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Evaluation of Insulin Resistance and Its Association with PCOS Symptoms

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Abstract

Introduction: PCOS is characterized by menstrual disorders due to chronic anovulation and hyperandrogenemia. It is considered as one of the most common endocrine disorders at reproductive ages. Hirsutism, menstrual disorders, hyperandrogenemia, obesity, infertility and spontaneous abortion are common in PCOS. This disease is often diagnosed clinically. According to the pathophysiology of the disease, insulin resistance can play a major role in PCOS etiology. The aim of this study was to evaluate the prevalence of diabetes, IFG and IGT, and their association with the symptoms of PCOS. Materials and methods: A total of 82 patients with PCOS were selected. FBS and OGTT were performed after prescribing 75 g glucose. The results of the study were evaluated using SPSS 21 software and Chi-square and one-way ANOVA statistical tests. Results: Hirsutism and menstrual disorders are the most common symptoms in PCOS patients. Although the frequency of diabetes, IFG and IGT increases with age and BMI in a PCOS family, but it is seen at any age and BMI. Insulin resistance was more common in patients with PCOS. Conclusion: The frequency of diabetes in our study was 9.7%, which is not significantly different from another study. The rate of IGT and IFG in patients was 14.6% and 9.8%, respectively, which is slightly lower than that of other studies and it is probably due to the low number of participants in the study and due the fact that our patients were new case of PCOS.

Keywords: PCOS, IFG, IGT, DM, Prevalence, Insulin Resistance.

Introduction

PCOS is the most common endocrine disorder among women at the reproductive age. Its prevalence is estimated to be 4-12% and its etiology is still unknown (Aghamohamadzadeh et al., 2010). The association of amenorrhea with PCOS was first described by Stein and Leventhal in 1935, so it has been known as Stein - Leventhal 's syndrome for many years (Yen, 1980). In PCOS, hyperandrogenemia are present and ovaries ovulate less or do not ovulate. Symptoms of PCOS appear when ovarian failure persists for a long time (Yildiz et al., 2003). For these reasons, this disease is also called hyperandrogenic anovulation. Patients with PCOS might experience various symptoms with varying degrees of severity. Some of the most important symptoms are hirsutism, menstrual disorders, acne, obesity, infertility and spontaneous abortion (Carmina & Lobo, 1999). Hormonal changes such as increased LH at the beginning of the menstrual cycle, hyperandrogenemia, decreased sex hormones globulins binding, and slight increases in insulin levels and cellular resistance to insulin are the main symptoms (Yildiz et al., 2003). In PCOS patients, disorder in glucose metabolism and insulin secretion is not observed until adulthood. Clear hyperglycemia and decreased insulin sensitivity may be the first manifestation of PCOS and type 2 diabetes in adult women (Ovalle & Azziz et al., 2002). The most common causes of insulin resistance are hyperinsulinemia and obesity (Yen, 1980).. Nearly ⅓ of patients with obese PCOS have impaired glucose tolerance test, and nearly 7.5-10% of them have type 2 DM. This form is even higher in non-PCOS women than that in the general population (Niafar et al., 2018). It has been reported that when one parent of PCOS women has DM, The probability of diabetes is higher in their family (Niafar et al., 2018). It is necessary for the prevention and treatment of PCOS patients and all aspects of the disease are assessed and investigated. The results of previous research showed impaired glucose tolerance and diabetes in the adult population of our country is high, but no study has been conducted on the relationship between insulin resistance and its association with PCOS symptoms. In this study, the common clinical symptoms were studied and the prevalence of diabetes, IFG and IGT was evaluated in PCOS patients.

Materials and Methods

This study was descriptive cross sectional research. In this study, 82 women with PCOS were selected. In all cases, the diagnosis of PCOS was based on clinical and paraclinical criteria and exclusion of other causes. Criteria of diagnosis of diabetes mellitus was fasting plasma glucose level of 126 mg/dL or higher; fasting is defined as no **caloric** intake for at least 8 hours, or a 2-hour **plasma glucose level** of 200 mg/dL or higher during

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a 75-g oral **glucose tolerance test. IGT** is defined as two-hour **glucose** levels of 140 to 199 mg/dL on the 75-g oral **glucose** tolerance test, and **IFG** is defined as **glucose** levels of 100 to 125 mg/dL in **fasting** patients. It should be noted that all our patients were not known cases of diabetes and their diabetes was diagnosed in this study. Statistical analysis was done by SPSS 21. The data is shown as Mean ± SD and 95% confidence interval. Chi-square and one-way ANOVA tests were used to determine statistical difference in qualitative variables. P value less than 0.05 was considered as statistically significant.

Results

In this study, the relationship between clinical symptoms (dysmenorrhea, oligomenorrhea, amenorrhea, infertility history, abortion, hirsutism, alopecia, acne) was compared by insulin resistance. The age of women was between 17 and 45 years and their mean age was 26.4 ± 7.8 years (Table 1). In this study, 51.2% women were married. The mean BMI of the patients was 27.6 ± 7 and 42 cases had BMI ≥30.

Table 1: Clinical characteristics and laboratory findings in PCOS patients

Parameters	PCOS	Mean±SD
Age (year)	17-45	26.4±7.8
BMI kg/m2	15.79-51.44	27.6±7
FBS mg/dL	72-135	91±16.6
BS after OGTT mg/dL	65-224	115.5±36.5
LH IU/L	2-20	11.27±5.2
FSH IU/L	2.5-18	7.5±3.5
Testosterone ng/dL	0.1-1.5	0.32±0.92
DHEA-S ng/dL	90-550	241.04±122.21

In this study, family history of diabetes and PCOS were evaluated. Sixteen cases had family history of diabetes and 34 cases had family history of PCOS. Eight cases had a history of PCOS and DM, and 24 cases had no family history of diabetes and PCOS. None of the 82 cases had a previous history of diabetes. Dysmenorrhea was found in 34 cases. Fifty people had the history of oligomenorrhea. Twenty women also experienced periods of amenorrhea. The history of hypermenorrhea was positive in only 4 cases. Out of 20 married women, 18 were infertile. Two married had history of spontaneous abortion once. Hirsutism was found in 70 people. Thirty two cases had a history of alopecia. Acne was reported in 50 cases. The mean LH in PCOS patients was 11.27 ± 5.2 ng / ml. the mean FSH was 7.5 ± 3.5ng/ml. The mean DHEA-S was 241.04 ± 122.21 ng/ml and the mean testosterone was reported 0.32 ± 0.92 ng/ml. FBS was obtained after 10-12 hours of fasting. The OGTT test was performed on all cases except those whose FBS test clearly diagnosed DM. FBS higher than 126 mg / dL was reported in 4 patients, so OGTT was not performed in these 4 cases. FBS was seen in range of 72 to 135 mg/dL and its mean was 91 ± 16.6 mg/dL, which 70 (85.4%) cases had normal FBS, 8 (9.8%) cases had IFG, and 4 cases (4.9%) had DM. (Table 2).

Table 2: The percentage of DM, IFG and IGT based on FBS and OGTT in PCOS

Parameters	Normal	IFG	IGT	DM
Based on FBS 82 People (%)	70 (85.4)	8 (9.8)	-	4 (4.9)
Based on OGTT 78 people (%)	62 (75.6)	-	12 (14.6)	4 (6.45)

Blood glucose in the OGTT test was in the range of 65 to 224 mg/dL, and its mean was 115.5 ± 36.5 mg/dL. Sixty two (75.6%) cases had normal glucose and 12 (14.6%) cases had IGT and 4 cases had DM.

The relationship between OGTT and BMI: 40 cases had BMI<30 and 38 cases had BMI≥30. Out of all cases who had BMI <30, 34 cases had normal BS and 6 of them had IGT. In a group with BMI<30, no subject with DM was reported. In the group with BMI≥30, 28 (73.6%) cases had normal BS and 6 (15.7%) cases had IGT, and 4 (10.5%) of them were clearly diabetic. No significant relationship was found between OGTT and BMI in our study (P-value>0.05) (Table 3).

OGTT and age: The mean age of cases with normal blood glucose was 24.3 ± 6.4 years. In addition patient with IGT, the mean age of cases was 33.3 ± 7.3 years and finally, the mean age of the OGTT group with DM was 38 ± 2.8 years. As seen, the highest mean age was in the group with diabetes (P value = 0.001) (Table 3).

OGTT and hirsutism: Seventy patients with PCOS had hirsutism in our study and 56 cases with normal blood glucose reported hirsutism, but 6 of them had no history of hirsutism. There was no significant relationship between OGTT and hirsutism in our study (P> 0.05) (Table 3).

Table 3: Relationship between OGTT and BMI, age and hirsutism in PCOS patients

Parameters	BMI<30 40 People	BMI≥30 38 People	Age 78 People	Hirsutism 70 People
Normal BS	34	28	24.3±6.4	56
IGT	6	6	33.3±7.3	8
DM	-	4	38±2.8	6
P value	>0.05	>0.05	0.001	>0.05

P value <0.05 was significance

FBS and BMI: A total of 40 cases had BMI>30 and 42 cases had BMI≥30 and 36 cases with BMI<30 had normal blood glucose and 4 had IFG. In BMI<30 group, no subject with DM was reported. In the group with BMI ≥30, 34 cases had normal FBS and 4 cases had IFG and 4 cases had diabetes. A significant relationship was not found between FBS and BMI in our study (p> 0.05) (Table 4).

FBS and age: In this study, among the cases with age less than 20 years, 18 had normal FBS and 2 had IFG. None of the people under the age of 20 had DM. In the age group of 20-29 years, 36 cases had normal FBS, 2 cases had IFG and 2 cases had DM. In the age group of 30-39 years, 10 cases had normal FBS, 4 cases

had IFG, and 2 cases had DM, and in the age group over 40 years, all cases had normal FBS. No significant relationship was found between age and FBS in our study (p> 0.05) (Table 4).

FBS and hirsutism: A total of 70 patients with PCOS had hirsutism. Sixty two cases with normal FBS had hirsutism, but eight of them had no history of hirsutism. Out of all cases with IFG, 2 cases had no hirsutism and 6 cases had hirsutism. No significant relationship was found between FBS and hirsutism in our study (p> 0.05) (Table 4).

Table 4: Relationship between FBS and BMI, age and hirsutism in PCOS patients

Parameters	BMI<30 40 People	BMI≥30 42 People	Age 82 People	Hirsutism 70 People
Normal BS	36	34	23.3±5.8	62
IGT	4	4	34.6±5.3	6
DM	-	4	37.5±1.8	2
P value	>0.05	>0.05	>0.05	>0.05

P value <0.05 was significance

Discussion

PCOS is considered as the most common endocrine disorder among women at their reproductive age, and its etiology has not been yet known (Aghamohamadzadeh et al., 2010). Patients usually experience different degrees of its severity. The most common clinical symptoms of this disease are hirsutism, menstrual disorders and obesity (Yen, 1980).. It is necessary to perform extensive studies on all aspects of PCOS because high prevalence and importance of this disease. The research findings carried out in this regard reveal that IGT, IFG and diabetes have high prevalence in Iran, while no research has been carried out on their prevalence in women with PCOS and their relationship with PCOS symptoms (Weerakiet et al., 2007). The age of women in our research ranged from 17 to 45 years and their mean age was 26.4 ± 7 years and the age group of 20-29 years was the most frequent age group.

Forty subjects had BMI ≥30 and more than half of the women with PCOS had BMI≥30 in our research and obesity played a major role in PCOS. In this regard, 58.5% of patients experienced dysmenorrhea, while dysmenorrhea was the most cause of referred to obstructive and gynecologist clinic (Naderpoor et al., 2015; Zhao et al., 2010). Thus, high rate of this clinical symptom in our study cannot explain the high prevalence of dysmenorrhea in patients with polycystic ovary syndrome. No significant relationship was found between dysmenorrhea and FBS or OGTT. In this study 68 (82.9%) of cases experienced the menstrual disorders such as oligomenorrhea or amenorrhea. Menstrual disorder is the key symptom of this disease.

It should be stated that 90% of the subjects who had insulin resistance in our study (all cases who had IGT, IFG or DM) experienced at least one of menstrual disorders. Out of the 38 patients with clinical symptoms of oligomenorrhea, 14 were identified as insulin resistance, that is, the prevalence of insulin resistance among 38 patients with oligomenorrhea was 36.8% in our study, which is comparable to another study. Roumain et al. found that the prevalence of insulin resistance was 33% among the 145 patients with a history of oligomenorrhea (Zhao et al., 2010). Infertility was also found in 42% of married women in our study, which is considered high percentage and it could be a sign of the high prevalence of this symptom in PCOS. Unfortunately, none of reviewed studies referred to rate of inferiority to compare the results and only infertility was reported as a significant manifestation of PCOS. Hirsutism is the most common manifestation of hyperandrogenism in women. In our study, hirsutism with a prevalence of 85.4% was the most common clinical symptom. Based on the research carried out, about 70% of patients with PCOS in the United States have hirsutism (Carmina et al., 2006) and a higher percentage obtained in our study can be due to these genetic differences. The prevalence of hirsutism among south China women is about 10-20%. (Huang et al., 2010) Alopecia and acne as a manifestation of hyperandrogenism were reported in 39% and 41% of the patients, respectively .The mean age of patients with PCOS in our study was 26.4 years, which the mean age of women with insulin resistance was 34.2 years. It reflects the role of age in development of insulin resistance. A significant relationship was found between FBS and age in our research, reflecting the fact that FBS test might be impaired with increasing the age. Hyperglycemia and decreased insulin sensitivity might be the first manifestation of PCOS and type 2 diabetes in adult women (Naser et al., 2010). Based on this study, 8 (9.7%) of patients with PCOS had DM. In a research carried out on 33 patients with PCOS by Karakas et al, the prevalence of DM was reported 15% (Karakas et al., 2010). In another research carried out on a group of 249 women with PCOS, the prevalence of DM was reported 7% (Lim et al., 2013). Another research on 302 women with PCOS, the prevalence of diabetes was reported 8.9% (Tehrani et al., 2011). Comparing the above finding with those found in our research reflects the fact that the rate of diabetes was different in various studies. In its last recommendation, ADA has reported that patients with PCOS are at high risk for development of glucose resistance disorder and diabetes and these patients should be screened (Garber et al., 2017). Results of our research revealed that about 12 (14.6%) patients had IGT, and in a research carried out on 249 patients with PCOS, the prevalence of IGT was reported 15.31% and in a research on 302 patients, the prevalence of this disorder was reported 31.7% (Tehrani et al., 2011). The difference in the prevalence of IGT can be due to small size of participants in our study compared to other studies, making it necessary to carry out extensive studies in this regard. Second, all people participated in our research were new case and IGT might increase significantly, if they are re-evaluated after 5-10 years.

Conclusion:

The results of this study are:

1- Hirsutism and menstrual disorders and infertility have significant prevalence in PCOS patients.

2- Although the prevalence of IFG, IGT, and DM increases with increasing the age and BMI in women with PCOS, there is a risk of developing these disorders at all age groups with any BMI.
3- Insulin resistance (DM, IFG, and IGT) has high prevalence in patients with PCOS.
4- The results of our research confirm the results of previous studies.

It is suggested that the risk of developing glucose metabolism disorders to be informed for all women with PCOS and it is recommended for these patients to modify their lifestyle. It is also recommended that all women with PCOS, without considering the age and BMI, to be screened in terms of insulin resistance and OGTT are recommended for their screening.

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Conflict of interest

All authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Ethical approval

The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran. The current study was performed according to the Institutional Committee for the Protection of Human Cases, which was adopted by the 18th World Medical Assembly, Helsinki, Finland and its later amendments.

Abbreviations:

DM: Diabetes Mellitus
IFG: Impaired Fasting Glucose
IGT: Impaired Glucose Tolerance
PCOS: Polycystic Ovary Syndrome
OGTT: Oral Glucose Tolerance Test
LH: Luteinizing Hormone
FSH: Follicle Stimulating Hormone
DHEA-S: Dehydroepiandrosterone-Sulfate

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