Original Article

Comparison of Effect of Exercise on Lipid Profiles of Overweight Normoglycemic Offspring of T2DM Parents and Non-diabetic Parents

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Background : The primary causes of Type 2 Diabetes Mellitus (T2DM) are largely unknown but abnormal lipid profile has been reported to be a risk factor for the T2DM through the alteration of lipid profile pattern.

Aims and Objectives : This study was designed to assess the effect of exercise on Lipid Profile (LP) on offspring of T2DM parents compared with offspring of Non-diabetic parents.

Discussion : This study involved 60 Offspring of T2DM parents (OODP) attending University College Hospital, Ibadan and 60 offspring of Non-diabetic parents (OONDP) who are undergraduate students of the University of Ibadan, Nigeria. Participants were randomly assigned into the two groups. Each participant followed a protocol of graded exercise using "tummy trimmer" everyday spending 45 minutes daily for 24 weeks. Blood samples were obtained after an overnight fasting for determination of lipid level using standard methods at baseline and at 24 weeks. Data were analyzed using descriptive statistics and student t test with significance at $p<0.05$).

Results : The most populated aged group was 26 to 35 years of which 47.3% (n=26) were OODP and 52.7% (n=29) were OONDP. However, all subjects were overweight with mean BMI of OODP and OONDP (29.30kg/m^2 ± 0.71 versus 26.37kg/m^2 ± 0.88) p=.0.035 In OODP, the mean Total Cholesterol (TC) reduced significantly from 131.29mg/dl ± 1.29 to 123.90 mg/dl ± 6.65 $p<0.001$ after 24 weeks of exercise. In OONDP, the mean TC also reduced significantly from 156.12 mg/dl + 6.38 to 147.73 mg/dl ± 5.93 $p<0.001$ after six months of exercise.

Conclusions : Serum Lipid improved after 24 weeks of exercise in the two groups. There was reduction of triglyceride and LDL- cholesterol while HDL-cholesterol increased.

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***Key words* : Exercise, Body Mass Index, Lipid Profile, Offspring of Diabetics, Offspring of Non-diabetics.**

Diabetes mellitus, commonly known as diabetes, is a disorder of intermediary carbohydrate, protein and lipid metabolism. It is characterized by hyperglycemia, glucosuria, polydipsia, polyuria, 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 and eventually leading 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. 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[1].

Obesity at younger age, significantly increased lifetime risk of Type 2 Diabetes Mellitus (T2DM)[1]. Family history of T2DM is associated with higher Body Mass Index (BMI), Dyslipidemia and Impaired Glucose Tolerance (IGT) in offspring[2, 3]. There seems to be a vicious cycle, where obesity increases risk for T2DM and a family history of T2DM increasing the risk for obesity[1, 4]. Parental history of T2DM is one of the dominant risk factors for development of T2DM[5]. The phenotype varies depending on which parent is affected and if the child was exposed to hyperglycemia in utero[5, 6]. β-cell dysfunction has been

Editor's Comment :

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- This study involved 60 Offspring of T2DM parents (OODP) attending University College Hospital, Ibadan and 60 offspring of Non-diabetic parents (OONDP) who are undergraduate students of the University of Ibadan, Serum Lipid improved after 24 weeks of exercise in the two groups. There was reduction of triglyceride and LDL- cholesterol while HDL-cholesterol increased.

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observed even in non-diabetic offspring of T2DM, more accentuated among those with maternal T2DM compared to paternal inheritance[7]. Here we report the effect of exercise on lipid profile in normoglycemic subjects.

In diabetes many factors may affect blood lipid levels, because of interrelationship between carbohydrates and lipid metabolism. Therefore, any disorder in carbohydrate metabolism leads to disorder in lipid metabolism and vice versa. Insulin resistance is a primary defect in the majority of patients with T2DM. In non-diabetic individuals insulin resistance in combination with hyperinsulinemia has a strong predictive value for future development for type 2 diabetes[8]. Several studies showed that insulin affects the liver apolipoprotein production and regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein, which causes dyslipidemia in diabetes mellitus. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase[9,10]. Hypertriglyceridaemia usually accompanies decreased HDL cholesterol, which is also a prominent feature of plasma lipid abnormalities seen in individuals with diabetes[11,12]. The cluster of lipid abnormalities associated with T2DM is defined by a high concentration of TG and small dense LDL and a low concentration of HDL cholesterol. The association between reduced HDL cholesterol levels and increased risk of heart disease is, on the other hand, well established, independently of TG levels and other risk factors[13, 14]. The possible mechanism responsible for hypertriglyceridaemia may be due to increased hepatic secretion of Very Low Density Lipoprotein (VLDL) and delayed clearance of triglyceride rich lipoproteins, which is predominantly due to increased levels of substrates for triglyceride production, free fatty acids and glucose[15].

Individuals who are obese are at high risk of developing T2DM, particular 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. There seems to be a connection between abdominal fat and diabetes, hence anything that will reduce abdominal fat will likely reduce diabetes[2]. Exercise has been known to ameliorate the effect of diabetes by improving insulin sensitivity and lipid profile .It is the aim of this to work to compare the effect of exercise on lipid profile of overweight normoglycemic offspring of patients with type 2 DM and non-diabetic parents.

Materials and Methods

This is a prospective study of a cross-section of 120 randomly selected subjects. All subjects are from South-west, Nigeria. The parents of the test group (normoglycemic offspring of Diabetic Parents) 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 control group, normoglycemic offspring of non-diabetic parents were randomly selected from the general population of Ibadan Community, Ibadan and undergraduate students of University of Ibadan.

Hypertensive and diabetic subjects were exempted from this study. The weight of subjects was recorded in kilograms (to the nearest 1.0 kg) without wearing any heavy clothing like a coat, jacket, shoes, or Agbada (a flowing wide-sleeved robe), using a calibrated bathroom scale (Soehnle Waagen GmbH and Co. KG, D 71540 Murrhardt/Germany) positioned on a firm horizontal surface. Height of subjects was measured in meters (to the nearest 0.1m) using a stadiometer. Subjects stood erect, without shoes and headgears, on a flat surface with the heels and occiput in contact with the stadiometer (Prestige HM0016D) (India). The bathroom weighing machine and stadiometer had the reliability test using Rasch modeling approach and Samuel Messick's method to test their validity. The Body Mass Index (BMI) was subsequently calculated using the formula: weight (kg)/ height^2 (m^2). There were two groups of subjects [control OONDP) and test group (OODP)]. Estimation of blood lipid levels was conducted in each of the subjects as described below. Blood samples were obtained after overnight fasting for determination of LP levels using standard methods, at baseline start of week 1 and after 24 weeks of exercise. The LP determined from the fasting blood was measured spectrophotometrically utilizing standard laboratory kits supplied by BIOLABO, France. Data were analyzed using descriptive statistics. Continuous variables were compared with student t test and level of significance set at $P<0.05$.

The following definitions were utilized: Underweight – BMI <18.5 kg/m^2. Normal weight – BMI 18.5-24.9 kg/m^2, Overweight – BMI 25.0-29.9 kg/m^2, Obesity – BMI $\geq$30 kg/m^2.

Tummy trimmer, a portable, aerobic exercise, lightweight equipment (European Home Choice Company, Lagos, Nigeria) was used for exercise in this study. It is an in-door aerobic equipment. It is compact and can fit right in the subject's hand-bag.

During each phase of exercise the Tummy trimmer, a portable lightweight equipment, is held at the two handles and the sole of the two feet are put inside the pedal rest while the subject assume different positions. 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. 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 subjects were trained to start slowly and work up with repetition as she/he feels comfortable with harmoniously. The subject was trained 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 subjects would later sit erect with legs straight horizontally, he/she raises handle to tummy height using arms only. Then finally, subject would to lie flat on the floor while he/she bends knees up to his/her chest. He/she makes circular motion push feet up and then round towards the floor again. The different positions were observed for exercise period of 45 minutes (a video clip of the exercise procedure was shown to the subject before the commencement of the exercise). Each subject was instructed as follows: (1) He/she to undergo the 4 phases of exercise for 45minutes daily (in the 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 weekly cell phone calls made to each of the subjects by the research assistant to ensure compliance with exercise schedule.

Experimental interventional study was carried out in which blood sample was collected from subjects in the test group and the control group after an overnight fasting.

10ml of venous blood specimen was obtained from each subject into plain bottles. Separation of serum at centrifugal force of 3,000 rpm 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- 20^{o}C in a refrigerator at IMRAT until used for the determination of lipid profile.

Determination of Total Cholesterol (TC):

TC level was measured spectrophotometrically using standard laboratory chemical supplied by BIOLABO, France. The cholesterol formed reacts with oxygen in the presence of cholesterol oxidase to form 4-cholesten-3-one 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. It was performed according to standard protocols.

Determination of HDL Cholesterol HDL-C:

HDL-C level was measured spectro-photometrically using standard lab kits supplied by BIOLABO, France. LDL contained in serum are precipitated by the addition of phosphotungstic acid and magnesium chloride. High-density Lipoproteins (HDL) which remain in the supernatant (obtained after centrifugation) react with the cholesterol reagent and proportionally with the cholesterol standard. It was conducted according to standard protocols. Determination of TG and LDL levels were also carried out according to standard protocols.

Sample size estimation :

This was performed using formula $(Z_{1-\alpha}/2)^2 \times SD^2/d^2$ where Z= normal variant, d= 5.0%, Type 1 error was used with SD of 25 mg/dl of fasting blood glucose from previous study. Attrition was 25%. This is equal to $\frac{1.96^2(25)^2}{5.0^2} = 96$

If we add 25% attrition (24) making a total of 120 subjects. Cochran's formula (1977).

Statistical Analysis :

Statistical analysis was done using SPSS version 15 software (Lead Technologies, Chicago, USA). The data were expressed as mean ± SD for various continuous parameters studied.

The study was approved by the Teaching Hospital Ethics Committee (UI/UCH joint IRB) and Catholic Hospital Ethics Committee prior to its implementation.

RESULTS

There were 120 participants in the study. Each of the 2 group had 60 subjects each with equal number of males and females. The most populated aged group was 26 to 35 years of which 47.3% (n=26) were OODP and 52.7% (n=29) were OONDP. However, all subjects were overweight with mean BMI of OODP and OONDP (29.30kg/m^2 ± 0.71 *versus* 26.37kg/m^2±0.88), p=0.035 significantly (Table 1).

In OODP, the mean TC reduced significantly from 131.29 mg/dl ± 1.29 to 123.90 mg/dl ± 6.65, p<0.001 at the end of exercise period (after the exercise). In OONDP, the mean TC reduced significantly from 156.12 ± 6.38 to 147.73 mg/dl ± 5.93, p<0.001 after the exercise. In OODP male subjects, the mean TC reduced significantly from 120.90 ± 7.71 to 117.20

mg/dl ± 7.07 p<0.001 after the exercise. In female OODP, the mean TC reduced significantly from 140.73 mg/dl ± 13.97 to 130.00 mg/dl ± 10.95, p<0.001 after the exercise (Table 2).

In OODP, the mean HDL increased significantly from 32.95 mg/dl ± 3.57 to 42.57 mg/dl ±3.82, p<0.001 after the exercise. In OONDP, the mean HDL increased significantly from 43.27 mg/dl ± 2.86 to 50.35 mg/dl ± 2.46, p<0.001 after the exercise. In OODP male subjects, the mean HDL increased significantly from31.90 mg/dl ± 4.38 to 38.30 mg/dl ±5.65 p<0.001 after the exercise. In female OODP, the mean TC increased significantly from 33.91± 5.72 to 46.45 mg/dl ± 5.15, p<0.001 after the exercise (Table 3).

In OODP, the mean LDL-C reduced significantly from 71.14 mg/dl ± 7.29 to 66.05 mg/dl ± 7.17, p<0.001 after the exercise. In OONDP, the mean LDL-C reduced significantly from 86.62 mg/dl ± 6.13 to 78.92 mg/dl ± 5.67, p<0.001 after the exercise. In OODP male subjects, the mean LDL-C reduced from 66.60 mg/dl ±8.05 to 62.00 mg/dl ± 7.44, p>0.001 after the exercise. In female OODP, the mean LDL-C reduced significantly from 85.90 mg/dl ± 9.35 to 75.10±7.87, p<0.001 after the exercise (Table 4).

Table 1 — *Anthropometric Parameters of 120 Study Subjects*

Variable	Category	Total	OODP	OONDP	P
Gender	Male	60 (50.0)	30 (50.0)	30 (50.0)	
	Female	60 (50.0)	30 (50.0)	30 (50.0)	
Age (years)	16-25	43 (35.8)	22 (36.7)	21 (35.0)	
	26-35	55 (45.8)	26 (47.3)	29 (52.7)	
	36-45	19 (15.8)	9 (15.0)	10 (16.7)	
	46-55	3 (2.5)	3 (5.0)	0 (0.0)	
Mean Weight (Kg)		69.80±1.59	73.28±2.38	67.00±2.01	0.185
Mean BMI (Kg/m²)		27.70±0.61	29.30±0.71	26.37±0.88	0.035*

P value significant at P<0.05.

Table 2 — *Variability of Total Cholesterol (TC) in the Study Groups*

Variable	Category	Before Ex	After Ex	T	P
TC/mg/dl	Total	145.02±5.37	137.09±4.71	4.048	0.001*
	OODP	131.29±8.29	123.90±6.65	3.015	0.007*
	OONDP	156.12±6.38	147.73±5.93	2.812	0.009*
	OODP-Male	120.90±7.71	117.20±7.07	2.924	0.017*
	OODP-Female	140.73±13.97	130.00±10.95	2.447	0.034*
	OONDP-Male	158.40±10.79	144.10±8.08	1.908	0.089
	OONDP-Female	154.69±8.13	150.00±8.36	5.825	0.001*

Table 3 — *Variability of High Density Lipoprotein (HDL) in the Study Groups*

Variable	Category	Before Ex	After Ex	T	P
HDL-C/mg/dl	Total	38.66±2.35	46.87±2.23	-6.574	0.001*
	OODP	32.95±3.57	42.57±3.82	-4.033	0.001*
	OONDP	43.27±2.86	50.35±2.46	-5.982	0.001*
	OODP-Male	31.90±4.38	38.30±5.64	-3.081	0.013*
	OODP-Female	33.91±5.72	46.45±5.15	-3.099	0.011*
	OONDP-Male	44.50±4.91	53.90±3.81	-4.572	0.001*
	OONDP-Female	42.50±3.60	48.13±3.18	-4.146	0.001*

Table 4 — *Variability of Low density Lipoprotein (LDL) in the Study Groups*

Variable	Category	Before Ex	After Ex	T	P
LDL-C/mg/dl	Total	79.70±4.79	73.17±4.50	5.679	0.001*
	OODP	71.14±7.29	66.05±7.07	4.329	0.001*
	OONDP	86.62±6.13	78.92±5.67	4.182	0.001*
	OODP-Male	66.60±8.05	62.00±7.44	1.884	0.092
	OODP-Female	75.27±12.10	69.73±11.95	9.114	0.001*
	OONDP-Male	85.90±9.35	75.10±7.87	2.381	0.041*
	OONDP-Female	87.06±8.30	81.31±7.92	6.446	0.001*

Discussion

There was reduction in the lipid profile in the two groups. The present study assessed the lipid profile among normoglycemic offspring of T2DM subjects and controls without family members with T2DM. We observed lower mean lipid profile in the subjects studied after six months of exercise in normo-glycemic offspring of individuals with T2DM compared to controls. Pimenta *et al*,[16] observed similar reduction in lipid profile in subjects with family history of DM compared to BMI-matched controls[17]. 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, abnormal lipid profile 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[18]. It is therefore likely that many of the beneficial effects of physical activity on cardiovascular risk are related to improvements in insulin sensitivity[18]. 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. Diabetes mellitus type 2 is typically associated with dyslipidaemia[19]. 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[20]. 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[21]. In type 2 diabetics, high TG levels and low HDL-C levels frequently co-exist, which are important factors for CHD. 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,[22] 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.

Conclusion

Regular exercise appear to significantly reduced serum lipid in overweight non diabetic individuals irrespective of diabetic status of their parents. People with family history of T2DM should engage in regular exercise to reduce their tendency to obesity and blood lipids.

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