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Mother-daughter genetic relationship in central obesity

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ABSTRACT

Central obesity is an important predictor of all-cause mortality. Children of obese parents bear a greater risk to develop obesity themselves.

Objective: To find possible correlations in central obesity and other cardio-metabolic parameters between mother and daughter.

Subjects and methods: The current study measured anthropometric, laboratory, radiologic and genetic data for 120 centrally obese mothers and their 200 daughters aged from 12 to 18 years old.

Results: Twenty-two percent of the daughters was overweight, 15.5% obese and 30% had central obesity. Genotype E3/E4 of apolipoprotein E was the most frequent genotype in mothers group (38.3%) and daughters with visceral obesity (46.7%) while E3/E3 was the most frequent genotype in daughters group without visceral obesity (42.9%). In both mothers and daughters, disturbed lipid profile was found in those with E3 allele, while increased BMI and weight were found among those with alleles E2 and E4 respectively. Daughters genotype E3/E4 had the highest significant values of most of the studied anthropometric measurements and lipid profile, while mother's genotype E4/E4 had the highest significant values of most of the studied anthropometric measurements and insulin.

Conclusion: A key role could be played by the mother in the primary prevention of central obesity due to the consistent association of central obesity indices between mothers and daughters.

Introduction

Obesity is now a severe universal problem for the public health. The International Obesity Task Force [1] stated that about 155 million children in school age are obese or overweight around the world. Egypt, United Arab Emirates, Saudi Arabia, Kuwait, Jordan, and Bahrain show the highest levels of obesity and overweight in the region with prevalence in these countries ranging from 69% to 77% in men and 74% to 86% in women [2].

Children of obese parents carry a greater risk to be obese themselves [3]. This pattern is evident even when children are raised away from their biological parents, suggesting a genetic contribution in adiposity [4]. When the individual is exposed to a specific environment, the genetic predisposition to fat gain is expressed. It is greatly important to investigate possible environmental factors that can act together with genetic factors to produce increase in the prevalence of obesity among children [5].

A dramatic increase in health care costs have been noticed in the last two decades due to obesity and related issues among adolescents and children, since obesity; especially central obesity, is an independent risk factor for chronic diseases such as type 2 diabetes and cardiovascular conditions. Obesity is associated with reduced life expectancy as well as an increased risk of morbidity and mortality [6].

So, this study aimed to find possible correlations between the mother-daughter dyads for central obesity and subsequent cardio-metabolic risk factors; and to understand the relative contributions of shared genes to the observed mother-daughter patterns. Also, to provide data for policy makers to spotlight daughters at high risk during childhood helping to develop healthy lifestyles as well as obesity prevention programs.

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Subjects and Methods

Subjects

This study is a cross sectional study. It comprised 320 Egyptian female subjects; 120 centrally obese mothers and their 200 daughters (ages range between 12 and 18 years). They were selected from the "Clinic of Management of Visceral Obesity and Growth Disturbances", "Medical of Excellence Research Centre (MERC)" at the National Research Centre (NRC), during the period from February 2013 to March 2016.

Tracing for daughters was done after screening of 800 mothers to choose those mothers exhibiting both exogenous and central obesity. Pregnant mothers were excluded from the study. Mothers and daughters were excluded if (a) obesity is secondary to syndromatic, endocrinological or neurological deficit, (b) there is a history of significant hepatic, renal, or thyroid dysfunction, (c) there are acute or chronic inflammatory diseases; recent surgical operations; myocardial infarction or a cerebro-vascular accident within the previous 3 months, (d) they are on corticosteroid use; anti diabetic medication use; or lipid-lowering medication use.

Ethical committee approval

Verbal presentation and explanation of the written informed consent form and information was supplied to patients. This was confirmed orally and by the personally dated signature of the parents. Approval of the Ethical Committee of National Research Centre was issued on 26/8/2012 number 12/090.

Methods

For all participants, a full history was taken and thorough physical examination was performed. Blood pressure was measured and classified: mothers were classified as normal (SBP $\leq$ 119, DBP $\leq$ 79), prehypertensive (SBP120-139, DBP 80–89), stage 1 hypertension (SBP 140–159, DBP 90–99) and stage 2 hypertension (SBP $\geq$ 160, DBP $\geq$ 100) [7] (Chobanian et al., 2003). For daughters, the data of the systolic and diastolic blood pressure were plotted on blood pressure tables for children and adolescents of the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents [8]. Pubertal development was assessed by the criteria of Tanner [9].

Anthropometric measurements

Body height was measured to the nearest 0.1 cm using a Holtain portable anthropometer (The Harpenden Portable Stadiometer, Wales, UK)). Body weight was determined to the nearest 0.01 kg using a Seca scale Balance (Seca Balance Beam Scale Model 700, Seca Deutschland Medical Scales and Measuring Systems Seca gmbh & co. kg. Hamburg, Germany) with the subject dressed minimum clothes and no shoes. Waist circumference was measured at the level of the umbilicus with female standing and breathing normally, hip circumference at the level of the iliac crest, using non-stretchable plastic tape to the nearest 0.1 cm. Skin fold thickness at the five sites was measured at left side of the body using Harpender Tanner-White house Holtain skin fold caliper to the nearest 0.2 mm. Each measurement was taken; by well-trained researcher and another one assisted to him; as the mean of three consecutive measurements, using standardized equipments and following the recommendations of International Biological Program [10]. The following indices were calculated: Body mass index (BMI): as weight (in kilograms) divided by height squared (in meters) and Waist/Hip ratio (cm/cm).

The terms overweight and obesity were used in mothers when their BMIs were 25 to <30 kg/m^2 and $\geq$30 kg/m^2 respectively, according to the World Health Organization Expert Committee classification [11]. For daughter's BMI, subscapular and triceps skin fold thicknesses they entered separately to the Egyptian growth charts for age and sex and percentiles and Z-scores were calculated [12]. For daughters (aged 12 to 18 years), based on the standardized percentile curves of BMI suggested for Egyptian children and adolescents; obesity was defined as $\geq$ 95th percentile, overweight as $\geq$ 85th to < 95th percentile, and normal weight is defined as 15th–<85th percentile of BMI for age and sex [11].

Abdominal ultrasound

Abdominal ultrasound was performed to assess visceral and subcutaneous fat. Using a 7.5 MHz linear-array probe; the rectus muscle to spine and rectus muscle to aorta distances were measured as indicative of visceral fat thickness, and the distance between skin to fat and fat to rectus muscle interfaces are measured as indicative of subcutaneous fat thickness using VIVID Three (GE, Health care, USA) ultrasound scanner with a high resolution B-Mode [13]. The term central obesity was used in mothers with umbilical visceral fat thickness $\geq$7 cm [14] and in daughters with umbilical visceral fat $\geq$4.4 cm [15].

Laboratory investigations

Venous blood samples were obtained to measure plasma glucose level and lipid profile in the morning by venipuncture; performed by Professional staff; after 12- hours overnight fasting. The blood samples were left to clot; sera were separated by centrifugation for 10 min at 5000 rpm then stored at −80 °C until assays. Plasma glucose was determined by the glucose oxidase method. Plasma concentrations of total cholesterol [16], triglycerides [17], and high-density lipoprotein-cholesterol (HDL-C) [18] were measured using commercially available kits provided by STANBIO Laboratory Inc. (1261 North Main Street Boerne Texas 78006 USA). LDL-C was calculated according to an equation developed by Friedewald et al. [19], as follows: LDL-C = Total cholesterol − Triglycerides/5 + HDL-C.

Molecular studies

Genomic DNA was extracted from whole blood using DNA extraction kit (QIAamp DNA Blood Kit; Qiagen). The purity of extracted DNA was checked. A 318 bp fragment from the ApoE gene was PCR amplified in a 50 µl reaction containing 10 µl (0.1–0.4 ng) purified genomic DNA, 1x Qiagen PCR Buffer, 0.25 µM each primer, 200 µM each dTNP, 1xQ-Solution, and 1.5U QIAGEN Taq DNA Polymerase. Two primers were used in the amplification: Upstream primer E2 (5′ ACT GAC CCCGGT GGC GGA GGA GAC GCG TGC) and downstream primer E3 (5′ TGT TCCACC AGG GGC CCC AGG CGC TCG). Reaction mixtures were incubated at 94oC for 3 min, subjected to 40 cycles of amplification (94oC, 10sec.; 65oC, 30sec; 72oC, 30sec), and incubated at 73oC for 7sec. The PCR product was digested with restriction enzymes AflIII (5.000 U/ml) and HaeII (20.000 U/ml), 10 × buffer, and 0.2 µl BSA. The contents were incubated for 24 h at 37 °C. The digests were resolved on ethidium bromide-stained agarose gel and the results were documented by photography and separation of the resulting DNA fragments on 4% agarose gel [20].

Statistical Analysis

Data were coded and entered using the statistical package SPSS version 16. Data was summarized using mean and standard deviation in quantitative data and using frequency (N) and relative frequency (percentage) for qualitative data. Comparisons between groups were done using ANOVA test. Correlations between