

Relationship of Epidemiologic Features and Risk Factors in Impaired Glucose Tolerance and Gestational Diabetes Mellitus

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Abstract

Introduction: To examine the relation of weight and parity with glucose intolerance during pregnancy.

Methods: This study was a prospective cohort survey of 365 women at 24-38 weeks of gestation who were attending the antenatal clinic in Istanbul Bakırköy region, between 1st January 2009 and 31st December 2009. Risk factors were determined using a questionnaire, and two steps oral glucose tolerance test (OGTT) were routinely performed. The statistical analysis was performed using Kruskal Wallis test, Mann-Whitney U test, Chi-square test and Oneway Anova test, Tukey HSD test. $P < 0.05$ value was statistically significant.

Results: Pregestational weight, gestational weight gain and parity of the women with GDM were significantly higher, and educational status was significantly lower than other groups ($p < 0.01$).

Discussion and Conclusion: Pregestational obese women and women who had higher gestational weight gain higher risk of GDM. Patient education is important for preventive medicine practice.

Keywords: Gestational diabetes mellitus; impaired glucose tolerance; risk factors.

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemia, which arises from an insufficient release of insulin and/or its inadequate effect due to various etiological reasons [1]. Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance that occurs for the first time or is noticed during pregnancy [2–5]. GDM is the most common metabolic disorder in pregnancy and is observed in 3%–7% of all pregnancies [4]. However, this frequency varies according to race, ethnic group, family history, age, number of births, obesity and diagnosis. It is one of the leading causes that significantly increase morbidity and perinatal mortality of the mother and the fetus during pregnancy.

Obesity, the presence of GDM in previous pregnancies, given birth to newborns weighing more than 4000 gr, family history of diabetes and polycystic ovary syndrome (PCOS) are risk factors for the development of GDM [6]. Insulin resistance is frequently seen in obese individuals [7].

Most of the GDM risk factors (such as race, family history, maternal age) are irreversible factors. The severity of GDM is directly related to weight gain during pregnancy. Weight gain during pregnancy can be modified by nutrition education, diet changes and exercise. Since it is associated with poor perinatal outcomes in patients with GDM receiving drug therapy, approaches to control weight gain in patients may be promising [8].

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Materials and Methods

This study was planned as a prospective, case-controlled study. Approval of the Ethics committee of Istanbul Bakirkoy Sadi Konuk Training and Research Hospital was obtained. Between January 1, 2009 and December 31, 2009, 365 pregnant women who applied to the Gynecology and Obstetrics Clinic of Sadi Konuk Training and Research Hospital and volunteered to participate were included in this study. The defined risk factors for gestational diabetes mellitus (GDM) are smoking, lack of exercise, parity, age of the pregnant woman, previous GDM history, first degree relatives having DM, history of giving birth to a large baby weighing more than 4000 grams, having a history of fetal loss, pre-pregnancy body mass index exceeding 26 kg/m² and hypertension. These risk factors were questioned in the whole case group.

In line with the main goal of this study, weight gain during pregnancy was questioned. Pregnant women with Type I or Type II DM, multiple pregnancies, established the diagnosis of endocrinopathy, kidney and liver disease, and pregnant women using drugs that could affect insulin secretion or sensitivity was not included in the study group.

Pregnant women at their 24-28 gestational weeks were admitted to our pregnancy polyclinic for GDM screening, and 50 g oral glucose loading test was performed. A 100 g Oral Glucose Tolerance Test (OGTT) was applied one week later to the patients whose glycemic levels in venous serum ranged between 130-195 mg/dl after 50 g oral glucose loading test. The threshold values in OGTT were 95 mg/dl (5.3 mmol/L) for serum fasting glucose, 180 mg/dl (5.3 mmol/L) at the first, 155 mg/dl (8.6 mmol/L) at the second, 140 mg/dl (7.8 mmol/L) at the third hours which were diagnostic criteria of Carpenter and Coustan^[9], as suggested by ADA in 2003^[9]. Two glycemic values exceeding threshold values or any glycemic value exceeding 200 mg/dL (11.1 mmol/L) established the diagnosis of gestational diabetes.

If only a single glucose value exceeded the threshold value, then the repetition of the test at 32-34 weeks is recommended. If only fasting blood glucose was at its maximum level in OGTT, namely over 126 mg/dl, and then fasting blood sugar was measured again on another day. If the result was still higher than 126 mg/dl, then the diagnosis of GDM was made.^[11] Although there is no clear definition in the literature for patients with glucose levels exceeding a single threshold value of 100 g in OGTT, this condition was evaluated as impaired glucose tolerance.

Plasma glucose levels were measured in the Central Laboratory of Bakirkoy Sadi Konuk Training and Research Hospital using a glucose oxidase method and an automatic de-

vice. (Hitachi model 917: Inter-sample exchange rates (CV) at 93.33 mg/dl and 238.6 mg/dl average concentrations of 0.90% and 0.77%, respectively). In-sample exchange rates (CV) are 98.9 mg/dl and 253,4, respectively. Average concentrations were 1.62% and 1.70%, respectively).

In addition, weight gain was recorded by asking pregnant women who applied for 50 g OGTT test about their pre-pregnancy weights, and weights at admission to record weight gain. Their Body Mass Indexes (BMIs) were calculated by dividing their pre-pregnancy weight (kg) by the square of their height (mt). Pre-pregnancy BMIs were evaluated as recommended by the WHO Committee of Experts in 1995 as follows^[12]. (<19.8 kg/m² = Thin, 19.8-26 kg/m² = Normal, 26-30 kg/m² = Overweight, >30 kg/m² = Obese)

Arterial blood pressures were measured from the right arms of the pregnant with a mercury sphygmomanometer, at least 15 minutes after resting. Pregnant women with two positive values in 100 gr OGTT were referred to the Internal Medicine Endocrinology Outpatient Clinic of Sadi Konuk Training and Research Hospital. Their appropriate dietary therapy and/or insulin treatment were initiated, and they were followed up by both outpatient clinics.

For statistical analyses, NCSS 2007 & PASS 2008 Statistical Software (Utah, USA) program was used. One-way Anova test and Tukey HSD test were used for the comparison of the quantitative data showing normal distribution among the groups. Kruskal Wallis test and Mann-Whitney U test were used for the comparison of non-normal parameters between groups. The chi-square test was used to compare qualitative data. The results were evaluated within a 95% confidence interval and a significance level of p<0.05.

Results

The demographic characteristics of the cases are shown in Table 1.

The distribution of the risk factors of the cases is shown in Table 2 and Figure 1.

The distribution of weight, height and BMI levels of the

Table 1. Distribution of descriptive characteristics

	Min-Max	Mean±SD
Age	17-43	27.78±4.68
Gravida	1-7	2.42±1.48 (2)
Parity	0-6	1.10±1.26 (1)
Abortion	0-2	0.24±0.49 (0)
Curettage	0-2	0.08±0.32 (0)
Gestational weeks	23-38	28.43±2.82
Years of education	0-16	6.30±3.05 (5)

Table 2. Distribution of risk factors

	n	%
Smoking status		
Yes	41	11.2
No	324	88.8
Exercising		
Yes	115	31.5
Hayır	250	68,5
Familial diabetes		
Yes	180	49.3
No	185	50.7
Diabetes in previous pregnancy		
Yes	5	1.4
No	360	98.6
Hypertension in a previous pregnancy		
Yes	35	9.6
No	330	90.4
Fetal death (IUMF)		
Yes	5	1.4
No	360	98.6
LGA infant		
Yes	20	5.5
No	345	94.5

LGA: large for gestational age; IUMF: intrauterine fetal death.

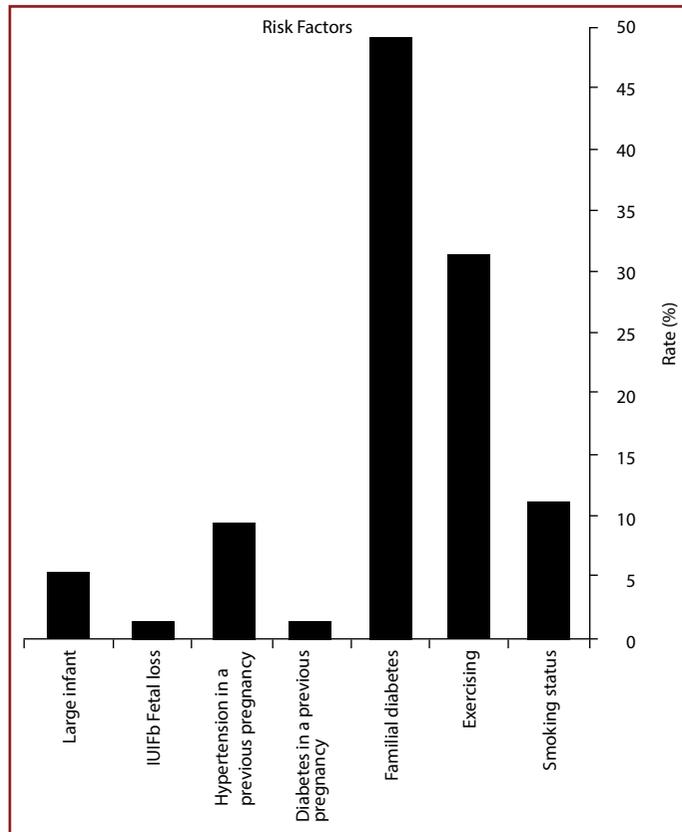


Figure 1. Distribution of risk factors.

cases before and after pregnancy is shown in Table 3 and Figure 2.

Normal glucose tolerance (NGT) was observed in 59.5% of the cases; 24.9% had impaired glucose tolerance (IGT), and gestational diabetes was seen in 13.2% of the cases. (Table 4, Fig. 3)

A statistically significant difference was found between the mean ages of the patients according to glucose tolerance types ($p < 0.01$). The mean ages of the patients in the GDM group were significantly higher when compared with the NGT and IGT groups ($p = 0.001$; $p < 0.01$). There was no significant difference between the mean ages of NGT, and IGT groups ($p > 0.05$).

A statistically significant difference was found between the number of pregnancies of the cases according to glucose tolerance types ($p < 0.05$). The gravida numbers of the GDM group were significantly higher than the NGT group ($p = 0.006$; $p < 0.01$). There was no significant difference between the gravida numbers of the patients according to

Table 3. Distribution of weight, height, and BMI levels before and after pregnancy

	Min-Max	Mean±SD
Pre-pregnancy weight	44-90	62.15±10.10
Post-pregnancy weight	53-104	72.55±10.64
Weight gain during pregnancy	4-24	10.41±4.11
Height	150-175	159.62±5.23
Pre-pregnancy BMI	18-36.9	24.41±3.96
Post-pregnancy BMI	21.8-40.3	28.56±4.11
BMI Difference	1.5-9.0	4.15±1.69

	n	%
Pre-pregnancy BMI		
Low weight	40	11.1
Normal weight	221	61.4
Overweight	99	27.5
Post-pregnancy BMI		
Normal weight	101	28.1
Overweight	259	71.9

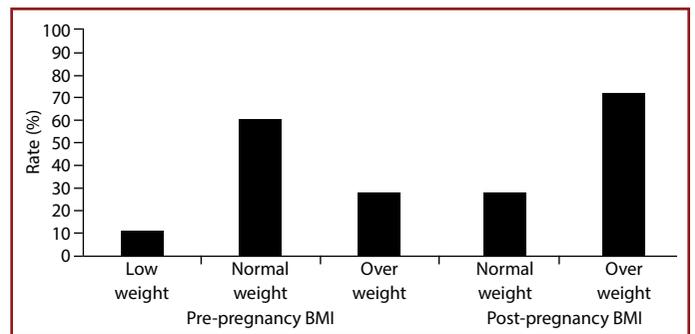


Figure 2. Distribution of pre-, and post-pregnancy BMI levels.

Table 4. Distribution of glucose tolerance types

	n	%
Normal Glucose Tolerance		
Yes	217	59.5
No	148	40.5
Impaired Glucose Tolerance		
Yes	91	24.9
No	274	75.1
Gestational Diabetes		
Yes	48	13.2
No	317	86.8

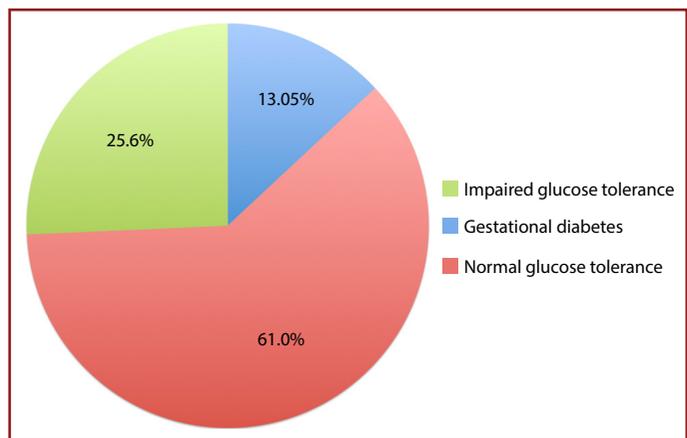


Figure 3. Distribution according to glucose tolerance types.

other glucose tolerance types ($p > 0.05$).

There was a statistically significant difference between parity numbers of the cases according to glucose tolerance types ($p < 0.01$). The parity numbers of the GDM group were significantly higher than the NGT and IGT groups ($p = 0.001$; 0.025 ; $p < 0.01$; $p < 0.05$). There was no significant difference between NGT and IGT groups as for parity numbers ($p > 0.05$).

There was no significant difference between the number of miscarriages and curettages according to glucose tolerance types ($p > 0.05$).

There was a statistically significant difference between the years of education according to the types of glucose tolerance ($p < 0.01$). The duration of education of the GDM group was significantly shorter than the NGT and IGT groups ($p = 0.001$; 0.008 ; $p < 0.01$). There was no significant difference between NGT and IGT groups for years of education ($p > 0.05$). (Table 5)

There was no significant difference between the number of abortions and curettages according to glucose tolerance types ($p > 0.05$). There was a statistically significant difference between the years of education according to the types of glucose tolerance ($p < 0.01$). The duration of education of the GDM group was significantly lower than the NGT and IGT groups ($p = 0.001$; 0.008 ; $p < 0.01$). There was no significant difference between the education periods of NGT and IGT groups ($p > 0.05$). (Table 5)

There was a significant difference between the rates of smoking according to the types of glucose tolerance ($p < 0.05$). Cigarette smoking rates were significantly lower in the IGT group than in the other groups. There was no significant difference between smoking rates of NGT and GDM groups ($p > 0.05$).

There was a significant difference between exercise rates according to glucose tolerance types ($p < 0.01$). Exercise rates of cases in the IGT group were significantly lower than the other groups. There was no significant difference between the exercise rates of NGT and GDM groups ($p > 0.05$).

There was no significant difference between the prevalence of diabetes in the family according to glucose tolerance types ($p > 0.05$).

A significant difference was found between the incidence of diabetes in the previous pregnancies according to the types of glucose tolerance ($p < 0.01$). While 10.2% of the GDM group had diabetes in their previous pregnancies; none of the cases in the NGT and IGT groups had diabetes in their previous pregnancies

Table 5. Evaluation of descriptive features according to glucose tolerance types

	NGT Mean±SD	IGT Mean±SD	GDM Mean±SD	P
+Age (yrs)	27.48±4.48	27.25±4.17	30.06±5.77	0.001**
++Gravida	2.25±1.26 (2)	2.60±1.90 (2)	2.88±1.46 (2)	0.032*
++Parity	0.94±1.05 (1)	1.19±1.54 (1)	1.67±1.43 (1)	0.006**
++Abortion	0.24±0.49 (0)	0.25±0.53 (0)	0.20±0.40 (0)	0.970
++Curettage	0.08±0.28 (0)	0.15±0.47 (0)	0.00±0.00 (0)	0.070
+Years of education	6.66±2.82 (5)	6.00±2.75 (5)	5.20±4.15 (5)	0.001**

+ One-way ANOVA test; ++ Kruskal Wallis test; * $p < 0.05$; ** $p < 0.01$.

There was a significant difference in the rate of hypertension in the previous pregnancies according to the types of glucose tolerance ($p < 0.01$). The incidence of hypertension in the previous pregnancies of the NGT group was significantly lower than the other groups. There was no significant difference between the rates of hypertension in the previous pregnancies of the cases in the IGT and GDM groups ($p > 0.05$).

There was no significant difference between the incidence of IUMF according to glucose tolerance types ($p > 0.05$). There was a significant difference in the incidence of large babies in the previous pregnancies according to the types of glucose tolerance ($p < 0.05$). In the NGT group, the incidence of infants large for their gestational age (LGA) in previous pregnancies was significantly lower than in the other groups. There was no significant difference between the incidence rates of LGAs in the previous pregnancies of the cases in the IGT and GDM groups ($p > 0.05$). (Table 6)

There was a significant difference between pre- and post-pregnancy weights of the patients according to glucose tolerance types ($p < 0.01$). The weights of the pregnant in the GDM group were significantly higher than the NGT and IGT groups. (Table 7)

There was a significant difference between BMI levels of the cases before and after pregnancy, according to glucose tolerance types ($p < 0.01$). The GDM, NGT and IGT groups were all significantly different from each other. (Table 8)

A statistically significant difference was found between the

weight differences of the patients according to glucose tolerance types ($p < 0.01$). The weight difference in the GDM group was significantly higher than the NGT and IGT groups ($p = 0.001$; $p = 0.008$). A significant difference was not observed between NGT and IGT groups ($p > 0.05$). (Table 9, Fig. 4)

There was a statistically significant difference between BMI differences of patients according to glucose tolerance types ($p < 0.01$). The BMI difference in the NGT group was significantly lower than the IGT and GDM groups ($p = 0.013$; $p = 0.003$). A significant difference was not seen between GDM and IGT groups ($p > 0.05$).

There was a statistically significant difference between the groups according to BMI classification before pregnancy ($p < 0.01$). The rate of overweightness before pregnancy was higher in the GDM group. However, the rate of normal

Table 6. Evaluation of risk factors according to glucose tolerance types

	NGT n (%)	IGT n (%)	GDM n (%)	p
Smoking	32 (14.3)	4 (4.3)	5 (10.2)	0.038
Exercise	82 (36.6)	10 (10.9)	23 (46.9)	0.001
Familial diabetes	111 (49.6)	39 (42.4)	30 (61.2)	0.103
In previous pregnancy				
Diabetes	0 (0)	0 (0)	5 (10.2)	0.001
Hypertension	12 (5.4)	14 (15.2)	9 (18.4)	0.002
IUMF	5 (2.2)	0 (0)	0 (0)	0.203
LGA infant	6 (2.7)	9 (9.8)	5 (10.2)	0.012

Chi-square test; * $p < 0.05$; ** $p < 0.01$.

Table 7. Evaluation of pre-, and post-pregnancy weights, and BMI levels according to glucose tolerance types

	NGT Mean±SD	IGT Mean±SD	GDM Mean±SD	p
Weight				
Pre-pregnancy	61.41±9.7	61.16±9.71	67.24±10.85	0.001**
Post-pregnancy	71.38±10.32	71.49±8.34	79.75±12.86	0.001**
BMI				
Pre-pregnancy	23.75±3.34	24.85±4.38	26.61±4.83	0.001**
Post-pregnancy	27.61±3.92	29.61±3.92	31.59±5.44	0.001**

One-way ANOVA test; ** $p < 0.01$.

Table 8. Evaluation of pre-, and post-pregnancy weights, and BMI levels according to glucose tolerance types

	NGT Mean±SD	IGT Mean±SD	GDM Mean±SD	P
Weight differences	9.98±3.94	10.33±3.62	12.51±4.98	0.001**
BMI differences	3.85±1.51	4.44±1.77	4.97±1.96	0.001**

One-way ANOVA test; ** $p < 0.01$.

Table 9. Evaluation of BMI classifications according to groups

	NGT n (%)	IGT n (%)	GDM n (%)	p
Pre-pregnancy BMI				
Low Weight	30 (13.4)	5 (5.7)	5 (10.2)	0.001**
Normal Weight	141 (62.9)	64 (73.6)	16 (32.7)	
Overweight	53 (23.7)	18 (20.7)	28 (57.1)	
Post-pregnancy BMI				
Normal Weight	76 (33.9)	20 (23.0)	5 (10.2)	0.002**
Overweight	148 (66.1)	67 (77.0)	44 (89.8)	

Chi-square test was used; **p<0.01.

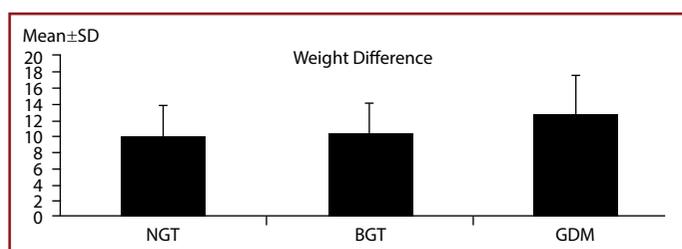


Figure 4. Distribution of weight differences.

weight was higher in the IGT group.

There was a statistically significant difference between the groups according to BMI classification after pregnancy (p<0.01). The rate of overweightness after pregnancy was higher in the GDM group when compared with NGT and IGT groups.

Discussion

Gestational diabetes mellitus (GDM) is one of the serious obstetric problems that affect the mother and the baby during pregnancy. When the participants were grouped according to glucose tolerance rates, normal glucose tolerance was observed in 59.5%, impaired glucose tolerance in 24.9%, and gestational diabetes in 13.2% of the cases.

GDM is the most common metabolic disorder in pregnancy and is observed in 3%-7% of all pregnancies [4]. There are no large series of studies on this subject in our country. In a study of 1000 pregnant women published in 1996 by Yalcin HR et al. [13] from Ankara, the frequency of GDM was found to be 6.6%. In another study published in Trabzon, including 807 pregnant women, the prevalence of GDM was found to be 1.23% [14]. In both studies, 50 g glucose screening test and 100 g OGTT were applied. In the study conducted in Ankara, the threshold value for 50g OGTT was taken as 130mg/dl and the threshold value of 140mg/dl was cited in the report from Trabzon [13, 14].

The difference between the findings can be attributed to

the choice of threshold values and given that they were determined in different geographical regions. In our study group, according to the recommendations of ADA's Committee of Experts in 2003, when the threshold values defined by Carpenter and Coustan [9] were used, the incidence of GDM was determined as 13.2%. The incidence of GDM varies with race, ethnic group, family history, age, number of births, obesity and diagnostic criteria used. Since our hospital serves Bakırköy and its surroundings, this value can be considered as a value belonging to the population in Bakırköy and its environs.

While investigating a characteristic feature that can be modified with local environmental conditions, demographic characteristics, gene pool, and socio-cultural characteristics, it is necessary to conduct studies in larger series. Although given that GDM is below 5% in many populations, which suggests that screening is unnecessary, screening seems to be worthwhile when the increase in the population in Bakırköy and its environs is considered [15].

In this case, screening, diagnosis and treatment of GDM are a public health problem. Therefore, many opinions have been suggested in GDM screening. Naylor et al. [16] reported that the incidence of GDM is less than 2% of the pregnant women without any risk factors. In this case, it is important to question the risk factors. In a study performed in Kayseri, Cihan et al. [17] found the incidence of GDM, according to Carpenter and Coustan criteria as 11.4%.

We found that pregnant women with GDM were relatively older, and the rates of gravida, parity, GDM, and hypertension in previous pregnancy were higher. There was no significant difference between the groups concerning the incidence of abortion and curettage. In the study of Naheed et al., it was reported that the most common risk factor associated with GDM was the presence of diabetes in the first degree relatives of the patients who underwent screening tests according to ADA criteria after risk factor screening

(Naheed et al. 2008). Risk factors that are detected less frequently were reported as a history of miscarriage and grand multiparity [18].

The mean years of education of the participants were 6.30 ± 3.05 years (median, 5 years). There was a statistically significant difference between the groups concerning the educational level ($p < 0.01$). The duration of education in the GDM group was significantly lower than the NGT and IGT groups ($p = 0.001$; 0.008 ; $p < 0.01$). This situation can be attributed to the positive change in health behaviors as the education level increases. Along with the increase in education level, eating habits change positively and awareness of going to a doctor for control during pregnancy enhances.

The financial possibilities of the patients affect their eating habits and access to a doctor during pregnancy and in all other conditions. In this respect, the cases were not homogeneous in our study. Studies should be carried out in larger series by adding these variables. In this way, the variable which mostly affects glucose metabolism can be determined in GDM or pregnancy. In a study by Maria Lindqvist et al. [19] unemployment and low educational level were found to be associated with an increased risk of GDM.

When the clinical features of normal and pregnant women with GDM were compared, pregnant women with GDM were statistically significantly more obese ($p < 0.01$). In obese pregnant women, the rate of cesarean and labor induction, hypertension, preeclampsia, stillbirth and risk of GDM are increased [20]. GDM and obesity are the most common metabolic disorders during pregnancy. Adipose tissue also has an endocrine function and is effective in many steps of metabolism, especially in the metabolism of glucose with adipocytokines, such as adiponectin, resistin and leptin.

There are more and more new findings of adipocytokines that are revealed every day. Even after pregnancy, there is an increase in insulin secretion and a decrease in insulin sensitivity depending on weight in GDM patients [21]. This condition tends to support the endocrine function of adipose tissue.

Concerning risk factors, most of the GDM risk factors are innate irreversible factors. In this sense, weight gain during pregnancy is important because it is a changeable risk factor. In our study, we found a significant difference between pre- and post-pregnancy weight of cases according to glucose tolerance types. Weight difference in GDM group was significantly higher than the NGT and IGT groups. We did not find any significant difference between NGT and IGT.

Preventive medicine is becoming increasingly important today. It can be predicted that when the weight gain is kept under control by informing the pregnant women starting from the first examination, a significant decrease in GDM and GDM related complications will be achieved.

There was a statistically significant difference between the groups according to BMI classification before pregnancy. We found that the rate of overweight before pregnancy was higher in the GDM group. The difference between the groups according to BMI classification after pregnancy was again statistically significant. The rate of overweight after pregnancy was higher in the GDM group than NGT and IGT group.

Insulin resistance and related hyperinsulinism develop in peripheral tissues with increasing obesity. The results of this study point to an increase in fasting insulin levels independent of weight in the third trimester of pregnancy and a decrease in the suppression of hepatic glucose production by insulin infusion [18]. Therefore, given that this effect is more pronounced in obese pregnant women, and that the incidence of GDM is more common in obese pregnant women is consistent with the data in the literature [21].

These findings emphasize the importance of weight gain in the management of pregnant women with GDM and suggest that diet and exercise will be promising approaches in preventing the development of GDM.

Conclusion

In our study, we found that the weight of GDM cases at the beginning of pregnancy was higher than the other groups. The difference in weight between the onset and the end of pregnancy in the GDM group was significantly higher than in the NGT and IGT groups.

The mean gravida and parity numbers of pregnant women with GDM were significantly higher than the other groups. Preventive medicine is an indisputable concept for both individual and public health and the national economy. In this context, the main approach should be to determine the risk factors of GDM and change the ones that can be changed and prevent the emergence of the disease.

Most of the GDM risk factors (such as race, family history, maternal age) are irreversible factors. However, the severity of GDM seems to be directly related to weight gain during pregnancy. Weight gain during pregnancy can be altered by nutrition education, diet and exercise. Since it is associated with poor perinatal outcomes in patients with GDM receiving drug therapy, approaches to control weight gain should be seriously considered [8].

Ethics Committee Approval: Approval of the Ethics committee of Istanbul Bakirkoy Sadi Konuk Training and Research Hospital was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: G.T.; Design: G.T.; Data Collection or Processing: G.T., M.H.; Analysis or Interpretation: A.K.; Literature Search: G.T.; Writing: G.T.

Conflict of Interest: None declared.

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