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A Cutoff for Age at Menarche Predicting Metabolic Syndrome in Egyptian Overweight/Obese Premenopausal Women

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Previous studies showed that early age at menarche is associated with increased risk of metabolic syndrome. However, the definition of early menarche at these studies was based on background data in the communities at which these studies was carried on. The aim of this work is to determine a cutoff for age at menarche discriminating presence or absence of metabolic syndrome in overweight/obese premenopausal women. This study included 204 overweight/obese women. Metabolic syndrome was defined according to NCEP-ATP III (National Cholesterol Education Program Adult Treatment Panel III) criteria. Of a total 204 participants, 82 (40.2%) had metabolic syndrome. By using receiver operating characteristic analysis, age at menarche ≤ 12.25 years discriminated individuals with from those without metabolic syndrome. The area under the curve was 0.76 (95% confidence interval, 0.70 to 0.83). Sensitivity, specificity, negative predictive value, and positive predictive value were 82%, 70%, 85%, and 64%, respectively. Age at menarche ≤ 12.25 years predicts the presence of metabolic syndrome in overweight/obese women.

Keywords: Menarche; Metabolic syndrome; Overweight

INTRODUCTION

Metabolic syndrome is a major health problem as it affects about 25% of the population worldwide [1]. The components of this syndrome are central obesity, high blood pressure, hyperglycemia, low levels of high density lipoprotein cholesterol (HDL-C) and hypertriglyceridemia [2].

Several studies showed a link between early age at menarche and increased risk of metabolic syndrome [3-6]. However, the definition of early menarche at these studies either below 12 years [3-5] or below 12.5 years [6] was based on background data in their communities. The aim of this work is to determine a cutoff for age at menarche predicting metabolic syndrome in premenopausal overweight/obese women.

METHODS

Participants

This is a cross-sectional study was conducted on 222 randomly selected premenopausal overweight/obese women (body mass index [BMI] ≥ 25 kg/m²) aged from 25 to 45 years attending Mansoura Specialized Medical Hospital outpatient obesity clinic. All study participants gave written informed consent and the study was approved by the Ethics Committee of the Mansoura Faculty of Medicine. Participants were asked about their age at which the first menstrual bleeding occurred in years and months. Women with lacking information about age at onset of menarche, those with menarche before 9 years or beyond 16 years were excluded. Women taking hypolipidemic

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or corticosteroid medications were also excluded. Finally, 204 subjects remained in this study.

Clinical evaluation

Assessment of anthropometric measurements was done while the participants wearing light clothes and no shoes. Height was measured to the nearest 0.5 cm and weight to the nearest 1 kg. BMI was estimated as weight (kg) divided by squared height (m^2). Waist circumference was measured at the upper border of the iliac crest to the nearest 0.5 cm. Blood pressure was measured in the right arm in a sitting position to the nearest 2 mm Hg and the average of the two measurements was used in the analysis.

Sampling and biochemical measurements

After at least 12 hours fast, 5 mL venous blood was withdrawn from each subject under complete aseptic conditions. After serum separation, blood glucose and lipid profile were assayed immediately. Fasting blood glucose, serum total cholesterol, triglycerides, and HDL-C were measured by enzymatic methods. Low density lipoprotein cholesterol was calculated using Friedewald equation [7].

Definition of metabolic syndrome

The National Cholesterol Education Program-Adult Treatment Panel III guidelines [8] was used to define participants who have metabolic syndrome if three or more of the following five criteria are present: (1) waist circumference ≥ 88 cm; (2) blood pressure $\geq 130/85$ mm Hg or treated for hypertension; (3) fasting blood glucose ≥ 100 mg/dL or treated for diabetes; (4) fasting triglycerides ≥ 150 mg/day; and (5) fasting HDL-C < 50 mg/dL. All study participants were divided into two groups according to presence or absence of metabolic syndrome.

Statistical analysis

Data were expressed as mean \pm standard deviation for continuous variables and as number (%) for categorical variables. Student *t*-test and chi-square tests were used to compare continuous and categorical variables respectively. Receiver operating characteristic (ROC) curve analysis was done to evaluate the ability of age at menarche to discriminate between individuals with and those without metabolic syndrome. The optimal cut-off was determined by Youden index [9]. All statistical analysis were done using SPSS version 20 (IBM Co., Armonk, NY,

USA). A two tailed *P* value less than 0.05 was considered significant.

RESULTS

Of a total 204 participants, 60 (29.4%) were overweight and 144 (70.6%) were obese. Prevalence of metabolic syndrome was 33.3%, 43.1%, and 40.2% in overweight, obese and all study participants respectively. Other characteristics of study popula-

Table 1. Characteristics of study population

Characteristic	Metabolic syndrome present (<i>n</i> =82) ^a	Metabolic syndrome absent (<i>n</i> =122) ^a	<i>P</i> value
Current age, yr	38.9 \pm 6.4	37.3 \pm 6.8	0.09
Age at menarche, yr	11.6 \pm 1.1	13.2 \pm 1.8	<0.01
BMI, kg/m ²	33.6 \pm 4.2	32.5 \pm 4.6	0.08
Overweight/obese			0.20
Overweight	20 (24.4)	40 (32.8)	
Obese	62 (75.6)	82 (67.2)	
Parity			0.07
0–2	47 (57.3)	85 (69.7)	
≥ 3	35 (42.7)	37 (30.3)	
Ever use of contraception (yes)	26 (31.7)	34 (27.9)	0.56
WC, cm	104.3 \pm 12.0	103.6 \pm 13.2	0.69
WC ≥ 88 cm	81 (98.8)	109 (89.3)	0.01
SBP, mm Hg	124.5 \pm 14.3	113.3 \pm 10.3	<0.01
SBP ≥ 130 mm Hg	41 (50.0)	9 (7.4)	<0.01
DBP, mm Hg	78.0 \pm 9.1	71.5 \pm 7.5	<0.01
DBP ≥ 85 mm Hg	18 (22.0)	3 (2.5)	<0.01
FBG, mg/dL	109.5 \pm 12.7	98.2 \pm 16.7	<0.01
FBG ≥ 100 mg/dL	69 (84.1)	46 (37.7)	<0.01
HDL-C, mg/dL	49.3 \pm 11.5	54.7 \pm 9.6	<0.01
HDL-C < 50 mg/dL	49 (59.8)	32 (26.2)	<0.01
TG, mg/dL	134.1 \pm 34.9	100.8 \pm 23.7	<0.01
TG ≥ 150 mg/dL	39 (47.6)	6 (4.9)	<0.01
LDL-C, mg/dL	132.2 \pm 31.5	126.0 \pm 30.6	0.16
TC, mg/dL	208.3 \pm 33.4	200.8 \pm 30.3	0.10

Values are presented as mean \pm standard deviation or number (%). BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol.
^aDefined by the National Cholesterol Education Program-Adult Treatment Panel III [9].

Table 2. Prediction of metabolic syndrome by age at menarche using receiver operating characteristic curve analysis

Age at menarche cutoff point, yr	AUC (95% CI)	P value ^a	Sensitivity, %	Specificity, %	NPV, %	PPV, %	Accuracy, %
≤12.25	0.76 (0.70–0.83)	<0.01	82	70	85	64	75

AUC, area under the curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

^aSignificance of AUC.

tion are summarized in Table 1. Age at menarche was significantly lower in individuals with metabolic syndrome when compared to those without metabolic syndrome ($P < 0.01$).

ROC curve analysis for prediction of metabolic syndrome by age at menarche is presented in Table 2. Age at menarche significantly discriminated overweight/obese individuals with from those without metabolic syndrome (P value of AUC < 0.01).

DISCUSSION

The presence of metabolic syndrome in overweight and obese individuals increases the risk of cardiovascular disease, type 2 diabetes mellitus, nonalcoholic fatty liver disease, obstructive sleep apnea, and polycystic ovarian syndrome [1]. In this study, prevalence of metabolic syndrome in overweight and obese women was 33.3% and 43.1% respectively which is slightly differ from what was reported by Park et al. [10] (28.1% and 50.0%, respectively).

In this study and by using of ROC curve analysis, age at menarche ≤ 12.25 years predicted presence of metabolic syndrome in overweight and obese women. This cutoff is about to be similar with that used for definition of early menarche in previous studies reporting its association with metabolic syndrome [3-6]. To best of our knowledge, this is the first time to define a cutoff for age at menarche that predicts metabolic syndrome using ROC curve analysis.

A possible explanation for the inverse association between age at menarche and metabolic syndrome is that childhood obesity enhances early sexual maturation possibly due to high leptin levels [11]. In addition, childhood obesity was found to be associated development of metabolic syndrome in adulthood [12]. Therefore, childhood obesity may mediate the link between age at menarche and metabolic syndrome.

Previous studies showed that certain parameters can be used in screening of metabolic syndrome such as waist-to-height ratio [13], lipid accumulation product which is estimated from waist circumference and plasma triglyceride levels [14] and triglyceride/HDL-C ratio [15]. In females, especially if obese or overweight, age at menarche may be one of such parameters.

This study conducted on overweight/obese women to ensure that a higher proportion of this study participants would have metabolic syndrome since prevalence of metabolic in overweight/obese individuals is higher than those with normal body weight [10]. Moreover, it may be appropriate to differentiate obese individuals who are metabolically healthy obese form those who have metabolic syndrome [16]. So, knowing age at menarche in overweight/obese women may be helpful in this differentiation.

One of the limitations of this study is that it is not a population based one and this due to lack of financial support. A second limitation is that determination of age of menarche was done using recall. However, menarche is a major physiological event, and age of menarche is memorable for many years [17]. A third limitation is that childhood BMI and waist circumference were not adjusted in regression models due to lack of data about these two parameters.

In conclusion, age at menarche less than or equal to 12.25 years predicts the presence of metabolic syndrome in overweight/obese women and can be used in screening of metabolic syndrome in females.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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