positions were observed for exercise period of 30 to 40 minutes (a video clip of the exercise procedure was shown to the subject before the commencement of the exercise).

Each subject was advised as follows:

(1) He/she to undergo the 4 phases of exercise between 30 and 40 minutes daily (either in the mornings or evenings).
(2) He/she to contact the researcher on cell phone anytime when he/she has any problems with the unit.
(3) There were regular cell phone calls made to each of the subjects by the research assistant to ensure compliance with exercise schedule.
(4) The research assistant called them on cell phone and sent s.m.s (Short Message Service) to them to keep return appointments every six weeks. This was done one or two days before appointment schedule.

The data obtained were analyzed using computer statistical programme package SPSS version 15.0. Data were analyzed using student t test. Probability value of P less than 0.05 was considered statistically significant.

RESULTS

TC/HDL Ratio is shown in Table 1 and figure 1. The total cholesterol and HDL ratio was reduced in all the groups. The p-values are shown in the last column of the table. In OODP, the ratio was reduced from 5.45 $\pm$ 1.14 to 3.33 $\pm$ 0.30. Only the statistical analysis between OONDP, OODP and NONDP is significant (P<0.05).

Figure 1 shows the reduction of TC/HDL ratio statistically significant (P<0.05) in ONDP and NONDP groups. There is reduction from 5.45±1.14 to 3.33±0.30 in OODP, 3.85± 0.42 to 3.26±0.33 in NODP, 4.01±0.31 to 3.07±0.16 in OONDP, 4.72±0.40 to 3.94±0.30 in NONDP.

Moreover, the reduction in OONDP, OODP and NONDP were statistically significant.

Table 1: TC/HDL ratio measurements in offspring of diabetic and non-diabetic parents before and after 6 months exercise.

	Before exercise Mean±SEM	After exercise Mean±SEM	P
Overweight/Obese offspring of diabetic parents (OODP) n=21	5.45±1.14	3.33±0.30	0.000*
Normal weight offspring of diabetic parents (NODP) n=21	3.85±0.42	3.26±0.33	0.095
Overweight/Obese offspring of Non-diabetic parents (OONDP) n=26	4.01±0.31	3.07±0.16	0.000*
Normal weight offspring of Non-diabetic parents (NONDP) n=27	4.72±0.40	3.94±0.30	0.000*

All values are mean±SEM
*Significant at p<0.05

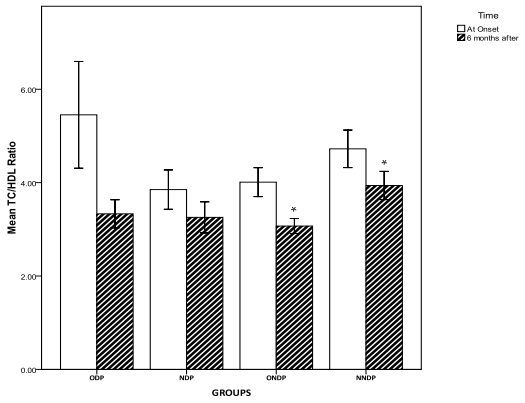

Figure 1: Showing mean TC/HDL ratio and different groups at onset and 24 weeks after exercise.

All values are mean±SEM
*Significant at p<0.05

DISCUSSION

There was reduction in this TC/HDL ratio in all the groups. This is the ratio between the level of total cholesterol and HDL (good cholesterol). In adults the ratio should be higher than 0.24,[9] however the ratio under 0.24 is low and less than 0.10 is dangerous while the ratio greater than 6.0 is too high. The ratio is most potent predictors of heart disease,[9] HDL is protective against heart disease,[9] Real et al, (2002) reported the importance of total cholesterol to HDL ratio. They advised that lowering total cholesterol prevented coronary heart disease in 33 out of 66 hypercholesterolaemic subjects that they studied. This is an important index when a physician is assessing the heart of a patient who has hypertension concurrently with diabetes mellitus. This signified that exercise can prevent or delay the onset of these twin diseases: (Hypertension and diabetes). In patients with T2DM, insulin resistance syndrome continues to gain support as an important risk factor for premature coronary disease particularly concomitant hypertension, hyperinsulinemia, central obesity and the overlap of metabolic abnormalities of hypertriglyceridemia, low HDL and elevated FFA.[10] Most studies show that these patients have low level of fitness compared with control patients, even when measured for level of ambient activity and that of poor aerobic fitness. Poor fitness is associated with many of the cardiovascular risk factors and improvement in many of these risk factors has been linked to a decrease in plasma insulin levels.[10] It is therefore likely that many of the beneficial effects of physical activity on cardiovascular risk are related to improvements in insulin sensitivity.[10]

The study was carried out on normoglycemic type 2 diabetics and non-diabetics controls to assess the role of individual parameters of lipid profile in the dyslipidaemia of type 2 diabetes mellitus, with particular emphasis on the lipid ratios. TG and HDL ratio may be better indicators of how the individual parameters correlate with each other, while in circulation during the postprandial state. Diabetes mellitus type 2 is typically associated with dyslipidaemia.[11] This is characterized by hypertriglyceridaemia and low HDL-C levels, while the levels of total cholesterol and LDL-cholesterol may not differ significantly from those in the non diabetics. However, patients with diabetes often have an abnormally high number of small dense LDL particles, which has been found to be related to the TG and HDL ratio.[12]

Many studies have also indicated an important predictive role of increased serum TG levels contributing to the risk for CHD, especially in type 2 diabetics.[13] In type 2 diabetics, high TG levels and low HDL-C levels frequently co-exist, which are important factors for CHD. In this regard, TG/HDL-C ratio is one of the important predictors of heart disease. It is generally considered that ratio below 2.5 represents a lower risk of heart disease. This ratio is also an indicator of LDL particle size[14] and a good predictor of LDL, phenotype B, that is associated with an increased atherogenic risk.[15,16] whereas, HDL has been assigned a protective role against the development of atherosclerosis because of its role in reverse cholesterol transport. HDL is also associated with the metabolism of the TG rich lipoproteins, since it is the reservoir of apoprotein C-2,[17] which is the activator of lipoprotein lipase – the enzyme

responsible for the metabolism of chylomicrons and VLDL in the peripheral tissues. During the postprandial metabolism of chylomicrons and VLDL in the peripheral tissues During the postprandial metabolism of these lipoproteins, there is an active exchange of lipids and apolipoproteins with HDL. Hence the TG and HDL ratio highlights the integrated role of these two parameters in the removal of a lipid load from the circulation in the postprandial state.

CONCLUSION

In conclusion, the present study shows that subjecting offspring of T2DM to exercise will improve their TC/HDL ratio which has a beneficial effect. More studies are required to ascertain this by using larger population.

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