Is There Any Relation Between Insulin Resistance and Menstrual Irregularity in Obese Women?

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Research note

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Abstract

Objectives: Menstrual irregularity is a common issue in obese women that can cause anovulation and infertility. Insulin resistance is also common in obese women. We aimed to find the relation between menstrual pattern and insulin resistance in obese women.

Results: The samples were 233 obese women 18-36 years old coming to obesity clinic for treatment of obesity. We checked Homeostatic Model Assessment for Insulin Resistance (HOMA – IR) and lipid profile in the clients and also we filled a form including the age, educational status, marital status, menstrual pattern and severity of hirsutism. Sample size was 233. The mean age of women was 25.6 ± 8 years. The mean Body mass index (BMI) was 44.6 ± 4.8 kg/m². 84.55% of women had insulin resistance. There was significant relation between menstrual pattern and fasting insulin level ($p=0.05$). There was no significant relation between presence of Insulin resistance and menstrual pattern ($p=0.28$). There was significant relation between age and menstrual pattern ($p=0.007$). Based on the results, there was no significant relation between HOMA- IR and menstrual pattern ($p=0.28$). Perhaps type of obesity (android) may have relation with menstrual pattern and also we need to a standard IR definition to explain the relation between different findings.

Introduction

Obesity is epidemic and even pandemic in the world and its prevalence is growing in adolescent. In 2013–2014 in USA, its prevalence in adolescent was 20.6% and in comparison in 1988–1994 in this age group was 10.5% [1–3]. The majority of overweight adolescence will become overweight adults. Obesity in girls will make advanced puberty and age at menarche has adverse relation with girls Body mass index (BMI) [4]. One third of women in USA are obese [5]. Obesity results to many complications like: Diabetes, Coronary diseases, hypertension,... and infertility.

Infertility in obese women is due to anovulation and menstrual irregularity. Insulin resistance (IR) is a common finding in obese women but it is not clear that the menstrual irregularity in obese women is due to IR or obesity by itself.

A survey was done on 36 women with Poly Cystic Ovarian (PCO) and 25 age and weight control women. Fasting insulin and oral glucose tolerance test (OGTT) and ovarian morphology by (trans-vaginal ultrasound) were assessed. There was no significant association between insulin sensitivity and ovarian morphology or between insulin sensitivity and menstrual frequency. They concluded that PCO is associated with insulin resistance (IR) but BMI, hyperandrogenism and hyperandrogenemia are independent predictors of insulin sensitivity [6].

In this study on obese women we assessed the IR prevalence and the pattern of menstrual cycles to answer this question that either this is obesity that makes irregular menstrual pattern or combination of obesity with IR?

Methods

This is a prospective cross sectional study on obese women that came to Minimally Invasive Surgery Research Center for treatment of obesity. After consultation and taking informed consent, the women with BMI > 30 that had the inclusion criteria entered the study.

Inclusion Criteria

Eighteen to 36 years old obese women that did not use exogenous insulin were included in the study.

A data collection form was completed by the general practitioner including age, menarche age, marital status, parity, educational status, job, use of metformin, the severity of hirsutism, BMI and menstrual pattern. After 10 hours of fasting, the patients returned to laboratory of Minimally Invasive Surgery Research Center for following blood tests: Fasting blood glucose (FBS), Fasting Insulin, Cholesterol, triglyceride, low-density lipoproteins (LDL), high-density lipoproteins (HDL).

We described normal pattern of menstruation as the regular menses with interval 21–35 days. Abnormal menses were intervals less than 21 or more than 35 days.

The severity of hirsutism was estimated by general physician according to the modified Ferriman – Gallwey Scoring System for Hirsutism [7].

Insulin resistance was estimated by calculation of HOMA – IR.

Homeostatic model assessment (HOMA) is a method for assessing β cells function and insulin resistance (IR) can be detected from fasting blood sugar and insulin concentration, that was first described in 1985 [8]. HOMA – IR calculation was by this formula: Fasting blood sugar (mg/dl) $\times$ fasting insulin (mU/lit)/405 .

In our study If HOMA – IR was more than 2.5, it was described as insulin resistance [9].

Data analysis:

All analysis was performed using SPSS software version 25. Quantitative variables are presented by mean $\pm$ standard deviation (SD).

Data distribution normality was assessed with Kolmogorov – Smirnov test. If a parameter was not normally distributed we used Mann - Whitney test. Independent sample T – test and one way analysis of variance were used for comparing measurements in two groups. P value of < 0.05 was considered significant.

Results

This is a prospective cross sectional study between Jan 2018 – March 2019. The samples were 233 obese women 18–36 years old that came to Minimally Invasive Surgery Research Center for treatment of obesity. The mean age of women was 25.6 ± 8 years. The mean BMI was 44.6 ± 4.8 . Table 1 shows quantitative variables.

Table 1
– Description of quantitative variables of women

Standard Deviation	Mean	Variables
8	25.6 years	Age
4.8	44.6 kg/m ²	BMI
1.9	12.9 years	Menarche age
14.8	99.3 mg/dl	FBS
12.07	21.04 mU/lit	Fasting insulin
3.06	5.1	HOMA - IR
29.3	113.5 mg/dl	LDL
11.2	45.7 mg/dl	HDL
36.7	188.7 mg/dl	Cholesterol
62.8	149.9 mg/dl	Triglyceride

Table 2 shows baseline variables.

Table 2
Baseline variables

Number (percent)	Variables
58 (24.9%)	Marital status:
175 (75.1%)	Single
	Married
183 (78.5%)	Profession:
43 (18.5%)	Housewife
4 (1.7%)	Employee
3 (1.3%)	Farmer
	Self - Employee
2 (0.9%)	Education :
10 (4.3%)	Illiterate
30 (12.9%)	Primary School
122 (52.4%)	Under Diploma
55 (23.6%)	Diploma
14 (6%)	Bachelor
	Upper than Bachelor
161 (69.1%)	Menstrual pattern:
4 (1.7%)	21–35 days
68 (29.2%)	< 21 days
	> 35 days
16(6.9%)	Metformin usage:
217 (93.1%)	Yes
	No

HOMA – IR in most of the women was more than 2.5 (N = 197) (Table 3).

Table 3
– Prevalence of HOMA – IR > 2.5

Percent	Number	HOMA - IR
15.45	36	≤ 2.5
84.55	197	> 2.5

There was significant relation between age and menstrual pattern ($p = 0.007$) (Additional file: Table S1).

There was significant relation between menstrual pattern and fasting insulin level ($p = 0.05$) (Additional file: Table S2).

There was no significant relation between BMI and menstrual pattern ($p = 0.08$) (Additional file: Table S3).

There was not significant relation between HOMA – IR and menstrual pattern ($p = 0.28$) (Additional file: Table S4).

There was not significant relation between HOMA – IR and severity of hirsutism ($p = 0.18$) (Additional file: Table S5).

Discussion

In this study there was no significant relation between HOMA- IR and menstrual pattern ($p = 0.28$).

In a survey on 57 morbid obese women the samples were in two groups. In group one the morbid obese women had not hirsutism or menstrual irregularity and group 2 had menstrual dysfunctions with or without hirsutism. Thyroid function tests, FBS and serum lipid profile in two groups had not significant difference but in group two HOMA – IR was significantly higher than group 1. They concluded that IR in morbid obese women can make menstrual irregularity even without elevated androgens [10]. But in our study in 82% of obese women with normal menstrual pattern and in 85.28% of obese women with abnormal menstrual pattern HOMA – IR was more than 2.5. On the other hand in some studies IR was not related with menstrual regularity [6].

The effectiveness of treatment with D – Chiro Inositol (DCI) in improving IR in patients with PCOS had been confirmed in several reports. In one retrospective study 47 women with PCOS were treated with DCI for 15 months. In 51.6% the serum AMH levels and IR indexes significantly decreased during the treatment. They concluded that DCI for treatment of PCOS makes improvement of IR and menstrual cycle irregularity [11].

In one study on biochemical characteristics of women with menstrual disturbances, the samples were 257 women with oligomenorrhea. Between women with oligomenorrhea 149 were hyper androgenic and 108 non hyper androgenic. They had 213 controls with normal cycles. Endocrine and metabolic parameters and IR were compared among different menstrual patterns. Hyper androgenic women with

amenorrhea had higher levels of androgens and more lipid profile disorders than hyper-androgenic women with oligomenorrhea. However in non-androgenic women with amenorrhea the degree of IR and metabolic disturbances were similar to hyperandrogenic women with oligomenorrhea. They resulted that in women without excess levels of androgens menstrual disturbance does not correlate with severity of IR and metabolic disturbances [12].

In one survey on 137 women with PCOS 84.7% had hyperandrogenism, 84.7% had oligo anovulation and 89% had PCO. 69.4% had classic phenotype of PCOS, 15.3% had ovulatory phenotype, 15.3% had normo androgenic phenotype. 71.4% of subjects were IR and IR frequency differed among phenotypes ($p < 0.001$). In normo androgenic phenotype there was not IR case and resulted that in normo androgenic PCOS women there is not IR and are different from other PCOS cases [13].

There is a survey on 70 non obese patients with hirsutism, to find the role of IR on hirsutism. The samples were in three groups. 30 women with idiopathic hirsutism (IH) and 20 with hirsutism due to PCO and 20 healthy controls were assessed.

16 with IH and 17 with PCOS had IR. There was significant difference in fasting Insulin levels and HOMA – IR in three groups, but there was no significant difference between IH and PCOS patients. Women with android fat deposition had higher fasting insulin levels and HOMA – IR. They concluded that IR occurs in non obese patients with IH, and may be related to android obesity [14].

By a research on 976 Korean people the cut of points for describing insulin resistance was calculated. The cut off point for fasting insulin was 12.94 mU/ml, for the quantitative insulin sensitivity check index (QUICKI) was 0.32 and for HOMA – IR was 3.04 [15]. In our research we described the IR as HOMA – IR > 2.5 . There is heterogeneity for IR definitions and in different studies HOMA – IR index cut off values to define IR was different. The IR cut off range in different studies was between 2 to 3.5 [16], and was dependent to gender, race, age, obesity, smoking and etc.

Triglyceride and glucose index (TYG index) also have been suggested for diagnosis of insulin resistance. In a review article with 69922 participants the TYG index was evaluated by HOMA as reference test. The highest specificity was 99% with HOMA – IR with a cut off value of 4.68 [16]. In one study optimal insulin resistance cut off was 2 [17]. In another study IR cut off was 2.8 [18]. Considering various normal IR cut off definitions, the relation between different variables is not reliable.

We concluded that the role of IR in obese women, on menstrual pattern is not clear.

Not only obesity by itself but also obesity with combination with hirsutism or IR does not have significant relation with menstrual pattern.

Limitations

Perhaps type of obesity (android) may have relation with menstrual pattern. But this is just half of the picture and we need to a standard IR definition to explain the relation between different findings.

Abbreviations

HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; BMI: Body mass index

PCO: PolyCystic Ovarian; OGTT: oral glucose tolerance test; FBG: fasting blood glucose

HDL: high-density lipoproteins; LDL: low-density lipoproteins; HOMA: Homeostatic model assessment; DCI: D – Chiro Inositol; PCOS: Polycystic ovary syndrome; IH: idiopathic hirsutism; QUICKI: quantitative insulin sensitivity check index; TYG index: Triglyceride and glucose index

Declarations

Ethical approval and consent to participate

The procedures of this study performed in accordance with the [Declaration of Helsinki](#) and were approved by Ethical Committee of Iran Registry of University of Medical Sciences (IR-IUMS.REC.1394.04.140.26833). All included patients were informed of the purpose of the study and signed the informed consent.

Consent for publication

Not applicable

Availability of data and materials

I had full access to all of the data in this study and I take complete responsibility for the integrity of the data and the accuracy of the data analysis. The authors agree with sharing, coping, and modifying the data used in this article, even for commercial purposes.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Study concept and design: FA; Acquisition of data: FS; Analysis and interpretation of data: FA; Drafting of the manuscript: PA and FS; Critical revision of the manuscript for important intellectual content: FA and FS; Statistical analysis: PA; Administrative, technical, and material support and study supervision: FA

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