**ARAŞTIRMA MAKALESİ /** *RESEARCH ARTICLE*

# Is Gestational Diabetes Mellitus Associated with the Metabolic Syndrome?

*Gestasyonel Diyabet, Metabolik Sendrom ile İlişkili midir?*

**Emel Arslan Yıldırım[1], Mehmet Bülbül[2], Kemal Özerkan[3], Osman Haldun Develioğlu[4]**

*[1]Health Sciences University, Bursa Educational Research Hospital, Bursa; [2]Department of Obstetrics and Gynecology, Adıyaman University Faculty of Medicine, Adıyaman; [3]Department of Obstetrics and Gynecology, Uludağ University Faculty of Medicine; [4]Assisted Reproductive Treatment (ART) Center, Bursa, Turkey*

## ABSTRACT

***Aim:*** *Gestational Diabetes Mellitus (GDM) accounts for 1-14% of pregnancies. Insulin resistance (IR) plays a role in pathophysiology as it is in Polycystic Ovary Syndrome (PCOS) and Metabolic Syndrome (MS). Therefore, these three clinical situations are thought to be related to each other.*

***Material and Method:*** *In this study, 27 women who were diagnosed with GDM and 30 healthy women were compared in terms of PCOS, MS and IR.*

***Results:*** *Weight and body mass index (BMI), waist and hip circumference were higher in the GDM group than in the control group (respectively 69.0±11,5 kg vs 62.0±10,3 kg, p:0,01; 27.0±4,7 kg/m$^2$ vs 23.0±3,5 kg/m$^2$, p:0,001; 82.0±8,5 cm vs 74.0±7,5 cm, p<0,001; 103.0±8,1 cm vs 98.0±8,7 cm, p:0,02). MS frequency was statistically higher in the GDM group than in the control group. The waist circumference, blood pressure, fasting blood sugar and triglyceride levels were higher than the control group. (respectively 55,6% vs 20%, p:0,006; 18,5% vs 0%, p:0,01; 29,6% vs 6,7%, p:0,02; 48,1% vs 10%, p: 0,002). HDL cholesterol levels were not statistically different between the groups (p> 0.05). When the threshold for HOMA was taken as 2.24, more insulin resistance was detected in the GDM group than in the control group (respectively 48,1% vs 20,0%, p: 0,02).*

***Conclusion:*** *As in GDM, the common problem in MS and PCOS is IR. As shown in many studies, in our study, MS was found higher in the GDM group. Therefore, metabolic syndrome should be screened in patients with GDM.*

**Key words:** *gestational diabetes; insulin resistance; metabolic syndrome; polycystic over syndrome*

## ÖZET

***Amaç:*** *Gestasyonel Diabetes Mellitus (GDM) gebeliklerin %1-14'ünü görülür. Polikistik over sendromu (PCOS) ve metabolik sendromda (MS) olduğu gibi patofizyolojisinde insülin direnci (IR) rol alır. Bundan dolayı bu üç klinik durumun birbiriyle ilişkili olduğu düşünülmektedir.*

***Materyal ve Metot:*** *Bu çalışmada GDM tanısı almış 27 kadın ve sağlıklı 30 kadın PCOS, MS ve IR açısından karşılaştırılmıştır.*

***Bulgular:*** *GDM grubunda kilo ve vücut kitle indeksi (BMI), bel ve kalça çevreleri kontrol grubundan daha yüksekti (sırasıyla 69.0±11,5 kg vs 62.0±10,3 kg, p:0,01; 27.0±4,7 kg/m$^2$ vs 23.0±3,5 kg/m$^2$, p:0,001; 82.0±8,5 cm vs 74.0±7,5 cm, p<0,001; 103.0±8,1 cm vs 98.0±8,7 cm, p:0,02). MS sıklığı GDM grubunda kontrol grubuna göre istatistiksel anlamlı olarak daha yüksekti. Bel çevresi, kan basıncı, açlık kan şekeri ve trigliserid düzeyleri yüksek olan hasta sayısı kontrol grubuna göre daha fazlaydı (sırasıyla %55,6 vs %20, p:0,006; %18,5 vs %0, p:0,01; %29,6 vs %6,7, p:0,02; %48,1 vs %10, p: 0,002). HDL kolesterol düzeyi açısından ise gruplar arasında istatistiksel olarak fark saptanmadı (p>0,05). HOMA için eşik değer 2.24 olarak alındığında GDM grubunda kontrol grubundan daha fazla insülin direnci saptandı sırasıyla (sırasıyla %48,1 vs %20 ,0, p: 0,02).*

***Sonuç:*** *GDM'de olduğu gibi MS ve PCOS'ta ortak problem IR'dır. Birçok çalışmada gösterildiği gibi bizim çalışmamızda da MS, GDM grubunda daha yüksek saptandı. Bundan dolayı GDM öyküsü olan hastalarda metabolik sendrom taranmalıdır.*

**Anahtar kelimeler:** *gestasyonel diyabet; insulin direnci; metabolik sendrom; polikistik over sendromu*

***İletişim/Contact:*** *Mehmet Bülbül, Adıyaman Üniversitesi Tıp Fakültesi, Siteler Mahallesi, Atatürk Bulvarı, No: 411, Adıyaman, Türkiye* • ***Tel:*** *0532 308 34 55* • ***E-mail:*** *mehmetbulbulmd@gmail.com* • ***Geliş/Received:*** *24.05.2018* • ***Kabul/Accepted:*** *24.05.2019*

***ORCID:*** *Emel Arslan Yıldırım, 0000-0002-6294-9559* • *Mehmet Bülbül, 0000-0001-5695-2586* • *Kemal Özerkan, 0000-0003-1460-6524* • *Osman Haldun Develioğlu, 0000-0003-2273-0701*

## Introduction

Glucose intolerence, which is the first time detected during pregnancy and currently seen in 18% of pregnancies with the increase of obesity, is called Gestational Diabetes Mellitus (GDM)[1]. The main pathogenetic mechanism of GDM is that the need for insulin increases due to decreased insulin sensitivity during pregnancy, which cannot be met by pancreatic β cells[2,3]. Patients undergoing a pregnancy complicated by GDM have an increased risk for Type 2 diabetes mellitus (Type 2 DM) later in life[4,5,]

Polycystic ovarian syndrome (PCOS) is a multi-systemic disease that can be accompanied by hyperandrogenaemia/hyperandrogenism and polycystic ovarian morphology, which is common with oligo-anovulation in women of reproductive age[6–8]. In addition to reproductive abnormalities, women with PCOS are at risk for various metabolic disorders, such as insulin resistance, Type 2 DM, obesity, hypertension, dyslipidaemia and cardiovascular diseases[9–11].

Metabolic syndrome (MS) is a disease that develops on the basis of abdominal obesity and insulin resistance (IR), including hypertension (HT), hyperglycemia and atherogenic dyslipidemia. Moreover, it is known that MS is associated with GDM and PCOS[12–14].

As the number of components of MS increases, the risk of morbidity and mortality increases. For this reason, there are many researches about the causes, results, prevention and prevention methods of this clinical complex, which is increasing in frequency both in the world and in our country. We aimed to compare the women who had complicated pregnancy with GDM with healthy women in terms of clinical, metabolic and endocrinological findings and ovarian morphology.

## Material and Method

This study was conducted prospectively in Uludag University Medical Faculty Obstetrics and Gynecology Clinic between March 2007 and September 2008. From hospital archieve, the records of 27 women (study group) who were diagnosed with GDM based on the results of the 100 g oral glucose tolerance test at 24–28 weeks of gestation of the last pregnancy and in the same period 30 women (control group) who were diagnosed healthy according to the normal 50 gram glucose screening tests were included into the study. Women with secondary hypertension, Cushing's syndrome, Addison's disease, congenital adrenal hyperplasia, and androgen-producing tumours and women who gave birth to twin pregnancy history were excluded. The study was approved by the Ethics Committee of Uludag University Medical Faculty (Approval No: 2007–6/13). Written informed consent was obtained from all the women who agreed to participate in the study.

Demographic data, physical examination findings and laboratory data of all the women were recorded. Height, weight, waist circumference and arterial blood pressure measurements were obtained. Patients were considered hypertensive if systolic blood pressure and diastolic blood pressure was over 135 mmHg and 85 mmHg respectively or existing antihypertensive medication usage.

Complete blood count, biochemical parameters, lipid profile, fasting insulin, hormone profile were studied in venous blood samples taken after a fasting period of at least 8 hours when there is no follicle above 10 mm in ultrasonography or 2–5$^{th}$ day of the menstrual cycle. All patients included in the study were evaluated with transvaginal ultrasonography (TVUSG) for the presence of PCO morphology. The diagnosis of PCOS was based on the 2003 Rotterdam criteria. International Diabetes Federation (IDF) 2005 criteria were used for the definition of MS. The creatinine and microalbumin levels of the urine samples were determined. In all urine samples, creatinine and microalbumin were studied.

The threshold value for hyperinsulinemia was 15 IU/Ml. The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) (fasting insulin (μU/ml) × fasting blood glucose/22.5) formula was used to determine insulin resistance, and the free androgen index (FAI); total testosterone (nmol/l) × 100/sex-hormone binding globulin (SHBG) (nmol/l), was used to determine abnormal androgen status. The microalbumin × 100/creatine formula was used for the spot urine test for microalbuminuria and a microalbuminuria level >30 mg/day was considered significant.

Statistics: Statistical Package for Social Sciences (SPSS, Version 13.0; SPSS Inc., Chicago, Il, USA) was used for statistical analysis. The t-test was used to measure the normal distribution, Mann-Whitney U-test was used to measure the non-normal distribution. The chi-square test was used to compare the ratios between the groups. A $p<0.05$ was considered to be statistically significant. Data were reported as mean ± (standard deviation) SD.

## Result

The demographic characteristics of the groups are presented in Table 1. The mean age, gravida and abortus numbers were significantly higher in the GDM group than the control group (35.4±6.2 vs 31.7±4.3, p: 0.01, 2.7±1.8 vs 1.9±1.2, p: 0.03; 0.7±1.0 vs 0.3±0.6, p0.03, respectively), and parity and the number of living children were similar in both groups (p>0.05). Concomitant diseases were significantly more frequent in the GDM group (44%) than the control group (3.3%) (p<0.001). (One patient with dyslipidemia, coronary artery disease, antiphospholipid syndrome, prothrombin mutation, two patients with infertility, three patients with chronic HT and four patients with hypothyroidism was accompanied by GDM.) The frequency of smoking, hirsutism, acne and oligomenorrhea were not different between the GDM group and the control group (p>0.05).

In both groups, the 50 grams of glucose screening test results were significantly higher in the GDM group (183±5.9 mg/dl) with similar gestational weeks (25.3±2.6 weeks vs 24.6±0.7 weeks for the GDM group and control group, respectively, p: 0.64), than the control group (101±4.1 mg/dl) (p<0.001). Pre-pregnancy weight and pre-pregnancy body mass index (BMI) were significantly higher in the GDM group than the control group (65.7±12.6 vs. 57.7±8.1 p: 0.01; 26.0±5.3 vs 21, respectively; 0±2.7, p<0.001). There was no significant difference between the groups in terms of weight gain during pregnancy (p: 0.16).

The mean gestational week at birth was significantly lower in the GDM group than the control group (37.8±1.7 vs 39.2±1.1, p: 0.001, respectively) (Table 1). However, there was no significant difference between the two groups in terms of newborn weight (3257±602 vs 3513±462, p: 0.77). The 1st and 5th minute APGAR scores were significantly lower in the GDM group (p: 0.01). There was no statistically significant difference between the Caesarean section rates (51.9% vs. 56.7%) and fetal gender (p>0.05).

Postpartum evaluation was performed at 107±18.1 weeks in the GDM group and at an average of 126±18.9 weeks in the control group (p=0.42) (Table 2). The mean postpartum weight, BMI, waist and hip circumference were significantly higher in the GDM group (69.0±11.5 kg vs. 62.0±10.3 kg, p: 0.01; 27.0±4.7 kg/m$^2$ vs 23.0±3.5 kg/m$^2$, p: 0.001; 82.0±8.5 cm vs 74.0±7.5 cm, p<0.001; 103.0±8.1 cm vs 98.0±8.7 cm, p: 0.02). However, height was significantly shorter in the GDM group (159±6 cm) than the control group (162±5 cm) (p: 0.01).

Mean arterial systolic and diastolic blood pressure values were significantly higher in GDM group than the control group (p<0.05) statistically. In the GDM group, mean total cholesterol, low density lipoprotein (LDL), very low density lipoprotein (VLDL) and triglyceride levels were significantly higher than the control group (209±40 vs 169±29, p<0.001; 128±35 vs 97±17, p<0.001; 29±16 vs 16±12, p: 0.004; 145±80 vs 83±61, p: 0.004). There was no statistically significant difference between the groups in terms of high density lipoprotein (HDL) cholesterol, CFH, dehydroepiandrosterone sulphate (DHEA-S), total and free testosterone levels (p>0.05).

The mean SHBG levels in the GDM group were significantly lower than the control group (31.0±0.3 vs

***Table 1.*** *Prepartum demographic data*

| | | GDM, n: 27 | Control, n: 30 | P |
|---|---|---|---|---|
| Age (Years) (mean ± SD) | | 35.4±6.2 | 31.7±4.3 | 0.01 |
| Gravida (mean ± SD) | | 2.7±1.8 | 1.9±1.2 | 0.03 |
| Parity (mean ± SD) | | 2.0±1.3 | 1.6±0.9 | 0.15 |
| Abortions (mean ± SD) | | 0.7±1.0 | 0.3±0.6 | 0.03 |
| Live (mean ± SD) | | 1.9±1.1 | 1.5±0.7 | 0.14 |
| Weight before pregnancy (kg) (mean ± SD) | | 65.7±12.6 | 57.7±8.1 | 0.01 |
| Pre-pregnancy BMI (mean ± SD) | | 26.0±5.3 | 21.0±2.7 | <0.001 |
| Weight taken during pregnancy (kg) (mean ± SD) | | 13.4±7.7 | 16.4±4.5 | 0.16 |
| Accompanying disease (n (%)) | | 12 (44.4) | 1 (3.3) | <0.001 |
| Cigarette (n (%)) | | 7 (25.9) | 7 (23.3) | 0.82 |
| Hirsutism (n (%)) | | 4 (14.8) | 3 (10) | 0.58 |
| Acne (n (%)) | | 2 (7.4) | 3 (10) | 0.73 |
| Oligo-menorrhea (n (%)) | | 3 (11.1) | 4 (13.3) | 0.80 |
| Week of pregnancy | | 37.8±1.7 | 39.2±1.1 | 0.001 |
| Birth | Apgar 1st minute | 8.3±1.6 | 9.0±0.0 | 0.01 |
| | Apgar 5th minute | 9.4±1.3 | 10.0±0.0 | 0.01 |
| | Weight | 3257±602 | 3513±462 | 0.77 |
| Birth Type | Cesarean Birth | 14 (51.9) | 17 (56.7) | 0.72 |
| | Vaginal Birth | 13 (48.1) | 13 (43.3) | |
| Baby gender | Girl | 14 (51.9) | 14 (46.7) | 0.69 |
| | Male | 13 (48.1) | 16 (53.3) | |

BMI, body mass index (kg/m$^2$), GDM, gestational diabetes mellitus

56.9±23.9, p<0.001) and the FAI was higher (2.0±1.1 vs 1.1±1.1, p:0.001). There was no statistically significant difference between the groups in terms of urine creatine, micro albumin and micro albuminuria levels (p>0.05).

According to IDF 2005 criteria, waist circumference, blood pressure, fasting blood glucos and triglyceride levels were higher in the GDM group compared to the control group (respectively 55.6% vs 20%, p: 0.006; 18.5% vs 0%, p: 0.01; 29.6% vs 6.7%, p: 0.02; 48.1% vs 10%, p: 0.002) (Table 3). There was no statistically significant difference in HDL cholesterol levels between the groups (p>0.05).

When the threshold level for hyperinsulinemia was taken as 15 IU/mL, seven (25.9%) patients in the GDM group and four (13.3%) patients in the control group had hyperinsulinemia (Table 4). This was not statistically significant (p=0.24). Similarly, there was no statistically significant difference between the groups in terms of glucose/insulin ratio (p>0.05) when the limit was taken as <4.5. The mean HOMA value was found as 3.2±3.6 in the GDM group and 2.0±2.2 in the control group. When the threshold value for HOMA was 2.24, it was found that 13 (48.1%) of the 27 patients in the GDM group and six (20.0%) of the 30 patients in the control group had insulin resistance. This difference was statistically significant (p=0.02).

The prevalence of metabolic syndrome was significantly higher in the GDM group than in the control group. There was no statistically significant difference between the two groups in terms of PCOS frequency. On the other hand, hyperandrogenism findings were found to be statistically more frequent in the GDM group than in the control group (Table 4). PCO appearance was

***Table 2.*** *Postpartum data of groups*

| | GDM, n: 27 | Control, n: 30 | p |
|---|---|---|---|
| Size (cm) | 159±6 | 162±5 | 0.01 |
| Weight (kg) | 69.0±11.5 | 62.0±10.3 | 0.01 |
| BMI (kg/m$^2$) | 27.0±4.7 | 23.0±3.5 | 0.001 |
| Waist circumference (cm) | 82.0±8.5 | 74.0±7.5 | <0.001 |
| Hip circumference (cm) | 103.0±8.1 | 98.0±8.7 | 0.02 |
| Systolic Blood Pressure (mmHg) | 111±17 | 101±10 | 0.01 |
| Diastolic Blood Pressure (mmHg) | 71±11 | 64±6 | 0.01 |
| Fasting plasma glucose (mg/dl) | 97±33 | 85±9 | 0.09 |
| Cholesterol (mg/dl) | 209±40 | 169±29 | <0.001 |
| HDL (mg/dl) | 52±11 | 59±23 | 0.12 |
| LDL (mg/dl) | 128±35 | 97±19 | <0.001 |
| VLDL (mg/dl) | 29±16 | 16±12 | 0.004 |
| Triglycerides (mg/dl) | 145±80 | 83±61 | 0.004 |
| DHEA-S (µg/dl) | 172±66 | 162±73 | 0.58 |
| Total Testosterone (nmol/l) | 0.55±0.22 | 0.46±0.22 | 0.14 |
| Free Testosterone (nmol/l) | 1.47±0.82 | 1.08±0.64 | 0.39 |
| SHBG (nmol/lt) | 31.0±0.3 | 56.9±23.9 | <0.001 |
| FAI | 2.0±1.1 | 1.1±1.1 | 0.001 |
| Urine Creatine (mg/dl) | 93±53 | 113±58 | 0.19 |
| Microalbumin (µg/ml) | 13.7±14.5 | 16.1±15.3 | 0.15 |
| Microalbuminuria (mg/gün) | 15.5±14 | 14.1±8.9 | 0.84 |

GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; FAI, free androgen index; DHEA-S, dehydroepiandrosterone sulfate; SHBG, sex hormone-binding globulin.

***Table 3.*** *Criteria for Metabolic Syndrome in Groups (IDF 2005)*

| | GDM, n: 27 | Control, n: 30 | p |
|---|---|---|---|
| Waist circumference (n (%)) | 15 (55.6) | 6 (20) | 0.006 |
| Blood pressure (n (%)) | 5 (18.5) | 0 (0) | 0.01 |
| HDL (n (%)) | 14 (51.9) | 12 (40) | 0.37 |
| Fasting plasma glucose (n (%)) | 8 (29.6) | 2 (6.7) | 0.02 |
| Triglycerides (n (%)) | 13 (48.1) | 3 (10) | 0.002 |

GDM, gestational diabetes mellitus; Waist circumference >80 cm;
Blood pressure ≥130/85 mmHg; HDL (low density lipoprotein) <50 mg/dl;
fasting plasma glucose ≥100 mg/dl; triglyceride ≥150 mg/dl

***Table 4.*** *Hyperandrogenism, PCOS, Metabolic Syndrome, fasting insulin, insulin/glucose ratio and HOMA frequency in groups*

| | GDM, n: 27 | Control, n: 30 | p |
|---|---|---|---|
| Fasting Insulin >15 IU/mL (n (%)) | 7 (25.9) | 4 (13.8) | 0.21 |
| Glucose/Insulin ≤4.5 (n (%)) | 4 (14.8) | 4 (13.8) | 0.60 |
| HOMA ≥2.24 (n (%)) | 13 (48.1) | 6 (20.0) | **0.02** |
| PCOS (n (%)) | 3 (11.1) | 3 (10) | 0.89 |
| Metabolic Syndrome (n (%)) | 10 (37) | 1 (3.3) | **0.01** |
| Hyperandrogenism (n (%)) | 18 (66.7) | 8 (26.7) | **0.003** |

GDM, gestational diabetes mellitus; HOMA, homeostasis model evaluation;
PCOS, polycystic ovary syndrome.

higher in GDM (11.1%) and control (10.0%) groups (p=0.89). According to t PCO appearance in ovaries, GDM (11.1%)) and control (10.0%) groups were similar (p=0.89).

## Discussion

The prevalence of metabolic syndrome varies between 27% and 56% [14,16]. In our study, although the prevalence of metabolic syndrome was found to be 19.2%, the prevalence of metabolic syndrome was 37% in the GDM group and 3.3% in the control group when self-evaluated. Diabetes mellitus and impaired FBG 17.5%, HT 8.7%, hypertriglyceridemia 28% HDL decreased 46% and abdominal obesity 37% was found as metabolic syndrome components. These rates were lower than other studies in the literature. The history of DM in the families of GDM pregnant women is seen in 26.9% and 45% [17–19]. However, in some studies, association with obesity was more frequent[20]. In our study, family history of DM, chronic HT and coronary artery disease was higher in the GDM group.

Obesity is the best predictor of metabolic syndrome. In addition, fat distribution is an important determinant regardless of body weight[21–25]. According to the IDF 2005 criteria, if the waist circumference is over 80 cm, this is the main criterion for the diagnosis of metabolic syndrome. As BMI increases, the risk of type 2 DM and glucose intolerance is increased up to 40 times[26–27]. When the body structures of the groups were compared, the mean weight, BMI and waist/hip circumference ratio were higher in the GDM group both before and after the delivery. Similarly, 48.1% of the GDM group and 10% of the control group had a BMI above 27 kg/m2. Waist circumference was over 80 cm in 55.5% of the GDM group and in 20% of the control group.

Insulin has important functions on normal vascular functions. With vasodilator effect, it increases blood flow and volume in skeletal muscles. In addition to its metabolic effects, it is one of the important mediators of endothelial function. Therefore, all of these effects are impaired and the risk of cardiovascular disease increases with IR[28–30]. It is also known to have IR in patients with GDM[2]. Because of that, patients with GDM have higher cholesterol, triglyceride, LDL and systolic blood pressure levels in their later lifes. This situation causes cardiovascular risk increase. The risk of developing type 2 diabetes, metabolic syndrome and cardiovascular disease is seven times higher in these patients[5,31–35]. In our study, mean arterial systolic and diastolic blood pressure values and total cholesterol, LDL, VLDL and triglyceride levels were higher in GDM group compared to the control group. However, no difference was found between the groups in terms of HDL cholesterol level. In addition, FBG was found to be 97±33 in the GDM group and 85±9 mg/dL in the control group and the difference was found to be close to the statistical significance. In both groups, the frequency of hyperinsulinemia, glucose/insulin ratios were not different, but when evaluated with HOMA, IR frequency was significantly higher in the GDM group (48.1%) than the control group (20.7%).

Perinatal mortality, cesarean rates and macrosomia risk are high in pregnant women with GDM and other neonatal morbidities such as birth trauma, hypoglycemia, hypocalcemia, polycythemia and hyperbilirubinemia are more common[36]. In our study, the mean gestational week at birth was significantly lower in the GDM group than in the control group, but there was no significant difference between the two groups in terms of new-born weight. The 1st and 5th minute APGAR scores were significantly lower in the GDM group. While cesarean delivery rate was 51.9% in GDM group, this rate was found to be 56.7% in the control group. There was no statistically significant difference between groups (p=0.72). There was no significant difference between the groups in terms of Cesarean indications (p=0.6).

Although some studies have shown otherwise[37], the incidence of GDM, pregnancy-related hypertension and neonatal hypoglycemia is higher in women with PCOS diagnosed[38–40]. Glucose, lipid and androgen metabolism disorders are known to be important risk factors in the development of GDM in women with PCOS[41]. Because of this close relationship, PCO appearance in patients with GDM is thought to be between 41 and 52% ratio[42]. In our study, the prevalence of PCOS in the GDM group was 11.1%, unlike the literature.

It is known that the fat storage pattern in obese individuals is influenced differently from androgenic and estrogenic sex hormones[43]. As in PCOS, women with high waist/hip ratio have high androgen levels and low SHBG levels[23]. In this study, no statistically significant difference was found between the groups in terms of hirsutism, cycle irregularities and PCO

appearance in ovaries which are typical findings of PCOS. On the other hand, the laboratory findings of hyperandrogenism were significantly more frequent in patients who had pregnancy complicated with GDM. In the GDM group, SHBG levels were found to be lower and FAI levels were higher, while DHEA-S, total and free testosterone levels were not significantly different.

The small study groups, the fact that the groups were not included into the study before pregnancy, the lack of long-term follow-up data of the women and non-homogeneous age distribution of both groups were the limitations of this study. However, it is important that PCOS, MS and GDM are evaluated together with all parameters.

As a conclusion, in our study, the prevalence of metabolic syndrome was 37% in the GDM group and 3.3% in the control group. Although no statistically significant difference was found between the groups in terms of PCOS, hyperandrogenism laboratory findings were observed more frequently in GDM group. However, there was able to be no difference in the prevalence of PCOS due to the fact that the patients in the GDM group were older and the PCO appearance decreased with the advanced age. Metabolic syndrome is becoming an important public health problem. Sedentary life and dietary habits changes in our country increase the frequency of metabolic syndrome. Although the data of our study is not sufficient to determine the prevalence of PCOS and metabolic syndrome in patients with GDM, it is thought that the rate of metabolic syndrome may be high in patients with a history of GDM in our society. While the importance of lifestyle changes, diet and exercise cannot be denied to reduce the incidence of metabolic syndrome, patients with different clinical reflections of the metabolic syndrome such as PCOS and GDM should be informed of the risk of metabolic syndrome and evaluated at regular intervals.

*Acknowledgements*

We would like to thank Dr. Mehmet Can Nacar for English editing.

## References

1. National Institute for Health and Welfare Ofcial Statistics of Finland; Health; 2014 [accessed 24 02 2018].
2. Damm P, Kuhl C, Bertelsen A, Molsted-Pedersen L. Predictive factors for the development of diabetes in women with previous gestational diabetes mellitus. Am J Obstet Gynecol 1992;167:607–16.
3. Powe CE, Allard C, Battista MC Doyon M, Bouchard L, Ecker JL et al. Heterogeneous contribution of insulin sensitivity and secretion defects to gestational diabetes mellitus. Diabetes Care 2016;39(6):1052–55.
4. Ryan EA, Imes S, Liu D, McManus R, Finegood DT, Polonsky KS et al. Defects in insulin secretion and action in women with a history of gestational diabetes. Diabetes 1995;44:506–12.
5. Huvinen E, Eriksson JG, Koivusalo SB, Grotenfelt N, Tiitinen A, Stach-Lempinen B et al. Heterogeneity of gestational diabetes (GDM) and long-term risk of diabetes and metabolic syndrome: findings from the RADIEL study follow-up. Acta Diabetol 2018;55(5):493–501.
6. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev 2012;33(6):981–1030.
7. Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocr Rev 2016;37(5):467–520.
8. Laven JS, Imani B, Eijkemans MJ, Fauser BC. New approach to polycystic ovary syndrome and other forms of anovulatory infertility. Obstet Gynecol Surv 2002;57:755–767.
9. Ehrmann DA. Polycystic ovary syndrome. N Engl J Med 2005;352(12):1223–1236.
10. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet 2007;370(9588):685–697.
11. Palomba S, Falbo A, Daolio J, Battaglia FA, LA Sala GB. Pregnancy complications in infertile patients with polycystic ovary syndrome: updated evidences. Minerva Ginecol 2018;Apr 11.
12. Homburg R. The management of infertility associated with polycystic ovary syndrome. Reprod Biol Endocrinol 2003;1:109.
13. Olah KS. The modern management of hirsutism. Rev in Gynecol Practice 2004;4:211–20.
14. Phipps WR. Polycystic ovary syndrome an ovulation induction. Obstet Gynecol Clin North Am 2001;28:165–82.
15. Speroff L, Fritz MA. Clinical Gynecologic Endocrinology and Infertility 7th ed. Lippincott Williams and Wilkins, Philadelphia 2005.
16. Homburg R. Management of infertility and prevention of ovarian hyperstimulation in women with polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol 2004;18:773–88.
17. Carmina E, Koyama T, Chang L, Stanczyk FZ, Lobo RA. Do- es ethnicity influence the prevalence of adrenal hyperandrogenism and insulin resistance in polycystic ovary syndrome? Am J Obstet Gynecol 1992;167:1807–12.
18. Zeev S and Ariel Weissman Kempers RD. Fertility and Reproductive Medicine 1998:263–292.

19. Lamain-de Ruiter M, Kwee A, Naaktgeboren CA, de Groot I, Evers IM, Groenendaal F et al. External validation of prognostic models to predict risk of gestational diabetes mellitus in one Dutch cohort: prospective multicentre cohort study. BMJ 2016;354: i4338.
20. Williamson K, Gunn AJ, Johnson N, Milsom SR. The im- pact of ethnicity on the presentation of polycystic ovarian syndrome. Aust N Z J Obstet Gynaecol 2001;41:202–6.
21. Paradisi G, Steinberg HO, Hempfling A, Cronin J, Hook G, Shepard MK et al. Polycystic ovary syndrome is associated with endothelial dysfunction. Circulation 2001;103:1410–15.
22. Husueh V. A, Lyon C. J, Quinones M. J. Insulin resistance and endothelium Am JMed 2004;117:109–17.
23. Ek I, Arner P, Rydén M, Holm C, Thörne A, Hoffstedt J et al. A unique defect in the regulation of visceral fat cell lipolysis in the polycystic ovary syndrome as an early link to insulin resistance. Diabetes 2002;51(2):484–92.
24. Suzuki M, Takamisawa I, Suzuki K, Hiuge A, Horio T, Yoshimasa Y et al. Close assosiation of endothelial dysfunction with insulin resistance and carotid wall thickening in hypertension. Am J Hypertens 2004;17(3):228–32.
25. Hernandez-Pampaloni M, Quinones M, Chon Y. Endothelial dysfunction is associated with subclinical atherosclerosis in insulin resistant patients. J Nucl Med 2002;80:140–51.
26. Julie L. Sharples. Polycystic ovary syndrome and the metabolic syndrome. Clin Diabetes 2003;21:154–60.
27. Kiddy DS, Sharp PS, White DM, Scanlon MF, Mason HD, Bray CS et al. Differences in clinical and endocrine features between obese and nonobese subjects with polycystic ovary syndrome: An analysis of 263 consecutive cases. Clin Endocrinol 1990;32(2):213–20.
28. Beharier O, Shoham-Vardi I, Pariente G, Sergienko R, Kessous R, Baumfeld Y et al. Gestational diabetes mellitus is a signifcant risk factor for long-term maternal renal disease. J Clin Endocrinol Metab 2015;100(4):1412–16.
29. Hardiman P, Pillay OS, Atiomo W. Polycystic ovary syndrome and endometrial carsinoma. Lancet 2003;361:1810–12.
30. Onat A, Senocak M. Obesity in Turkish adults: prevalence, validity as a coronary risk factor and interrelation with other risk factors. Int J Ang 1995;4:94–8.
31. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009;373(9677):1773–79.
32. Puhkala J, Kinnunen TI, Vasankari T, Kukkonen-Harjula K, Raitanen J, Luoto R. Prevalence of metabolic syndrome one year after delivery in Finnish women at increased risk for gestational diabetes mellitus during pregnancy. J Pregnancy 2013:139049.
33. Hakkarainen H, Huopio H, Cederberg H, Paakkonen M, Voutilainen R, Heinonen S. The risk of metabolic syndrome in women with previous GDM in a long-term follow-up. Gynecol Endocrinol 2016;32(11):920–925.
34. Lauenborg J, Mathiesen E, Hansen T, Glümer C, Jørgensen T, Borch-Johnsen K et al. The prevalence of the metabolic syndrome in a danish population of women with previous gestational diabetes mellitus is three-fold higher than in the general population. J Clin Endocrinol Metab 2005;90(7):4004–10.
35. McKenzie-Sampson S, Paradis G, Healy-Proftos J, St-Pierre F, Auger N. Gestational diabetes and risk of cardiovascular disease up to 25 years after pregnancy: a retrospective cohort study. Acta Diabetol 2018;55(4):315–322.
36. Yildirim B and Kaleli B. Relation of intra-abdominal fat distribution to metabolic disorders in lean women with polycystic ovary syndrome. Fertil Steril 2003;79:1358–64.
37. Yılmaz Ö, Pala HG, Artunç Ülkümen B. Comparison of Insulin Sensitivity Levels in Women with PCOS and Women with Regular Menses. Kafkas J Med Sci 2017;7(2):102–106. doi:10.5505/kjms.2017.24582.
38. Lo JC, Feigenbaum SL, Escobar GJ, Yang J, Crites YM, Ferrara A. Increased prevalence of gestational diabetes mellitus among women with diagnosed polycystic ovary syndrome: a population-based study. Diabetes Care 2006;29(8):1915–17.
39. Joham AE, Ranasinha S, Zoungas S, Moran L, Teede HJ. Gestational diabetes and type 2 diabetes in reproductive-aged women with polycystic ovary syndrome. J Clin Endocrinol Metab 2014;99(3): E447–E452.
40. Sawada M, Masuyama H, Hayata K, Kamada Y, Nakamura K, Hiramatsu Y. Pregnancy complications and glucose intolerance in women with polycystic ovary syndrome. Endocr J 2015;62(11):1017–23.
41. Li G, Huang W, Zhang L, Tian Z, Zheng W, Wang T et al. A prospective cohort study of early-pregnancy risk factors for gestational diabetes in polycystic ovarian syndrome. Diabetes Metab Res Rev 2018:e3003.
42. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes 1989;38:1165–74.
43. Catalano PM, Bernstein IM, Wolfe R, Srikanta S, Tyzbir E, Sims EA. Subclinical abnormalities of glucose metabolism in subjects with previous gestational diabetes. Am J Obstet Gynecol 1986;155:1255–6.