ZKTB

ORIGINAL RESEARCH

Evaluation of Obesity and Metabolic Status in Polycystic Ovary Syndrome in Fertile and Infertile Groups

Polikistik Over Sendromunda Obezite ve Metabolik Durumun Fertil ve İnfertil Gruplarda Değerlendirilmesi

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ABSTRACT

Objective: *The aim of our study was to compare the BMI and metabolic values of fertile and infertile groups in patients with polycystic ovary syndrome (PCOS) and to determine the effect of obesity and metabolic status on fertility and infertile groups and the fertility effect of obesity.*

Material and Methods: *The clinical and metabolic data of 230 patients who presented to the gynecology outpatient clinic of our hospital between 2013 and 2018 and were diagnosed with PCOS according to the Rotterdam Diagnosis Criteria were evaluated. Body mass index (BMI), waist ratio, menstrual period, fertility status, fertility duration, parity status, presence and degree of hirsutism were evaluated. 75 g oral glucose tolerance test (OGTT) was performed following appropriate diet and fasting period. Fasting glucose and insulin levels and insulin resistance cases were determined. Total cholesterol, HDL and LDL cholesterol levels were determined. Patients with BMI; The patients were divided into two groups as fertile and infertile, evaluated for obesity and metabolic data, and data on the relationship with BMI were calculated statistically. These metabolic disorders were compared to BMI and fertility status.*

Results: *The mean age of the patients was 26.7 years. The mean BMI was 28.92 ± 5.95 kg / m2. Only 25% of the patients had normal weight and 73% were overweight. 4 (1.7%) cases in the weak group with BMI less than 18.5, 58 (25.2%) cases in normal weight group with BMI 19-24.9, 71 (30.9%) in overweight group with BMI 25-29.9 There were 86 cases (37.4%) in obese group with BMI 30-39.9 and 11 cases (4.8%) in morbidly obese group with BMI of 40 and above. u (21.5%) is fertile. The duration of infertility ranged from 12 to 196 months, with a mean of 33.92 ± 24.25 months and a median of 24 months. The waist circumference is between 62 and 135 cm and the average is 87.76 ± 13.48 cm. The waist / hip ratio ranged from 0.65 to 0.98 and the mean was 0.80 ± 0.06. The distribution of BMI was similar in the fertile and infertile groups. 99 (43.1%) of the patients had insulin resistance, 77 (33.5%) had impaired glucose tolerance and 12 (5.2%) had DM. Mean blood lipid levels were not significantly different between fertile and infertile groups. The distribution of glucose metabolism disorders was similar in both groups.*

Conclusion: *Obesity and metabolic disorders are more common in PCOS cases. There was no significant difference between fertile and infertile groups according to BMI.*

Keywords: *polycystic ovary syndrome, fertility, metabolic situations.*

ÖZET

Amaç: *Polikistik over sendromunda(PKOS) fertil ve infertil gruplarin BKİ ve metabolik değerleri karşılaştırılarak obezite ve metabolik durumun fertilite üzerine etkisini belirlemektir. Polikistik over sendromunda(PKOS) fertil ve infertil grupların beden kitle indeksi (BKİ) ,metabolik değerleri karşılaştırılarak obezite ve metabolik durumun fertilite üzerine etkisini belirlemektir.*

Gereçler ve Yöntem: *2013- 2018 döneminde Rotterdam Tanı Kriterlerine göre PKOS tanısı alan 230 hastanın, klinik ve metabolik verileri retrospektif olarak değerlendirilmiştir. Beden kitle indeksi (BKİ), bel –kalça oranı , mensturasyon süreleri, fertilite durumu, fertilite süresi, parite durumu, hirsutizm varlığı ve derecesi ile hastalara uygun diyet ve açlık süresini takiben 75 gr oral glikoz tolerans testi (OGTT) yapılmıştır.İnsulin direnci HOMA-IR ile belirlenmiştir. Total kolesterol,HDL ve LDL kolesterol düzeyleri belirlenmiştir. BKİ'ne göre hastalar ; normal kilolu,fazla kilolu ve obez olarak gruplara ayrılmış ve fertilite durumuna göre sonuçlar değerlendirilmiştir.Metabolik bozukluklar BKİ ve fertilite durumlarına uygun olarak karşılaştırılmıştır. Rotterdam tanı kriterlerine göre PKOS tanılı 230 hastanın klinik ve metabolik verileri retrospektif olarak değerlendirildi.Beden kitle indeksi (BKİ), bel / kalça oranı,mensturasyon,fertilite durumu, infertilite süresi,parite, hirsutizm, 75 g oral glukoz tolerans testi (OGTT), HOMA –IR değeri, total kolesteroll, HDL, LDL kolesterol düzeyleri belirlendi.BKİ'ne göre; normal kilolu, fazla kilolu ve obez gruplar fertilite durumuna göre gruplandırıldı ve değerlendirildi. Metabolik bozukluklar BMI ve fertilite durumuna göre karşılaştırıldı.*

Bulgular: *Yaş ortalaması 26,7'dir. BKİ ortalaması 28.92±5.95 kg/m2 'dir. Olguların %25'i normal kiloda olup,%73'ü normalden fazla kilodadır. Olguların 181'i (%78.5) infertildir, 49'u (%21,5) fertildir. İnfertilite süreleri 12 ile 196 ay arasında değişmekte olup, ortalaması 33.92±24.25 ay, medyanı 24 aydır. Bel çevresi 62 ile 135 cm arasında değişmekte olup, ortalaması 87.76±13.48 cmdir. Bel/kalça oranı 0.65 ile 0.98 arasında değişmekte olup, ortalaması 0.80±0.06 saptanmıştır. BKİ dağılımı fertil ve infertil grupta da benzerdir. Olguların 99'unda (%43.1) insülin direnci, 77'sinde (%33.5) bozulmuş glikoz toleransı, 12'sinde (%5.2) DM saptanmıştır.Lipid düzeyleri gruplar arasında anlamlı farklılık göstermemiştir. Glikoz metabolizması bozuklukları her iki grupta benzerdir. Yaş ortalaması 26.7, Ortalama BKİ 28.92 ± 5.95kg/m2 idi. Olguların% 25'i normal kilolu,% 73'ü fazla kilolu olduğu belirlendi. Olguların 181'i (% 78.5) infertil, 49'u (% 21.5) fertil ve infertilite süresi 12 ile 196 ay arasındaydı (ortalama 33.92 ± 24.25 ay, median 24 ay). Hastaların 99'unda (% 43.1) insülin direnci, 77'sinde (% 33.5) bozulmuş glukoz toleransı ve 12'sinde (% 5.2) DM vardı. Glikoz ve lipit metabolizması ve bozuklukları her iki grupta da benzerdir.*

Sonuç: *PKOS olgularında obezite ve metabolik bozukluklar daha sık görülmektedir. Ancak bu durumun fertilite üzerine etkisi, saptanmamıştır.*

Anahtar Kelimeler: *polikistik over sendromu, fertilite, metabolik durum*

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common gynaecologic disorders encountered in reproductive age. Although the frequency varies according to the population studied, it is approximately 5-10% (1). In PCOS, gynecological symptoms such as anovulation, infertility and hirsutism are seen. In addition to these clinical symptoms, the incidence of certain metabolic disorders, which have recently been clearly associated with the pathophysiology of the syndrome, has increased, including hyperinsulinemia, type 2 diabetes, obesity and hyperlipidemia etc. These metabolic disorders also increase the severity of gynecological symptoms. In particular, these disorders in infertile patients seem to be closely related to anovulation (2). The role of metabolic values of PCOS in etiopathogenesis; Although it cannot be fully elucidated, it is believed that the frequently observed insulin resistance inhibits the production of liver sex hormone-binding globulin (SHBG) and this situation is thought to cause the androgen secretion of ovarian and adrenal (3, 4). In clinical practice, this is the case with hyperandrogenemia or hyperandrogenism.

Insulin resistance, which plays a role in the etiopathogenesis of PCOS and is a risk factor for the development of metabolic syndrome and long-term diabetes, appears to be a social problem that causes more anxiety with obesity (5, 6). For example, hyperinsulinemia and insulin resistance was evaluated in this patient group; while the rate of insulin resistance in obese patients was 57%; The prevalence of non-obese patients was 9.3%. Insulin sensitivity decreased by about 50% in obese patients (7). In addition, glucose intolerance occurs at an earlier age than in non-PCOS (8). Environmental and genetic -epigenetic factors also play a role in the development of PCOS (4).

In the light of these data, the prevalence of obesity, which plays an important role in the pathogenesis of polycystic ovary syndrome, increases throughout the world and increases in the rate of pandemic. (9-11). About 40-70% of these patients are overweight or obese (10,12). The prevalence of PCOS is almost four times higher in the overweight and obese patients than in the weak individuals (13). However, other studies reported that obesity only increased the risk of PCOS (10, 14). In addition, it has been reported that PCOS will increase the risk of obesity, potentially decrease in basal metabolic rate and impaired satiety (15, 16).

It was concluded that exercise and weight loss may have positive effects on ovulation and insulin resistance in PCOS (17). Mild weight loss (5 to 10 percent reduction in body weight) can lead to the onset of normal ovulation and to be associated with better pregnancy rates in short-term studies (18-20).

In our study, we examined the effect of obesity and metabolic status on the fertility of PCOS cases in our country.

MATERIAL and METHODS

We retrospectively evaluated the data of 230 patients with PCOS who applied to our clinic between March 2013 and March 2018. The patients were diagnosed with polycystic ovary syndrome according to 2003 Rotterdam criteria (21); age of patients, body mass index, application complaints, family history, ultrasonographic findings, blood hormone profiles (Follicular stimulane hormone-FSH, Luteinizing hormone-LH, total and free testosterone, prolactin, thyroid stimulating hormone-TSH) and biochemical parameters (low-density lipoprotein -LDL, high density lipoprotein-HDL, triglyceride, cholesterol and fasting blood glucose levels were recorded.

According to the kilogram / (height)2 (m^2) formula of all cases, body mass index was calculated. 5 -24,99 kg / m^2 normal weight, BMI 25-29,99 kg / m^2 overweight kg / m^2, BMI 30-39,99 kg / m^2 obese, BMI 40 and above were considered as morbid obese. Insulin resistance was calculated with Homeostatic Model Assesment -HOMA index- (fasting insulin X fasting glucose) / concentrate. The concentration was calculated as 450 mg / dl and the limit value was taken as 2.4 (22). Above .2.4 values were considered as insulin resistance. 75 grams Oral Glucose tolerance test was performed after the appropriate diet and duration and serum glucose levels were measured at 0, 1, 2 and 2 hours. Diabettus mellitus was diagnosed at 200 hours. OGTT 2. Values between 140 and 199 were considered as impaired glucose tolerance. Total cholesterol, HDL and LDL cholesterol levels were measured. For total cholesterol, 200mg / dl and above, for LDL values above 100 mg/dl and less than 50mg/dl for HDL were accepted as dyslipidemia.

RESULTS

The study was conducted with 230 patients between March 2013 and March 2018. The ages of the cases ranged from 18 to 40 years, with a mean of 26.72 ± 5.60 years. BMI levels ranged from 17.6 to 47 kg / m^2 and the mean was 28.97 ± 5.95 kg / m^2. Only 25% of the patients had normal weight and 73% were overweight; 4 (1.7%) cases in the weak group with BMI less than 18.5, 58 (25.2%) cases in normal weight group with BMI 19-24.9, 71 (30.9%) in overweight group with BMI 25-29.9 There were 86 cases (37.4%) in obese group with BMI 30-39.9 and 11 cases (4.8%) in morbidly obese group with BMI of 40 and above. u (21.5%) is fertile.

The infertility period varies between 12 and 196 months, the mean is 33.92 ± 24.25 months and the median is 24 months. Waist circumference ranged from 62 to 135 cm and the mean was 87.76 ± 13.48 cm. The waist / hip ratio ranged from 0.65 to 0.98 and the mean was 0.80 ± 0.06.

Table 1: Distribution of Clinical and Metabolic Properties.

		Min-Max (median)	Ort±SS
Age (year)		18-40	26.72±5.60
BMI (kg/m²)		17.60-47.0	28.97±5.95
Waist Circumference (cm)		62-135	87.76±13.48
Waist/Hip Ratio		0.65-0.98	0.80±0.06
Duration of Infertility (month)		12-196 (24)	33.92±24.25
		n	**%**
BMI groups	**Lean**	4	1.7
	Normal	58	25.2
	Over Weight	71	30.9
	Obese	86	37.4
	Morbid obese	11	4.8
İnfertility	**No**	49	21.5
	Yes	181	78.5
İnsülin **resistance**	**No**	131	56.9
	Yes	99	43.1
Impaired Glucose Tolerance	**No**	153	66.5
	Yes	77	33.5
DM	**No**	218	94.8
	Yes	12	5.2

99 (43.1%) of the cases had insulin resistance, 77 (33.5%) had impaired glucose tolerance and 12 (5.2%) had DM.

Table 2: Relationship of Metabolic Conditions with Infertility.

		Fertil	Infertil	p
BMI	**Normal +Lean**	17 (%27.9)	45 (%72.1)	**0.259**[1]
	Over Weight	13 (%18.5)	58 (%81.5)	
	Obese	15 (%17.7)	71 (%82.3)	
	Morbid obese	4 (%36,6)	7 (%63,4)	
Insulin Resistance	**No**	29 (%22.1)	102 (%77.9)	**1.000**[2]
	Yes	21 (%21.5)	78 (%78.5)	
Impaired Glucose Tolerance	**No**	36 (%23.5)	117(%76.5)	**0.516**[2]
	Yes	14 (%18.3)	63 (%81.7)	
DM	**No**	46 (%21.2)	172 (%78.8)	**0.705**[3]
	Yes	3 (%27.3)	4(%72.7)	
		Ort±SS (medyan)	**Ort±SS (medyan)**	
Waist Circumference		91.05±14.97	88.98±12.84	**0.397**[4]
Waist/Hip		0.82±0.05	0.81±0.06	**0.508**[4]
HDL		48.51±18.45	46.30±11.32	**0.370**[4]
LDL		104.37±28.58	109.05±32.18	**0.432**[4]
Total Cholesterol		173.35±35.40	178.74±40.98	**0.474**[4]

***1** Pearson Ki-Kare test **2** Yates test **3** Fisher's Exact test **4** Student t test **5** Mann-Whitney U test*

According to the evaluation of BMI, waist circumference and waist / hip ratio, no statistically significant difference was found between fertile and infertile groups (p> 0.05). 0.05).Total cholesterol, HDL and LDL levels were not statistically different according to the fertility of the cases (p> 0.05).

Table 3: The Effect of Metabolic Conditions on Duration of Infertility.

		Infertilite Süresi (ay)	
		Ort±SS (medyan)	**p**
BMI	**Normal+Lean**	32.58±22.01 (24)	**0.109**[1]
	Over Weight	37.68±31.67 (28)	
	Obese	33.55±20.12 (25)	
	Morbid obese	19.57±5.28 (22)	
Insulin Resistance	**No**	33.74±22.95 (24)	**0.569**[2]
	Yes	35.11±27.06 (28)	
Impaired Glucose Tolerance	**No**	32.96±24.99 (24)	**0.306**[2]
	Yes	35.40±23.20 (26)	
DM	**No**	34.16±24.86 (24)	**0.683**[2]
	Yes	29.75±8.10 (30)	
		r	**p**
Waist Circumference		0.032	**0.697**
Waist/Hip		0.033	**0.727**
HDL		0.014	**0.870**
LDL		0.069	**0.406**
Total Cholesterol		0.138	**0.096**

***1** Kruskal Wallis test **2** Mann-Whitney U test **r:** Spearman's rho correlation coefficient.*

Duration of infertility and BMI, waist circumference, waist / hip ratio was evaluated, there was no significant difference between the groups. There was no statistically significant relationship between insulin resistance, impaired glucose tolerance and duration of DM and infertility (p> 0.05).

Statistical Analysis

While evaluating the findings obtained in the study, IBM SPSS Statistics 22.0 program was used for statistical analysis. The fit of the parameters to normal distribution was evaluated by Shaphiro Wilk test. Kruskal-Wallis test was used for the comparison of descriptive statistical methods (mean, standard deviation) and non-normally distributed parameters in the comparison of quantitative data. Student t-test was used to compare normal distribution parameters and Mann-Whitney U test was used for the comparison of parameters that did not show normal distribution. Chi-Square test, Fisheracts Exact test and Continuity Correction (Yates) test were used to compare qualitative data. Spearman arasındakis rho correlation analysis was used to examine the relationships between parameters which do not conform to normal distribution. Significance was evaluated at p <0.05.

DISCUSSION

In PCOS, obesite, metabolic syndrome and insulin resistance are frequently observed (23-25). In our study population, obesity rate was 42% and insulin resistance was 43%. According to the literature, approximately half of the patients are obese and at least one third of non-obese patients have intraabdominal fat increase (33, 34). Obesity is a risk factor for anovulation, ovulatory disorder, subfertility, low pregnancy rates and polycystic ovary syndrome (26, 27). In patients with infertile PCOS, the

success rate is lower in patients treated with obesity. During the infertility treatment of this patient group, a higher dose of medication is required (28). 78% of patients with PCOS were infertile. This is due to the fact that the situation that caused the application was prioritized by the patient and his / her social links; A significant number of patients have learned the presence of metabolic disorders, such as insulin resistance, for the first time when they are referred for gynecological symptoms. The literature on infertility and PCOS is examined, it has been reported in some studies that lower oocytes were collected during in vitro fertilization treatment in this patient group (29, 30). Abortion in the obese group and low pregnancy rate, cancellation of the cycle is more common (30).

The negative relationship between obesity and anti-Müllerian Hormone level, which is a marker of ovarian reserve, has been shown in many studies (31, 32). Pregnancy carries serious risks for women who are obese; increase in congenital anomalies (neural tube defects and cardiac defects), increase in abortion risk, gestational diabetes, hypertension and increase in risk of intrapartum intervention (35, 36). Pregnancy increases insulin resistance in PCOS patients by increasing insulin resistance (37). Considering these findings, some authors argue that patients who are obese and who cannot lose weight should not be treated in terms of infertility (38). In our case group, we found no statistically significant difference between the fertile and infertile groups. In Table 2, when glucose metabolism disorders were re-examined, it was not possible to reach a meaningful result when we looked at it more carefully and calculated. In addition, it may be possible to reach a real result with a prospective and long term follow-up study comparing the metabolic status of the patients with metabolic status immediately before conception and the metabolic status of infertile patients.

CONCLUSION

Obesity and metabolic disorders are more common in PCOS cases. There was no significant difference between fertile and infertile groups according to BMI.

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