İstanbul Med J 2017; 18: 210-7
DOI: 10.5152/imj.2017.55823

Original Investigation

Incidence of Metabolic Syndrome and Long-Term Chronic Health Problems in Infertile Women

Ruhuşen Kutlu[1], Derya Işıklar Özberk[1], Hüseyin Görkemli[2]

Abstract

Introduction: Infertility is a condition wherein there is no pregnancy within 1 year despite regular sexual intercourse without birth control. The aim of this study was to evaluate the incidence of metabolic syndrome (MetS) and chronic long-term health problems in infertile female patients.

Methods: This cross-sectional and analytical study was retrospectively conducted on 701 women who applied to family medicine outpatient clinic and received a medical report with the complaint of female infertility. The weight, height, waist circumference, blood pressure, and laboratory results of subjects were recorded from the information in the files. MetS was diagnosed according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guideline.

Results: The mean age of the 701 infertile women in the study was 29.9±4.4 (20–42) years; 81.6% (n=572) were housewives and 56.8% (n=398) completed primary school and were undergraduates. Of the patients, 78.9% (n=553) were admitted due to primary infertility. The incidence of MetS was 19.8% in the subjects of this study. The risk of MetS was 6,389 times higher in obese than in non-obese individuals [odds ratio (OR)=6,389; %95 confidence interval (CI): (4,260–9,581)], and this difference was statistically significant (p<0.001). The most common MetS components were triglyceride elevation (59.6%) and fasting blood glucose (55.0%). MetS was detected in 50.3% of hypertensive patients. Of the participants, 22.8% had hypothyroidism and 2.7% were found to have brucella seropositivity.

Conclusion: Obesity, long-term health problems, smoking, and some infectious diseases, which are among the replaceable factors associated with infertility, should be excluded before infertility treatment. Healthy lifestyle changes such as well-balanced and correct nutrition, physical activity, giving up smoking and alcohol will reduce the risk of obesity and increase the chances of infertility treatment.

Keywords: Metabolic syndrome, female ınfertility, obesit

Introduction

Infertility is the inability to conceive for at least 1 year despite regular unprotected sexual intercourse. Approximately 10%-15% of couples worldwide have infertility problems. Primary infertility is defined as not being pregnant previously, and secondary infertility is defined as having trouble conceiving again despite unprotected intercourse, even though pregnancy has been previously achieved (1).

In developed countries, the diseases causing infertility have been attributed to women at a rate of 37%, men at a rate of 8%, and both partners at a rate of 35%. The cause of infertility has not been found in 5% of couples (unexplained infertility). The most common causes of infertility are ovulatory disorders (25%), pelvic adhesions (12%), tubal occlusion (11%), other tubal anomalies (11%), hyperprolactinemia (7%), and endometriosis (15%). A cause has not been found in 20% of cases (2).

Before initiating infertility treatment, the patient should be evaluated in terms of obesity. It has been observed that obesity can lead to many problems including chronic oligo-anovulation, menstrual irregularity, subfertility, increased risk of miscarriage, and negative pregnancy results. It has been demonstrated that obesity-related infertility or decreased fertility results from the effects of impaired hypothalamic–pituitary–ovarian axis seen in each step from the selection of the ovarian follicle to implantation (3).

Metabolic syndrome (MetS) is defined as the presence of three or more criteria among abdominal obesity, hypertension (HT), hyperglycemia, increased triglyceride (TG) level, and decreased high-density lipoprotein (HDL) cholesterol level. These components used for the diagnosis of MetS are also very important for the risk of the development of cardiovascular disease (CVD) and type II diabetes mellitus (DM) (4).

The present study was performed to evaluate the frequency of MetS and related long-term chronic health problems (such as DM, thyroid dysfunction, HT, hyperlipidemia, and anemia) in infertile

[1]Department of Family Medicine, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey
[2]Department of Gynecology and Obstetrics, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey

Address for Correspondence:
Derya Işıklar Özberk
E-mail: derya_isiklar@hotmail.com

Received: 01.06.2017

Accepted: 21.07.2017

women applying to the outpatient clinic of family medicine for receiving health report before beginning in vitro fertilization (IVF) therapy.

Material and Methods

Method and population of the study

Infertile women are asked to obtain a health board report before starting IVF therapy for the sake of the procedure. This descriptive and cross-sectional study was performed by retrospectively evaluating the files of 740 women who applied to the outpatient clinic of family medicine for female infertility between January 2013 and January 2016. Those with lacking examinations and sociodemographic data in their files were excluded from the study. The files of 701 patients, who were suitable for the study, were examined (701/740).

Ethical approval for the study

Before beginning the study, ethical approval was obtained from the ethics committee of Meram Medical Faculty, Necmettin Erbakan University (number 2016/647 on 06/24/2016). Since our study was conducted by scanning files of patients retrospectively, informed consent was not obtained from the patients.

Collection of data

Based on the information obtained from the patients' files, ages, educational levels, patients' and their husbands' jobs, history of pregnancy, the presence of kin marriage, the presence of any chronic disease, and smoking and alcohol habits were recorded on the questionnaire form developed by the researcher. The participants who smoked at least once a day were accepted as addicted, and the amount of smoking was calculated as pack/year for these participants with smoking addiction. The presence of related long-term chronic diseases (such as DM, thyroid dysfunction, HT, hyperlipidemia, and anemia) was evaluated. Blood pressure (BP), height, weight, waist circumference (WC), and hip circumference of all patients were measured and recorded. To measure BP, systolic BP of 130 mm Hg and above and diastolic BP of 85 mm Hg and above were evaluated to be increased (4).

Anthropometric measurements

Anthropometric measurements of the patients were performed after taking off the shoes for height and jacket and extra clothes for weight by using a standard bascule and stadiometer. After anthropometric measurements (height, weight, WC, abdominal circumference, and hip circumference), body mass index (BMI) and waist-to-hip ratio (WHR) were calculated based on these data.

WC measurement

WC was measured from the narrowest part of the waist while the volunteer was standing upright in a relaxed manner with the arms hanging loosely at the sides and legs closed and after breathing out normally. The measurement value was recorded with 0.1 cm sensitivity. The values of WC >88 cm and WHR >0.85 were accepted as abdominal obesity (5).

Hip circumference measurement

The measurement was performed with a measuring tape in parallel to the floor, while the volunteer was standing upright with the arms hanging loosely at the sides and legs closed, from the widest part of both hips by ensuring no jamming tissue. The value was recorded with 0.1 cm sensitivity.

Waist-to-hip ratio

WHR was calculated by the formula: Waist/Hip Ratio=Waist circumference (cm)/Hip circumference (cm). To detect fat distribution, WHR was obtained by calculating the ratio of the narrowest part of the waist to the widest part of the hip.

Body mass index

BMI was obtained by the formula: Body Mass Index (BMI)=Body weight (kg)/Height $(m)^2$. BMI values were evaluated as underweight ($\leq$18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese ($\geq$30 kg/m^2).

Diagnosis of MetS

To diagnose MetS, the presence of three or more of the National Cholesterol Education Program Adult Treatment Panel III criteria was considered below (4):

- abdominal obesity (WC >102 cm in men and WC >88 cm in women)
- hypertriglyceridemia (TG >150 mg/dL)
- low HDL-C (<40 mg/dL in men and <50 mg/dL in women)
- HT (systolic BP ≥130 and diastolic BP ≥85 mm Hg)
- hyperglycemia (fasting plasma glucose (FPG) ≥100 mg/dL).

Since our study was conducted on women, WC and HDL-C values defined for women were taken into consideration.

Laboratory analyses

From the files of the patients, the values of FPG, complete blood, thyroid-stimulating hormone (TSH), total cholesterol (T-cholesterol), HDL-C, low-density lipoprotein cholesterol (LDL-C), TG, C-reactive protein (CRP), aspartate transaminase (AST), alanine transaminase (ALT), *Brucella* agglutination test, hepatitis B surface antigen (HBsAG), anti-HBsAG, anti-hepatitis C virus (HCV), urea, creatinine, prothrombin time (PT/INR), activated partial thromboplastin time (APTT), and complete urine analysis (CUA) were recorded. FPG <100 mg/dL was evaluated as normal, FPG between 100 mg/dL and 125 mg/dL as impaired fasting glucose (IFG), and FPG 126 mg/dL and above as overt DM (6).

Statistical evaluation

While evaluating the obtained data, Statistical Package for Social Sciences 20.0 (IBM Corp.; Armonk, NY, USA) software was used for statistical analyses. Frequencies, mean, minimum and maximum, standard deviation, median values, and odds ratios were calculated. Chi-square test was used for comparing qualitative data. Non-normally distributed quantitative data were compared with Mann–Whitney U test and Kruskal–Wallis test. The results were evaluated with 95% confidence interval and significance level of $p<0.05$. For correlation among parameters, Pearson's correlation analysis was used. The correlation coefficient (r) between 0.00 and 0.24 was evaluated as poor relationship, between 0.25 and 0.49 as moderate, between 0.50 and 0.74 as strong, and between 0.75 and 1.00 as very strong.

Results

In 701 women who participated in the study, the mean age was 29.9±4.4 (20–42) years; the mean age of marriage was 22.2±4.1 years; and the mean length of marriage was 7.6±4.0 years. Among them, 81.6% (n=572) were housewives, 56.8% (n=398) were elementary school graduates and below, 7.6% (n=53) were smokers,

Table 1. Comparison of sociodemographic features in participants with and without metabolic syndrome

		Existent MetS[1] (n=139)		Non-existent MetS (n=562)		Total			
Sosyodemografik özellikler		**n**	**%**	**n**	**%**	**n**	**%**	χ^2	**p**
Age group	≤29 years	53	14.9	302	85.1	355	100	10.860	0.001
	>29 years	86	24.9	260	75.1	346	100		
Professional status	Housewife	118	20.6	454	79.4	572	100	1.253	0.263
	Working	21	16.3	108	83.7	129	100		
Educational level	Elementary school graduate and below	89	22.4	309	77.6	398	100	3.716	0.054
	Above elementary school graduate	50	16.5	253	83.5	303	100		
Smoking state	Smoking	7	13.2	46	86.8	53	100	1.581	0.209
	Not smoking	132	20.4	516	79.6	648	100		
Smoking state of husband	Smoking	62	17.9	284	82.1	346	100	1.567	0.211
	Not smoking	77	21.7	278	78.3	355	100		
Occupation of husband	Worker	67	24.1	211	75.9	278	100	10.472	0.015
	Civil servant	32	17.8	148	82.2	180	100		
	Tradesman	30	14.2	181	85.8	211	100		
	Unemployed	10	31.3	22	68.7	32	100		
Presence of kin marriage	Yes	26	25.0	78	75.0	104	100	2.054	0.152
	No	113	18.9	484	81.1	597	100		
Presence of HT2 in family	Yes	67	21.9	239	78.1	240	100	1.459	0.227
	No	72	18.2	323	81.8	395	100		
Presence of DM3 in family	Yes	61	26.1	173	73.9	234	100	8.602	0.003
	No	78	16.7	389	83.3	467	100		
Presence of cancer in family	Yes	23	18.0	105	82.0	128	100	0.341	0.559

[1]MetS: metabolic syndrome. [2]HT: hypertension. [3]DM: diabetes mellitus.

and the husbands of 49.4% (n=346) were smokers. Of the participants, 14.8% (n=104) had kin marriage, 39.7% (n=278) of the husbands were workers, 25.7% (n=180) were civil servants, and 30.1% (n=211) were tradesmen.

Of the women, 78.9% (n=553) applied for primary infertility, and 21.1% (n=148) for secondary infertility. According to their BMI values, 2.4% (n=17) were underweight, 42.7% (n=299) were normal weight, 32.1% (n=225) were overweight, and 22.8% (n=160) were obese. WC was more than 88 cm in 34.2% of patients (n=240), and WHR was more than 0.85 in 47.5% of them (n=333). The rate of MetS was found to be 19.8% (n=139). The frequency of MetS development was 46.3% in those with BMI ≥30 kg/m^2. The frequency of MetS was 6.389 times higher in obese patients than others [OR=6.389, 95% CI (4.260–9.581)]. This difference was statistically significantly increased (p<0.001).

The women with and without the diagnosis of MetS were compared in terms of professional status, educational level, their and their husbands' smoking state, kin marriage, and the familial history of HT and cancer, and no statistically significant difference was detected (p>0.05) (Table 1).

There was no significant correlation between the diagnosis of DM and frequency of MetS in the participants, but the rate of MetS was significantly higher in those having a history of HT (p<0.001). In the comparison of women with and without the diagnosis of MetS with regard to marriage age, infertility type, and history of labor and miscarriage, no statistically significant relationship was detected between the groups (p>0.05). There was a statistically significant relationship only between the length of marriage and diagnosis of MetS (p=0.043). Comparison of some parameters in those with and without the diagnosis of MetS is shown in Table 2.

In the examination of the correlation between systolic BP and WC values (r=0.260, p<0.001) in our study, a positive moderate correlation was found. With regard to the correlation between BMI and systolic BP (r=0.387, p<0.001) and diastolic BP (r=0.303, p<0.001), a positive moderate correlation was observed. Moreover, a positive moderate correlation was found between BMI and TG (r=0.250, p<0.001). There was a positive strong correlation between BMI and WC (r=0.618, p<0.001). In the linear regression analysis, 38.2% of increased BMI values were attributed to increased WC values (R^2=0.382) (Figure 1).

In our study, the values of the median age (p=0.002), systolic BP (p<0.001) and diastolic BP (p<0.001), FPG (p<0.001), T-cholesterol (p<0.001), LDL-C (p=0.004), TG (p<0.001), WC (p<0.001), BMI (p<0.001), and WHR (p<0.001) were found to be significantly higher in those with MetS than in those without MetS. Moreover, the

Table 2. Comparison of some parameters in patients with and without metabolic syndrome

	Existent MetS[1] (n=139)		Non-existent MetS (n=562)		Total (n=701)			
Parameters	**n**	**%**	**n**	**%**	**n**	**%**	χ^2	**p**
Hypertension								
≥130/85 mm Hg (abnormal)	77	50.3	76	49.7	153	100	114.513	0.000
<130/85 mm Hg (normal)	62	11.3	486	88.7	548	100		
Waist circumference								
>88 cm (abnormal)	115	47.9	125	52.1	240	100	181,113	0,000
≤88 cm (normal)	24	5.2	437	94.8	461	100		
Fasting plasma glucose								
≥100 mg/dL (abnormal)	60	55.0	49	45.0	109	100	100.696	0.000
<100 mg/dL (normal)	79	13.3	513	86.7	592	100		
Triglyceride								
≥150 mg/dL (abnormal)	84	59.6	57	40.4	141	100	175.393	0.000
<150 mg/dL (normal)	55	9.8	505	90.2	560	100		
HDL cholesterol								
<50 mg/dL (abnormal)	137	27.8	356	72.2	493	100	66.227	0.000
≥50 mg/dL (normal)	2	1.0	206	99.0	208	100		
Body mass index (kg/m²)								
<18.5 underweight	1	5.9	16	94.1	17	100	101.783	0.000
18.5–24.99 normal	22	7.4	277	92.6	299	100		
25–29.99 overweight	42	18.7	183	81.3	225	100		
≥30 obese	74	46.3	86	53.7	160	100		
Waist/hip circumference ratio								
>0.85 (abnormal)	100	30.0	233	70.1	333	100	41.524	0.000
≤0.85 (normal)	39	10.6	329	89.4	368	100		
Fasting plasma glucose								
<100 mg/dL (normal)	79	13.3	513	86.7	592	100	108.796	0.000
100–125 mg/dL (IFG[2])	47	50.5	46	49.5	93	100		
>126 (overt DM[3])	13	81.3	3	18.7	16	100		

[1]MetS: Metabolik sendrom; [2]BAG: Bozulmuş açlık glukozu; [3]DM: Diyabetes mellitus

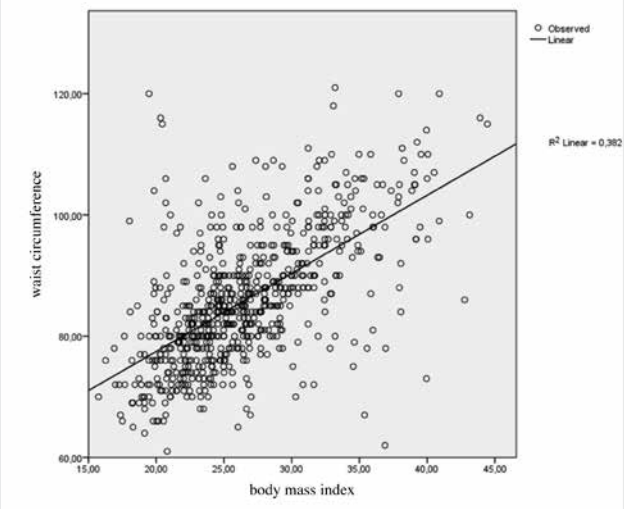

Figure 1. Linear regression analysis between body mass index and waist circumference

median HDL-C level of patients diagnosed with MetS was significantly lower than those without the diagnosis of MetS (p<0.001) (Table 3).

When the participants were grouped according to their BMI values, no statistically significant relationship was detected among the groups in terms of the median erythrocyte count, hemoglobin, hematocrit (HCT), mean erythrocyte volume, mean platelet volume, APTT, TSH, urea, and creatinine levels (p>0.05). In the comparison of the groups in terms of median white blood cell (WBC), platelet (PLT), PT/INR, AST, ALT, and CRP values, it was found that the WBC, PLT, AST, ALT, and CRP values of the normal weighted group were significantly lower than those of the overweight and obese groups (p<0.05). In addition, the PT/INR value of the normal weighted group was significantly higher than that of the overweight (p=0.020) and obese (p=0.015) groups (Table 4).

In our study, considering the reference interval of 0.32-5.4 μIU/mL for TSH level, TSH value was increased in 11 patients and de-

Table 3. Comparison of some parameters in patients with and without metabolic syndrome

	Existent MetS[1] (n=139)	Non-existent MetS (n=562)		
Parameters	**Median (min–max)**	**Median (min–max)**	**Z**	**P***
Age	31.00 (21.00–40.00)	29.00 (20.00–42.00)	-3.104	0.002
Systolic BP[2] (mm Hg)	132.00 (98.00–190.00)	122.00 (87.00–160.00)	-7.766	0.000
Diastolic BP (mm Hg)	83.00 (60.00–110.00)	78.00 (57.00–104.00)	-7.871	0.000
FPG[3] (mg/dL)	97.00 (68.00–258.00)	89.00 (62.00–183.00)	-7.886	0.000
T-cholesterol (mg/dL)	188.00 (125.00–304.00)	174.00 (85.00–336.00)	-4.345	0.000
LDL cholesterol (mg/dL)	116.00 (55.00–215.00)	109.00 (43.90–323.00)	-2.909	0.004
TG[4] (mg/dL)	158.00 (25.00–390.00)	85.00 (29.00–399.00)	-10.732	0.000
HDL cholesterol (mg/dL)	39.00 (22.00–62.00)	45.05 (22.00–87.00)	-7.636	0.000
WC5 (cm)	95.00 (67.00–121.00)	82.00 (61.00–120.00)	-12.101	0.000
BMI6 (kg/m^2)	30.73 (17.36–43.91)	24.78 (15.74–44.44)	-10.085	0.000
WHR7	0.88 (0.73–1.02)	0.83 (0.52–1.13)	-7.325	0.000

*Mann–Whitney U test. 1MetS: metabolic syndrome. 2BP: blood pressure. 3FPG: fasting plasma glucose. 4TG: triglyceride. 5WC: waist circumference. 6BMI: body mass index. 7WHR: waist-to-hip ratio.

Table 4. Values of some parameters according to body mass indices (BMI=kg/m^2)

	BMI[1] <25 (a) (n=316)	BMI 25–29.9 (b) (n=225)	BMI ≥30 (c) (n=160)	
Parameters	**Median (min–max)**	**Median (min–max)**	**Median (min–max)**	**p***
WBC[2] (10^3/µL)	6.87 (1.02–15.00)	7.78 (1.37–13.62)	7.57 (1.08–19.00)	0.000[ab]
				0.000[ac]
				0.043[bc]
RBC[3] (106/µL)	4.82 (3.10–5.83)	4.84 (3.75–6.10)	4.78 (3.86–6.10)	0.100
HGB[4] (g/dL)	12.70 (8.72–17.00)	13.20 (9.70–18.20)	12.85 (7.92–16.30)	0.719
HCT[5] (%)	39.00 (30.00–51.00)	39.25 (29.70–47.00)	38.40 (30.60–45.00)	0.642
MCV[6] (fL)	83.70 (59.00–96.30)	84.75 (57.30–97.00)	83.00 (74.40–95.00)	0.114
PLT[7] (103/µL)	255.00 (139.00–472.00)	262.50 (105.00–520.00)	291.50 (105.00–504.00)	0.006[ab]
				0.001[ac]
MPV[8] (fL)	7.00 (4.72–11.70)	7.00 (5.00–12.90)	7.05 (4.93–12.30)	0.933
PT/INR[9]	1.08 (0.50–12.60)	1.05 (0.89–13.40)	1.04 (0.50–1.88)	0.020[ab]
				0.015[ac]
APTT[10] (s)	29.00 (1.09–36.90)	30.00 (1.02–37.10)	29.10 (13.50–41.80)	0.733
AST[11] (u/L)	18.00 (8.00–40.00)	18.50 (8.00–35.00)	20.00 (9.00–49.00)	0.003[ac]
ALT[12] (u/L)	16.00 (8.0–45.00)	18.00 (6.00–35.00)	20.00 (7.00–48.00)	0.036[ab]
				0.000[ac]
				0.001[bc]
TSH[13] (µIU/mL)	1.6 (0.02–13.92)	1.68 (0.03–11.61)	1.80 (0.05–6.02)	0.435
Urea (mg/dL)	18.00 (8.00–34.00)	18.75 (7.00–41.00)	18.00 (6.00–48.00)	0.617
Creatinine (mg/dL)	0.66 (0.17–0.90)	0.60 (0.40–1.18)	0.60 (0.46–1.00)	0.096
CRP[14]	3.00 (0.18–10.10)	3.50 (0.00–18.00)	3.46 (0.50–19.00)	0.000[ab]
				0.000[ac]

*Kruskal–Wallis test. 1BMI: body mass index. 2WBC: white blood cell. 3RBC: red blood cell. 4HGB: hemoglobin. 5HCT: hematocrit. 6MCV: mean erythrocyte volume. 7PLT: platelet. 8MPV: mean platelet volume. 9PT/INR: prothrombin time. 10APTT: activated partial thromboplastin time. 11AST: aspartate transaminase. 12ALT: alanine amino transaminase. 13TSH: thyroid-stimulating hormone. 14CRP: C-reactive protein.

creased in 7 patients. No statistically significant relationship was found between the existence of MetS and TSH values (p>0.05). While the value of urea was increased only in one patient (urea >44 mg/dL), no increased value of creatinine was observed in any patient. The result of CUA revealed infection in 8% (n=56) of the participants, and treatment was arranged. *Brucella* agglutination test result was positive in 2.7% (n=19) of women, anti-HCV was positive in one patient, and HBsAg was positive in 11 patients. In

6.1% of the participants (n=43), anti-HBsAg was sufficient. Hepatitis B vaccination was recommended to other patients. Abnormality was found in the electrocardiography of five patients. Consultation was done with the Department of Cardiology, and echocardiography results were normal. Posteroanterior lung radiographies were evaluated to be abnormal in six patients. They were assessed in favor of infection by the clinic of chest diseases, and treatment was arranged for them.

Discussion

Obesity negatively affects fertility in women and causes impairments in menstrual cycle, chronic oligo-anovulation, and infertility. It also affects the success of infertility treatment negatively. In addition, in obese women, the results of pregnancy obtained with assisted reproduction techniques can be negative (7).

According to the Metabolic Syndrome Research conducted on 4259 patients in Turkey in 2004, the overall prevalence of MetS was reported as 35% in adults and 41.1% in females (8). Similarly, in the CARDIOMETRY study performed by the Metabolic Syndrome Association, the frequency of MetS was found to be 36% (9). On the other hand, it was reported as 22% in adults in the 2009 MetS guideline of the Turkish Society of Endocrinology and Metabolism (10). The frequency of MetS was 19.8% in infertile female patients included in our study. Similarly, in the study by Panidis et al. (11) conducted on 1223 female patients diagnosed with polycystic ovarian syndrome, the prevalence of MetS was found to be 15.8%. Ford et al. (12) reported the prevalence of MetS as 23.4% in women. In the literature review performed by the researcher, no study on the frequency of MetS in infertile female patients was found in Turkey within our knowledge. Further studies are needed on this topic.

In the present study, the frequency of MetS was significantly higher in patients older than 29 years than in those younger than 29 years. Similar to our study, Doğan et al. (13) conducted a study on the prevalence of obesity in Afyon and found the frequency of obesity higher in women older than 29 years than in those at the age range between 19 and 29 years.

While the frequency of obesity was found to be 22.3% in the study conducted for determining the epidemiology of diabetes, obesity, and HT in 1998, it was observed to increase by 40% and reached 31.2% in 2010 (14). In TURDEP-I study (Turkish Diabetes Epidemiology Study), abdominal obesity increases to 34.9% when WC is taken as a basis (88 cm for women and 102 cm for men) (15). Similarly, obesity frequency was found to be 22.8% in infertile women, and abdominal obesity rate was 34.2% in our study. The results of our study are consistent with the results of other studies demonstrating that fertility decreases in overweight and obese women. Koning et al. (16) conducted a study on 1000 anovulatory women and investigated the effect of overweight and obesity on fertility, cost of infertility treatment, and pregnancy results. They demonstrated that the possibility of successful infertility treatment was decreased in overweight and obese sub-fertile women, their pregnancy periods included more complications, and treatment costs were higher.

Especially in recent years, increased abdominal fat and frequency of MetS, unhealthy nutrition, sedentary lifestyle, and increased rate of smoking also among women increase morbidity and mortality associated with CVDs in women (17). In our study, the prevalence of MetS was found to be 46.3% in patients with obesity, and the rate of MetS was 6.389 times higher in patients with BMI ≥30 kg/m^2 than in those with BMI <30 kg/m^2. Similarly, in the study by Kutlu and Çivi (18), the prevalence of MetS was reported to be 59.7% in the obese group, and the frequency of MetS was found to be 3.467 times higher in obese patients than in non-obese ones.

In our study, MetS was detected in 50.5% of participants with IFG and in 81.3% of those with overt DM. In infertile female patients with MetS, the frequency of increased TG was 59.6%, and the frequency of elevated FPG was 55.0%. Similarly, in the study by Kozan et al. (8), they reported that 63.1% of women with MetS had hypertriglyceridemia and 53.3% had hyperglycemia.

In our study, Mets was found in 50.3% of patients with HT. Moreover, a positive moderate correlation was detected between BMI and systolic and diastolic BP values. Similarly, in the study by Hatemi et al. (19) performed in 11 provinces, the prevalence of obesity was reported to be 24.6% in women, and a positive linear correlation was reported between BMI and BP.

Abdominal obesity is the most important indicator of insulin resistance. Insulin resistance is generally observed in the etiology of essential HT. Moreover, as insulin resistance increases, TG level increases and HDL-C level decreases (10). In our study, a positive strong correlation was detected between BMI and WC. In the linear regression analysis, 33.5% of increased BMI values were attributed to increased WC. A positive correlation was observed between BMI and the values of FPG, TG, and LDL-C in the patients included in our study.

In the evaluation of HBG level in infertile patients, causes of anemia such as celiac disease should be kept in mind. Anemia was found in 25.8% of the participants in our study. In the literature review by the researcher, no study on anemia in infertility patients was encountered within our knowledge. In infertile patients, the treatment of anemia is important before the formation of pregnancy. In the meta-analysis by Pena-Rosas et al. (20), it was reported that iron replacement therapy in anemic parturients decreased low birth weight and preterm labor.

Obesity can be considered as a systemic inflammatory disease. In obese individuals, inflammatory markers such as CRP are specified to be associated with risk factors for insulin resistance and CVDs (21). In our study, WBC and CRP values were found to be increased in overweight and obese patients, supporting this datum.

In the study by Goldstajn et al. (22), IVF treatment, formation of pregnancy, and coagulation anomaly were investigated in infertile women, and it was recommended to scan the most common mutations in the society and to use low-molecular-weight heparin prophylaxis during pregnancy for patients having IVF failure and long-term infertility. In our study, PLT count was decreased in 8 patients and increased in 20 patients, but PT/INR value was decreased in 17.5% of the participants and increased in 2.6%. In the literature, there are no precise data on PLT and PT/INR values in infertile women, and further studies on this subject are needed.

In our study, TSH value was increased in 11 patients and decreased in 7 patients. For women planning to conceive, the upper limit of TSH is given as 2.5 mIU/L in the 2016 guideline for Diagnosis and

Treatment of Thyroid Diseases by Turkish Society of Endocrinology and Metabolism (23). In accordance with this guideline, hypothyroidism (TSH level >2.5 mIU/L) was detected in 22.8% of the patients. Thyrotoxicosis is primarily associated with hypomenorrhea and polymenorrhea, and hypothyroidism is mainly associated with oligomenorrhea. Thyroid dysfunction is also associated with decreased fertility (24). Therefore, it is important to evaluate TSH level in women applying for infertility. In the study by Altunoğlu et al. (25), which was performed to demonstrate the effect of thyroid hormones on obesity, no significant relationship was reported between thyroid hormones and obesity. Similarly, in our study, there was no statistically significant difference among normal weighted, overweight, and obese groups in terms of TSH values.

In the studies examining TSH value and the existence of MetS, MetS parameters including obesity and MetS were reported to be more common particularly in patients with TSH value of >2.5 mU/L compared with those having lower TSH value (26). However, in our study, no significant relationship was detected between the presence of Mets and TSH level.

In our study, no patient with chronic renal failure was found. In women with chronic renal failure, hypothalamic-pituitary-gonadal axis disorders can be seen, which can be resulted in anovulatory menstrual cycles and thus infertility (27).

Urinary tract infection was detected in 8% of women in our study. Early diagnosis and treatment of existent urinary system infections before pregnancy are important. It is specified that urinary system infections, for example, acute pyelonephritis, can have serious consequences both for fetus and for mother. Here the aim of the present study is to maintain sterility during pregnancy and prevent urinary system-related complications. This can mostly be prevented by the identification of asymptomatic bacteriuria in early pregnancy period. The rate of premature labor is reported as 20%–50% in pregnant cases with acute pyelonephritis (28).

In our study, *Brucella* seropositivity was observed in 19 patients. It is reported that brucellosis can cause amenorrhea, dysmenorrhea, tubo-ovarian abscess, and cervicitis in the genitourinary system (29). Therefore, while taking history of patients admitted for infertility, they should also be evaluated for *Brucella*. In our study, anti-HCV positivity was found in one patient, and HBsAg positivity was found in 11 patients. Moreover, the evaluation of hepatitis virus infections, which are among sexually transmitted infections, is also important. They are important because they can lead to infertility and have consequences such as ectopic pregnancy, which have social and vital importance. Identification of their contagion ways is essential for solving acute or long-term health problems that they can cause and for determining late sequelae (30).

Study Limitations

The limitations of our study are: it was designed as a retrospective study instead of a prospective one and it was conducted only on female infertile group, not including male infertile patients.

Conclusion

The results of our study have demonstrated that the frequency of MetS was increased in infertile women participating in our study although the program for fighting against obesity, diabetes, and HT is being carried out effectively. It is necessary to eliminate infertility-related changeable factors including obesity, long-term health problems, smoking, and some contagious diseases before infertility treatment. Obesity is a disease that is increasing worldwide. The detection of overweight without coexistence with other diseases and the implementation of preventive medicine such as lifestyle changes are important. Healthy lifestyle changes such as balanced and appropriate diet, physical activity, and fight against smoking and alcohol addiction will reduce the risk of obesity and increase the chance of infertility treatment.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Necmettin Erbakan University Meram Medical Faculty.

Informed Consent: Informed consent is not obtained due to the retrospective nature of this study

Peer-review: Externally peer-reviewed.

Author contributions: Concept - R.K.; Design - R.K., D.I.Ö.; Supervision - R.K., D.I.Ö., H.G.; Resource - H.G.; Materials - H.G.; Data Collection and/or Processing - D.I.Ö.; Analysis and/or Interpretation - R.K., D.I.Ö.; Literature Search - D.I.Ö.; Writing - R.K., D.I.Ö.; Critical Reviews - R.K., D.I.Ö., H.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Sipahi M, Parlak A. İnfertil Çifte Yaklaşım. Aydoğan Ü, Koç B. (eds.) Temel Aile Hekimliği. Güneş Tıp Kitapevleri Ltd. Şti, Ankara 2016: 527-8.
2. Günaydın G, Tıraş B. İnfertil Hastaya Yaklaşım. Çiçek MN, Mungan MT. (eds.) Klinikte Obstetrik ve Jinekoloji. Güneş Tıp Kitapevleri Ltd. Şti, Ankara 2007: 851-63.
3. Talmor A, Dunphy B. Female obesity and infertility. Best Pract Res Clin Obstet Gynaecol 2015; 29: 498-506. [CrossRef]
4. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 106: 3143-421.
5. Pekcan G. Beslenme durumunun belirlenmesi. Tüfekçi ME. (eds.) Hastalıklarda Beslenme Tedavisi. 2. Baskı, Alphan Hatipoğlu Yayınları, Ankara 2014: 85-134.
6. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33: 62-9. [CrossRef]
7. Jungheim ES, Travieso JL, Hopeman MM. Weighing the impact of obesity on female reproductive function and fertility. Nutr Rev 2013; 71: 3-8. [CrossRef]
8. Kozan O, Oğuz A, Abacı A, Erol C, Ongen Z, Temizhan A, et al. Prevalence of the metabolic syndrome among Turkish adults. Eur J Clin Nutr 2007; 61: 548-53. [CrossRef]
9. Gundogan K, Bayram F, Capak M, Tanriverdi F, Karaman A, Ozturk A, et al. Prevalence of metabolic syndrome in the Mediterranean region of Turkey: Evaluation of hypertension, diabetes mellitus, obesity, and dyslipidaemia. Metabolic Syndrome and Related Disorders 2009; 7: 427-34. [CrossRef]
10. Türkiye Endokrinoloji ve Metabolizma Derneği Metabolik Sendrom Kılavuzu 2009. Erişim tarihi: 16 Ocak 2017. http://www.turkendokrin.org/files/pdf/metabolik sendrom.pdf

11. Panidis D, Macut D, Tziomalos K, Papadakis E, Mikhailidis K, Kandaraki EA, et al. Prevalence of metabolic syndrome in women with polycystic ovary syndrome. Clin Endocrinol 2013; 78: 586-92. [CrossRef]
12. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. JAMA 2002; 287: 356-9. [CrossRef]
13. Doğan N, Toprak D, Demir S. Prevalence of Obesity and Associated Risk Factors in Afyonkarahisar-Turkey. Turkiye Klinikleri J Med Sci 2011; 31: 122-32. [CrossRef]
14. Satman I, Omer B, Tutuncu Y, Kalaca S, Gedik S, Dinccag N, et al. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013; 28: 169-80. [CrossRef]
15. Satman I, Yilmaz T, Sengul A, Salman S, Salman F, Uygur S, et al. Population-based study of diabetes and risk characteristics in Turkey: results of the turkish diabetes epidemiology study (TURDEP). Diabetes Care 2002; 25: 1551-6. [CrossRef]
16. Koning AM, Kuchenbecker WK, Groen H, Hoek A, Land JA, Khan KS, et al. Economic consequences of overweight and obesity in infertility: a framework for evaluating the costs and outcomes of fertility care. Hum Reprod Update 2010; 16: 246-54. [CrossRef]
17. Çengel A. Cardiovascular risk factors in women. Turk Kardiyol Dern Ars 2010; 38: 17-24.
18. Kutlu R, Çivi S. Frequency and Associated Factors of Metabolic Syndrome in Adults Older than 20 Years of Age who applied to Family Medicine Outpatient Clinic. Konuralp Tıp Dergisi 2014; 6: 47-54.
19. Hatemi H, Yumuk VD, Turan N, Arik N. Prevalence of overweight and obesity in Turkey. Metab Syndr Relat Disord 2003; 1: 285-90. [CrossRef]
20. Pena-Rosas J, Viteri FE. Effects and safety of preventive oral iron or iron+folic acid supplementation for women during pregnancy. Cochrane Database Syst Rev 2009; 7: CD004736. [CrossRef]
21. Vendrell J, Broch M, Vilarrasa N, Molina A, Gómez JM, Gutiérrez C, et al. Resistin, adiponectin, ghrelin, leptin, and proinflammatory cytokines: relationships in obesity. Obes Res 2004; 12: 962-71. [CrossRef]
22. Goldstajn MS, Kovacević D. The effect of trombophilia on pregnancy outcome and IVF success. Coll Antropol 2014; 38: 1153-61.
23. Türkiye Endokrinoloji ve Metabolizma Derneği. Tiroid Hastalıkları Tanı ve Tedavi Kılavuzu. Gebelik ve Tiroid Hastalıkları. 5.Baskı. Ankara: 2016. Erişim tarihi: 20 Ocak 2017 http://www.turkendokrin.org/files/TIROID_web.pdf
24. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocr Rev. 2010; 31: 702-55. [CrossRef]
25. Müderrisoglu C, Ülgen E, Altunoğlu E, Erdenen F, Boz M. Obesity and Thyroid Functions. Istanbul Tıp Dergisi 2009; 1: 24-5.
26. Topsakal S, Yerlikaya E, Akin F, Kaptanoglu B, Erürker T. Relation with HOMA-IR and thyroid hormones in obese Turkish women with metabolic syndrome. Eat Weight Disord 2012; 17: 57-61. [CrossRef]
27. Kuczera P, Adamczak M, Wiecek A. Endocrine Abnormalities in patients with chronic kidney disease. Pril (Makedon Akad Nauk Umet Odd Med Nauki). 2015; 36: 109-18. [CrossRef]
28. Sobel JD, Kaye D. Urinary tract infections. Mandel GL, Bennett JE, Dolin R (eds). In: Principles of practice of ınfectious diseases. Fifth edition, volume 1. 2000 USA: Churchill Livingstone 773-805.
29. Madkour MM. Kasper DL, Brucellosis. In : Harrison's Principles of Internal Medicine. Braunwald E, Fauci AS, Kasper DL, et al (eds). Me Graw-Hill Co, 15th edition, International edition, 2001, pp: 986-90.
30. Zarakolu P, Ünal S. Cinsel yolla bulaşan hastalıklar. Topçu AW, Söyletir G, Doğanay M, eds. İnfeksiyon hastalıkları ve mikrobiyolojisi. İstanbul: Nobel Tıp Kitabevi,2002;1111-5.

Cite this article as: Kutlu R, Özberk DI, Görkemli H. Incidence of Metabolic Syndrome and Long-Term Chronic Health Problems in Infertile Women. İstanbul Med J 2017; 18: 210-7.