International Journal of Endorsing
HEALTH SCIENCE RESEARCH

IJEHSR

Original Article

Insulin Resistance in young obese females with and without Polycystic Ovary Syndrome.

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Doi: 10.29052/IJEHSR.v10.i1.2022.31-35
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Received 02/09/2021
Accepted 20/12/2021
First Published 18/01/2022

OPEN ACCESS

Abstract

Background: The present study intends to determine the comparative insulin resistance (IR) among young obese females with and without polycystic ovary syndrome (PCOs) using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR).

Methodology: During this comparative cross-sectional study, a total of 300 young obese females were evaluated for the presence of PCOS and insulin resistance. Based on the PCOs diagnosis, 250 obese PCOs females were included in group 1, and group 2 comprised 50 obese non-PCOs females. With the demographic details, patients' diabetic and lipid profiles were also evaluated, and the difference in the inference between the groups was drawn using SPSS version 22.0.

Results: It is to note that more than 90% of the young obese PCOs females were diagnosed with type 2 diabetes mellitus (T2DM) while none of the obese non-PCOs females had diabetes. Furthermore, the HOMA-IR score was significantly high among young obese females diagnosed with PCOs (16.30 ± 1.62) as compared to those without PCOs (3.47 ± 0.37) ($p<0.01$).

Conclusion: It is concluded from the study results that young obese females with PCOS are more prone to develop insulin resistance than those without PCOs.

Keywords

Obesity, Polycystic Ovary Syndrome, Insulin Resistance, HOMA-IR.

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Introduction

Polycystic ovarian syndrome (PCOs) is a heterogeneous endocrine gland disorder affecting females in their reproductive age[1]. It has no specific etiology and can cause reproductive, endocrine, metabolic, and/or psychological dysfunctions in females[2]. Some significant manifestations of PCOs are irregular menstrual cycles, infertility, eating disorders, unstable mood, hormonal imbalance levels, obesity, and type 2 diabetes mellitus (T2DM)[3].

Metabolic syndrome and PCOs have a bi-directional impact on each other and share some common pathogenic factors that make females with PCOs more vulnerable to getting some sort of metabolic disorders[4]. The incidence rate of metabolic syndrome increases worldwide, and the scenarios are even worse for females diagnosed with PCOs[5]. Obesity plays a crucial role in intensifying insulin resistance (IR). It may also induce glucose intolerance in patients with PCOs, leading to the assumption that obesity may increase the risk of PCOs and their metabolic complications[6]. A study conducted in Karachi reportedly states that 35.6% of women with PCOs suffer from metabolic syndrome than those without PCOs[7]. The coexistence of PCOs and obesity affects insulin sensitivity of the body and increases the chances of T2DM[8]. Other comorbidities are also linked with this triad, like cardiovascular disorders[9].

PCOs and T2DM are both interlinked via complicated pathways. As PCOs increase the risk of T2DM, T2DM also increases the risk of PCOs onset. The reduced insulin sensitivity and increased resistance promote hyperandrogenism by initiating a cascade of biochemical reactions in the body, leading to PCOs[9]. According to research, IR contributes to the onset of PCOs in up to 90% of cases. Due to the compensatory effect to insulin sensitivity, hyperinsulinemia occurs that turn synergistically with other reproductive hormones, i.e., Luteinizing hormone (LH) in the form of co-gonadotrophin along with ovarian theca tissues[10]. As a result, CYP17A1 enhances the production and secretion of testosterone[11], promoting the production of pre-antral follicle[12]. Hyperinsulinaemia is also responsible for pleiotropic effects of the ovaries, which finally increase LH pulse amplitude[13], activation of adrenal p450c17a action with lowering the concentration of sex hormones released from the liver by conjugation with globulin[14].

A considerable amount of literature has been published on the prevalence of IR among women with PCOs in Pakistan. Hence the focus of the present study was to compare the insulin sensitivity in obese young females with and without polycystic ovary syndrome

Methodology

This comparative cross-sectional study was conducted at Government College Women University, Faisalabad, Pakistan between June 2020 to March 2021. A total of 300 obese females were recruited and divided into two groups based on PCOs diagnosis. According to NIH criteria, the PCOs diagnostic criteria included amenorrhea, physical signs of hyperandrogenism, excluded with other diagnosed health problems like prolactinoma, late-onset congenital adrenal hyperplasia, adrenal tumor, and hypothyroidism. Group 1 included 250 obese PCOs females while 50 obese non-PCOs females were included in group 2.

Patient's data, including age, weight, height, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), and family history of T2DM (primary and secondary degree), were recorded using a structured questionnaire. The diabetic and lipid profiles were evaluated by taking respective samples. Diabetes diagnosis criteria were set as per the American diabetes association 2020-2021. Serum glucose level was determined by enzymatic assay, while immunoassay was used to assess the level of insulin. The cross-reactivity of insulin was > 0.05% as compared with proinsulin.

Written informed consent was obtained from the patients after explaining the purpose of the study. The ethics committee of Government College Women University Faisalabad approved the study

protocol [Reference no. 21-1224/ BCH-1/R&D/GCWUF/2020; Dated: 11th May 2020]. Statistical analysis was performed on SPSS version 22.0. The difference in all the continuous variables between the study groups was assessed using an independent sample T-test. A chi-square test was applied for all the categorical variables, and the p-value < 0.05 was considered statistically significant.

Results

It was observed that more than 90% of subjects had a family history of T2DM. Around 92% subjects of group one had insulin > 15 µu/ml (hyperinsulinemia) and 90% had hypercholesterolemia i.e. cholesterol level > 150 mg/dl. There was a statistically significant difference in the mean BMI, blood pressure, and T2DM incidence between these two groups (p<0.05) as shown in table 1.

Table 1: Patient's baseline demographic and clinical characteristics.

Variables		Group 1 (n=250)	Group 2 (n=50)	Total (n=300)	p-value
Age; years		14.71±1.74	14.41±1.51	14.66±1.70	0.051*
Weight; kg		80.92±13.77	97.44±8.90	83.68±14.45	0.000*
BMI; kg/m2		39.07±4.75	41.12±6.70	39.41±5.17	0.000*
SBP; mmHg		140.04±12.84	128.40±10.17	138.10±13.16	0.048*
DBP; mmHg		71.22±7.80	70.00±7.35	71.01±7.72	0.142
T2DM family history	No	8(3.20)	5(10)	13(4.30)	0.031*
	Yes	242(96.80)	45(90.0)	287(95.70)	
Diagnosed T2DM	No	9(3.60)	50(100)	59(19.70)	0.000*
	Yes	241(96.40)	-	241(80.30)	
Normal Glucose Tolerance	No	126(50.40)	24(48.0)	150(50)	0.757
	Yes	124(49.60)	26(52.0)	150(50.0)	
Impaired Glucose Tolerance	No	250(100)	26(52.0)	276(92.0)	0.000*
	Yes	-	24(48.0)	24(8.0)	

Group 1- Obese PCOs; Group 2 - Obese Non-PCOs; BMI – Body Mass Index; SBP – Systolic Blood Pressure; DBP - Diastolic Blood Pressure; T2DM – Type 2 Diabetes Mellitus
Values are given as Mean ± SD or n(%).
*p<0.05 is considered significant.

There was a statistically significant difference in all the assessed biochemical parameters except cholesterol, as the subjects in both groups were obese (p<0.05). The score of HOMA-IR was found highly significant in PCOs obese group (16.30 ± 1.62) than the non-PCOs obese group of young females (3.47 ± 0.37) (Table 2).

Table 2: Biochemical parameters in obese women with and without PCOs.

Variables	Group 1 (n=250)	Group 2 (n=50)	Total (n=300)	p-value
Fasting Insulin	52.24±6.02	21.50±1.13	47.11±12.73	0.000*
FBS	118.36±12.09	81.12±3.37	112.15±17.80	0.000*
FGIR	2.26±0.17	3.99±0.36	2.55±0.68	0.000*
Random Insulin Level	175.09±8.89	149.36±3.78	170.80±12.66	0.000*
RBS	174.96±14.45	129.96±2.24	167.46±21.37	0.000*

HOMA IR score	16.30±1.62	3.47±0.37	14.16±5.01	0.000*
Cholesterol	184.09±9.03	190.44±7.96	185.15±9.16	0.752
TG	86.36±6.99	82.32±3.55	85.68±6.71	0.000*
HDL	41.52±5.02	47.94±3.40	42.59±5.35	0.018*
LDL	109.58±6.00	93.18±6.45	106.84±8.62	0.886

FBS – Fasting Blood Sugar; FGIR - Fasting Glucose Insulin Ration; RBS – Random Blood Sugar; HOMA IR - Homeostatic Model Assessment Of Insulin Resistance; TG – Triglyceride; HDL – High-Density Lipoprotein; LDL – Low-Density Lipoprotein. *p<0.05 is considered significant.

Discussion

PCOs is a concerning health issue for young females as it affects their reproductive life, disrupts the metabolic system, and makes them more prone to T2DM, cardiovascular disorders, and other metabolic syndromes[15]. Indeed, co-occurrence of PCOs and obesity are linked to IR, but IR might also be present among PCOs females irrespective of obesity[16], increasing the risk of T2DM. More than 50% of the females with PCOs develop T2DM by the age of 40 years, according to the Center for Disease Control and Prevention (CDC)[17].

A study also reports that irrespective of age and overall BMI score, women with PCOs are at higher risk of getting T2DM due to compromised insulin sensitivity[18]. The present study also supported the co-occurrence of PCOs and diabetes, i.e., T2DM was frequent among females with PCOs as compared to those without PCOs. A population-based study from Finland reported that obese females with PCOs are twice more likely to develop T2DM than the normal PCOs females[19].

Although IR is traditionally not considered a PCOs diagnostic criterion, the alteration in the insulin sensitivity and acanthosis nigricans accompanied by hyperandrogenic signs collectively indicate this syndrome[20]. An Indian study represents similar findings, indicating that the metabolic dysfunctions are more distinct in obese females with PCOs than those without PCOs[21]. Furthermore, atherogenic dyslipidemia is also more common among obese females with PCOs than females without PCOs[22]. Obese females with PCOs showed a substantially high score on HOMA-IR as compared to the obese females without PCOs. Behboudi-Gandevani et al., in a review article, revealed a significantly higher mean HOMA-IR in obese PCOs females than their non-obese counterparts (p<0.05)[23]. Another study reported IR in 72% of the obese women with PCOs as compared to 23% lean PCOs females[24].

Among the major limitations of the present study were the data generalizability as the study was focused to a single center of a particular geographical region.

Conclusion

In conclusion, the majority of the obese PCOs females had higher HOMA-IR scores, elevated fasting, and random insulin concentration than the obese non-PCOs counterparts. Hence, indicating that obese PCOs women are more prone to IR. However, to formulate improved management and treatment approaches focusing on better life quality and fertility outcomes, further studies are required to understand the true relationships between these co-existing conditions and associated morbidities.

Conflicts of Interest

The authors have declared that no competing interests exist.

Acknowledgement

The authors wish to acknowledge the Medical Affairs department of Getz Pharma for their technical assistance during the study.

Funding

The author(s) received no specific funding for this work.

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