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Heritability of Obesity-Related Variables in Tehran Families: Tehran Lipid and Glucose Study

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Background: Obesity is a complex disease resulting from interaction between genetic, environmental and behavioral factors.
Objectives: In this study, we aimed to estimate the heritability for obesity-related variables among nuclear families of Tehran Lipid and Glucose Study (TLGS).
Patients and Methods: This cross-sectional family-based study was conducted on 769 TLGS families in Iran. All families with two biological parents, at least one offspring (nuclear family) and at least two overweight or obese members were eligible for this study. Participants, who lacked the complete family and demographic variables were excluded. Consequently, 529 two-generation nuclear families (1066 parents and 1394 offspring) remained. Obesity-related variables, including waist circumference (WC), waist to hip ratio (WHR), body mass index (BMI), resting energy expenditure (REE), and body size (BS) were determined. Variance component method was used to estimate the age and sex adjusted heritability for obesity-related variables using SOLAR software.
Results: Recruited families consisted of 2460 individuals (493 fathers, 573 mothers, 720 sons, and 674 daughters). Parents and offspring were aged 45.7 ± 10.2 and 18.4 ± 9.7 years respectively. The age and sex adjusted heritability for all obesity-related variables were significant ($P < 0.0001$) and varied from 0.21 (hip) to 0.51 (BS). The heritability for body size considerably surpasses the heritabilities, which were estimated in this study.
Conclusions: This study indicates that Tehran families are genetically predisposed to obesity; although, inappropriate lifestyle may interfere with genetic patterns.

Keywords: Obesity; Anthropometry; Inheritance Patterns

1. Background

Obesity in human arises from the interaction of multiple genes, environmental factors and behavior (1). It is considered a complex disease, which is a major risk factor for type 2 diabetes, cardiovascular disease, stroke, cancer and premature death. Obesity is becoming an increasingly important clinical and public health challenge worldwide. There are over one billion overweight adults in the world, of whom at least 300 million are obese. Recent studies showed the overall prevalence of obesity in Iranians has increased from 13.6% in 1999 to 19.6% in 2005 and 22.3% in 2007 (2). In addition, assessing the trend of obesity in Tehran population showed that approximately 21% of men and 38.6% of women are obese (3, 4). Family history has long been recognized as an important risk factor for obesity (5, 6) and quantitative genetic analysis using twin, family and adoption design have demonstrated that familial resemblance in body mass index (BMI) is largely due to the genetic similarity, with the higher heritability, reported from twin studies (47-90%) to moderate estimate for family studies (24-81%) (7, 8). Differences in heritability (h^2) of obesity-related variables in various populations, could be related to numerous environmental factors, including geographical and social conditions, and climate as well as age, body composition, body size, and hormonal status (9).

2. Objectives

Since there are limited available data related to the heritability of obesity from Middle East, this study aimed to estimate the heritability of obesity-related variables among Tehran Lipid and Glucose Study (TLGS) families.

3. Patients and Methods

The families for this cross-sectional study were selected from the participants of Tehran Lipid and Glucose Study in Iran; an ongoing prospective population-based longitudinal cohort study which is conducted to determine the prevalence of noncommunicable diseases among a representative urban population of Tehran and to de-

velop population-based measures to decrease the prevalence or prevent the rising trend of diabetes mellitus and dyslipidemia (10, 11). In the present study, a total of 769 families were recruited from phase III of TLGS (2005-2008). All families with two biological parents and at least one offspring (1174 parents, and 2336 offsprings) (nuclear family) and at least two overweight or obese members were eligible for this study. Individuals who lacked the complete data for demographic variables or family data were excluded from the study. Finally, 529 families (1066 parents and 1394 offspring) remained.

Written informed consent was obtained from all participants, and approval for the study was granted by the institutional ethnics committee of the Research Institute for Endocrine Sciences (code 750), affiliated to Shahid Beheshti University of Medical Sciences, and especially for using personal information in the genetic projects, written informed consent was obtained.

Demographic data collection and anthropometric examination were undertaken by trained personnel. Weight was measured by using digital scales and recorded to the nearest 100 g, while the subjects were minimally clothed, without shoes. The digital scale calibration was periodically checked by the company. Height was measured in a standing position, without shoes, using a tape measure while the shoulders were in a normal position. Body mass index was calculated by dividing weight (kg) by height squared (m). Waist circumference (WC) was measured at the umbilical level over light clothing by using an unstretched tape with no pressure to the body's surface; measurements were recorded to the nearest 0.1 cm. Body size (BS) index was calculated as height divided by the wrist in centimeter. Resting energy expenditure (REE) was measured as determined in other similar studies (9).

3.1. Definition of Obesity-Related Variables

In adults, BMI was categorized as normal (BMI < 25 kg/m^2), and overweight/obese (BMI ≥ 25 kg/m^2). Abdominal obesity was defined as waist circumference ≥ 89 and ≥ 91 cm for males and females, respectively (10). For offspring, obesity was defined based on the standardized percentile curves of BMI suggested for Iranian children and adolescents. Overweight/obese individuals were defined as ≥ 85th percentile of BMI for age and sex, while normal weight was determined as < 85th percentile of BMI for age and sex (11). Abdominal obesity for offspring was determined as WC ≥ 90th percentile for age and sex, according to the national reference curve (12). For all individuals, WHR ≥ 0.95 and ≥ 0.8 were classified as high for males and females, respectively (9).

3.2. Statistical Analysis

The Kolmogorov-Smirnov goodness-of-fit test, skewness and Q-Q plot were used to assess the normal distribution of the continuous data. Normally distributed continuous variables are reported as the mean ± standard deviation (SD) whereas categorical variables were summarized as frequencies and percentage. If necessary a logarithmic transformation was performed to normalize the distribution of variables. The means of obesity-related variables, within generations, and among genders were assessed by independent sample t test analysis. Partial correlation coefficient (Pearson), adjusted for sex and age, were used to compare the relationship between obesity-related variables. Statistical analyses were performed by SPSS software (version 15.0; SPSS, Chicago, IL, USA). Genetic analysis was carried out using SOLAR (Sequential Oligo genic Linkage Analysis Routines) software package to assess the heritability for obesity-related variables. The heritability of each continuous variable was estimated after adjusting for sex and age; for variables which lacked normal distribution, the tdist function was used to estimate the heritability. The heritability of discrete traits was examined using a threshold model. For this analysis, if an underlying genetically determined risk exceeds a certain cut-off point; it was assumed that an individual belongs to a specific affection status (13). The null hypothesis of no genetic effect ($h^2 = 0$) was tested by comparing the likelihood of the restricted model; h^2 is constrained to zero with a general model in which the same parameter is estimated. Evidence of a non-zero estimate for a given parameter was considered statistically significant at $P < 0.05$.

4. Results

This family-based study included 2460 participants (493 fathers, 573 mothers, 720 sons, and 674 daughters). Parents and offspring were aged 45.7 ± 10.2 and 18.4 ± 9.7 years, respectively. In the parent group, females were younger than males and had higher levels of BMI, body size, hip, and lower levels of WHR, waist, REE, height, and weight; these differences were statistically significant ($P < 0.05$). Among the offspring, girls had higher levels of body size and hip; they, however, had the lower levels of age, BMI, WHR, waist, REE, height, and weight. In contrast to other variables, no significant difference was observed for age and hip circumference (Table 1). To determine the most prevalent contributions of combinations for obesity-related variables, the adjusted for sex and age Pearson partial correlation was calculated (Table 2), according to the observation on the obesity-related variables, waist and REE showed a strong direct correlation with hip and weight, respectively ($r = 0.923$, $P = 0.000$ and 0.936, $P = 0.001$). By contrast, BMI demonstrated the lowest and inverse correlation with waist ($r = -0.006$, $P = 0.652$).

All phenotypes were influenced by genetic factors, and significant heritable components ranging from 0.21 (hip) to 0.51 (BS) for the studied phenotypes. The heritability for BS as a skeletal trait, (0.51, p: $5.91 \times 10\text{-}47$) considerably surpasses the heritability estimated in this family-based study. The genetic basis of the daily energy expenditure, namely resting energy expenditure (REE) may predispose to obesity; the heritability for REE among the Tehran fami-

lies was estimated as 0.26. Estimating the heritability for obesity-related variables as discrete traits showed that h2 were 0.57 (P = 5.8 × 10-6), 0.48 (P = 1.1 × 10-13), and 0.33 (P = 0.1 × 10-6) for high BMI, waist and WHR, respectively (Table 3).

Table 1. Demographic and Anthropometric Variables of Participants Based on Their Generation [a,b,c]

Variables	Parent (n = 1066)			Offspring (n = 1394)		
	Father (n = 493)	Mother (n = 573)	P value	Boy (n = 720)	Girl (n = 674)	P value
Age, y	48.5 ± 9.3	43.3 ± 10.4	0.045	18.9 ± 10.4	17.4 ± 8.9	0.067
BMI, kg/m^2	27.4 ± 3.6	28.6 ± 4.1	0.012	22.1 ± 5.4	21.3 ± 4.7	0.013
WHR	0.97 ± 0.05	0.85 ± 0.08	0.002	0.89 ± 0.06	0.77 ± 0.07	0.003
Waist, cm	96.6 ± 9.4 [c]	88.8 ± 11.1	0.008	78.8 ± 16.2	68.9 ± 11.5	0.005
REE, Kcal	1671 ± 210	1407 ± 120	0.000	1535 ± 387	1319 ± 162	0.000
Body size	9.43 ± 0.51	9.9 ± 0.6	0.056	9.90 ± 0.66	10.5 ± 1.2	0.024
Hip, cm	99.4 ± 6.14	104.6 ± 7.8	0.003	87.9 ± 15.1	89.3 ± 14.1	0.087
Height, cm	169.1 ± 6.2	156.2 ± 5.3	0.000	158.1 ± 23.1	150.5 ± 16.3	0.000
Weight, kg	79.2 ± 11.9	70.2 ± 10.5	0.038	58.8 ± 24.1	49.8 ± 16.9	0.002
High BMI	276 (49.5)	353 (59.1)	0.011	137 (18.4)	73 (10.5)	0.038
Abdominal Obesity	378 (67.7)	282 (47.2)	0.001	237 (31.9)	84 (12.1)	0.002
High WHR	333 (59.7)	435 (72.7)	0.004	137 (18.4)	236 (34.1)	0.007

[a] Abbreviations: BMI, Body mass index; WHR, Waist-hip ratio; REE, resting energy expenditure.
[b] Data are presented as Mean ± SD or No. (%).
[c] log transformed.

Table 2. Pearson Partial Correlation Coefficients for Obesity-Related Variables [a,b,c]

	BMI	REE (P Value)	Body size (P Value)	Waist (P Value)	Hip (P Value)	Height (P Value)	Weight (P Value)	WHR (P Value)
BMI		0.715[c] (0.009)	0.331 (0.032)	0.006 (0.652)	0.814 (0.003)	0.301 (0.030)	0.743 (0.009)	0.298 (0.041)
REE			0.62 (0.012)	0.285 (0.049)	0.869 (0.002)	0.819 (0.002)	0.936 (0.001)	0.065 (0.050)
Body size				0.019 (0.085)	0.007 (0.124)	0.397 (0.039)	0.074 (0.010)	0.342 (0.026)
Waist					0.923 (0.000)	0.012 (0.116)	0.100 (0.026)	0.978 (0.000)
Hip						0.702 (0.002)	0.936 (0.000)	0.070 (0.033)
Height							0.852 (0.003)	0.264 (0.011)
Weight								0.013 (0.096)
WHR								

[a] Abbreviations: BMI, Body mass index; REE, Resting energy expenditure; WHR, Waist-hip ratio.
[b] Values for different parameters were adjusted for age and sex.
[c] Correlation Coefficient

Table 3. Heritability Estimates (%) for Obesity-Related Variables [a,b]

Variables	h^2, % [c,d]	P Value	Variation Explained by Covariate
BMI	0.30 ± 0.038	7.3×10^{-19}	0.51
WHR	0.27 ± 0.034	8.02×10^{-17}	0.52
Waist	0.32 ± 0.038	9.1×10^{-22}	0.60
REE	0.26 ± 0.038	4.55×10^{-12}	0.67
Hip	0.21 ± 0.035	1.57×10^{-10}	0.65
Height	0.23 ± 0.034	2.4×10^{-13}	0.35
Weight	0.33 ± 0.038	6.9×10^{-24}	0.65
Body size	0.51 ± 0.037	5.91×10^{-47}	0.31
High BMI	0.57 ± 0.13	5.8×10^{-6}	0.034
Abdominal Obesity	0.48 ± 0.06	1.1×10^{-13}	0.20
High WHR	0.33 ± 0.06	0.1×10^{-6}	0.19

[a] Abbreviations: BMI, Body mass index; h^2, heritability estimate; REE, resting energy expenditure; WHR, Waist-hip ratio.
[b] Estimated heritability is adjusted for sex, age.
[c] $P < 0.05$.
[d] Data are presented as mean ± SE.

5. Discussion

Body shape has a great variability in human population. It is determined by genetic factors, dietary patterns, physical activity, cultural or environmental factors as well as sex and age (14). It is reported that anthropometric variables are convenient factors to determine the body phenotype. Some aspects, which examined the variability of the anthropometric variables, have been studied; however, the heritability estimation of these variables is neglected. Attitudes towards weight gain or preferences for slim body images are mediated by social and cultural factors. It is determined that dietary habits, physical activity and cultural factors are associated with the body phenotype.

On the other hand, a few studies of family resemblance in twins or in nuclear families indicated that the heritability of anthropometric variables may be moderate. In this study we aimed to examine the heritability of obesity-related variables among TLGS nuclear families (15). This study confirms that genetic factors contribute to

familial aggregation of obesity. All obesity phenotypes were influenced by genetic factors with heritabilities ranging from 21% to 51%. In general, skeletal traits exhibit the higher level of heritability, whereas phenotypes defining the amount of adipose tissue, particularly central fat, are less determined by genetic factors. The familial correlation and heritability for body morphology and composition in TLGS families were approximately within the range observed in other studies; exception is the heritability for height, as the best-known skeletal trait, which was lower than previous h^2 reported in other populations. Additionally, among the obesity-related variables, height had the lower level of heritability compared with circumference traits; this difference could be explained by environmental and behavioral factors.

Sanchez-Andres et al. examined the heritability for a set of anthropometric variables in 261 Spanish families; the estimation computed for parents, and offspring showed a clear defined pattern as higher heritability for longitudinal traits, followed by breadths, circumferences, and skinfolds. They mentioned that fat-related traits are more attributed to common environmental factors (16). Another study in 2002 showed that the heritabilities for all anthropometric traits varied from 25% (BMI) to 61% (bizygomatic breadth); therefore, in this population, anthropometric phenotypes are under appreciable additive genetic influences (17). According to a quantitative genetic study for human obesity-related phenotypes in the nuclear families from Spain, all obesity variables were influenced by additive genetic factors with narrow sense heritabilities ranging from 0.28 to 0.69, and adipose tissues, were less determined by genetic factors (18). Another study, which considered the REE as a mostly heritable trait, showed that the heritability for REE is approximately 30% (19) and the study, which assessed the familial influences of obesity associated metabolic risk factors in 149 families, showed the similar results for REE heritability (20). The heritability estimated for this phenotype in TLGS families was also within the range observed in other studies.

Taken together, these results demonstrate the underlying genetic susceptibility to obesity-related variables. This study had a few limitations though. First, we could not consider the role of some common environmental factors such as smoking, physical activity and nutritional patterns. Second, the SOLAR program may underestimate the heritability that is caused by the genetic effects because of the interaction between genetic and environmental factors. However, to our knowledge, this is the first report of heritability for obesity phenotype in the population of Tehran, and the results of this study are generally consistent with those of the previous similar studies, which were conducted in different populations. According to the results of this study, families living in Tehran are genetically predisposed to obesity; although, inappropriate lifestyle may interfere with the genetic pattern.

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Authors' Contributions

Study concept and design: Bita Faam, Maryam Sadat Daneshpour; Acquisition of the data: Amir Abbas Momenan; Analysis of the data: Bita Faam, Maryam Zarkesh, Nima Hosseinzadeh, Kamran Guity; Drafting the manuscript: Bita Faam, Mohammad Sadegh Fallah, Maryam Zarkesh; Critical revision: Bita Faam, Maryam Sadat Daneshpour; Material supported: Somayeh Hosseinpour-Niazi, Amir Abbas Momenan; and Study supervision: Farhad Hosseinpanah, Fereidoun Azizi, and Maryam Sadat Daneshpour.

Financial Disclosure

There was no conflict of interests.

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