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CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

Long-term Outcomes of Gestational Diabetes Mellitus, a Retrospective Cohort Study

Gestasyonel Diabetes Mellitusun Uzun Dönem Sonuçları, Retrospektif Kohort Çalışma

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Abstract

Objective: Gestational diabetes mellitus (GDM) is defined as glucose intolerance that begins or is first detected during pregnancy. GDM is associated with adverse outcomes in pregnancy and infants. Postpartum outcomes have been introduced in recent studies. In our study, we report long-term complications of GDM.

Methods: In our study, pregnant women between 19 and 35 years old who were diagnosed with GDM for the first time and healthy pregnant were compared. In these patients, we assessed gestational age, type of delivery, birth weight fasting plasma glucose, postprandial plasma glucose, HbA1c, alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, creatine, urinalysis and thyroid stimulating hormone, lipid profile, diagnosis and pharmacological agents prescribed between indexed pregnancy and 5th year postpartum screening.

Results: One hundred-fifty two GDM cases and 202 healthy pregnant' data were recruited. We demonstrated that fasting and postprandial plasma glucose, HbA1c, ALT, AST, urea, creatine, urine protein, glucose, ketone, total cholesterol, triglyceride and low-density lipoprotein were significantly higher in pregnant with a history of GDM in the 5th year follow-up. Furthermore, we observed pregnant with GDM were diagnosed significantly higher with diabetes mellitus, hypertension, obesity, hyperlipidemia, coronary hearth diseases, angina, cerebrovascular disease in follow-up. These post-GDM patients were also found most probably using anti-diabetic, anti-hypertensive, anti-lipidemic, and anti-platelet agents.

Conclusion: Women with a history of GDM are at increased risk of diabetes and related diseases. Postpartum GDM follow-ups should include ALT, AST, urea, creatine, urine analysis in addition to well-documented tests as fasting glucose, postprandial glucose, HbA1c and lipid screenings.

Keywords: Gestational diabetes mellitus, long-term, outcomes

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Öz

Amaç: Gestasyonel diabetes mellitus (GDM); gebelikte ortaya çıkan, çeşitli derecelerde hiperglisemiye neden olan karbonhidrat intoleransıdır. GDM gebelikte olumsuz sonuçlarla ilişkilendirilmiştir. Postpartum sonuçlar ise yakın zamanda ortaya koyulmaya başlanmıştır. Amacımız GDM'nin uzun dönemde yaratabileceği komplikasyonları değerlendirmektir.

Yöntem: Çalışmamızda 19-35 yaş arasındaki ilk kez GDM tanısı almış ve doğum yapmış hastalar, sağlıklı bireyler ile karşılaştırılmıştır. Hastaların yaş, doğum haftası, doğum şekli, bebek doğum kilosu, açlık ve tokluk plazma glikozu, HbA1c, alanin aminotransferaz (ALT), aspartat aminotransferaz (AST), üre, kreatin, idrar analizi, tiroid uyarıcı hormon (TSH), lipid profili, aldığı tanılar ve ilaçları incelenmiş ve 5. yıl takipleri de değerlendirilmiştir.

Bulgular: Çalışmaya dahil edilen 152 GDM ile komplike olmuş gebelik ve 202 sağlıklı gebenin verileri çıkarılmıştır. GDM hastalarının açlık ve tokluk kan glikozu, HbA1c, ALT, AST, üre, kreatin; idrarda protein, glikoz ve keton, total kolesterol, trigliserid ve LDL değerlerinde 5. yıl takiplerinde anlamlı yüksek saptanmıştır. Beşinci yılda GDM olgularının anlamlı olarak daha fazla diyabet, hipertansiyon, obezite, hiperlipidemi, koroner arter hastalığı, anjina ve serebrovasküler hastalık tanısı aldığı görülmüştür. Bu hastaların aynı zamanda daha çok antidiyabetik, antihipertansif, antilipidemik ve antiplatelet ajan kullandığı izlenmiştir.

Sonuç: GDM öykülü kadınlar diyabet ve ilişkili hastalıklar açısından risk altındadır. Postpartum taramalarda çokça araştırılmış açlık glikozu, tokluk glikoz, HbA1c ve lipid profili yanında ALT, AST, üre, kreatin testleri de yer almalıdır.

Anahtar Kelimeler: Gestasyonel diabetes mellitus, uzun dönem, sonuçlar

Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance that is first identified during pregnancy[1]. The prevalence of GDM varies between 6% and 25%[2,3]. Prevalence has been increasing over the years, possibly due to increases in the maternal age, weight. Pregnant women with any following characteristic appear to be at increased risk of developing GDM are personal history of impaired glucose tolerance, family history of diabetes, obesity, older maternal age, previous GDM, previous birth of an infant with macrosomia or malformation, previous unexplained perinatal loss, multiple gestation[4].

The basis of recommendations for postpartum follow-up in patients with GDM is an increased risk estimated at up to the 70% chance of developing diabetes (predominantly type 2) later in life[4]. Therefore, screening at 4-12 weeks postpartum is recommended for all women who had GDM[5]. Furthermore leading organizations recommend long-term follow-up of women with gestational diabetes[1,4]. The American Diabetes Association also suggest re-evaluation of the glycemic status of the patient in 1 or 3 years. More frequent assessment is essential in terms of preconceptional and prenatal care for those whom planning future pregnancy. 1-2 years screenings should be used for women with risk factors as; diabetes, family history of diabetes, oral anti-diabetics or insulin use in pregnancy[1].

A history of GDM is predictive of an increased risk of developing type 2 diabetes, type 1 diabetes, metabolic syndrome and related cardiovascular complications[6,7]. Our study's objective is the assessment of the outcomes in 5th year follow-up of women with GDM.

Materials and Methods

A retrospective cohort research was conducted at the Obstetrics and Gynecology Clinic at the Tepecik Education and Research Hospital in İzmir. Eligible GDM subjects considered as gave singleton live birth without congenital anomalies between 2009 and 2014, between 19 and 35 years old to avoid age-related complications, the first time diagnosed as GDM and no previous diagnosis of diseases with glucose intolerance or any chronic disease. Control cases singleton live births with no infants' congenital anomalies, between 19 and 35 years old to avoid age-related complications, no previous chronic disease or newly diagnosed disease (gestational diabetes, hypertension etc.) in pregnancy. Follow-up data recruited 5th year of patients' birth date between 2014 and 2019. Patients with incomplete follow-up data were excluded from the study. Information has recruited from clinical data systems. This study was approved by the Ethics Committee of Tepecik Education and Research Hospital (decision no: 2019/6-12, date: 10.04.2019).

In our study, we recruited age, gestational age, type of delivery, infant birth weight, maternal alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, creatine, fasting blood glucose, postprandial blood glucose, HbA1c, whether the glycemic target reached or not in pregnancy, TSH, urine screening positivity range with number codes in the second or the third trimester. GDM diagnose were recruited from the clinical data diagnose system. Pregnancy glycemic targets are defined as the following: fasting 70-100 mg/dL; peak postprandial 1st hour glucose <140 mg/dL, 2nd hour glucose <120 mg/dL, HbA1c: 6-6.5%. In 5th year follow-up we extract biochemical results, glycemic

status, anti-diabetic treatment, whether the glycemic target reached or not, additionally total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglyceride results. Non-pregnancy glycemic targets are defined as fasting 80-130 mg/dL, postprandial <160 mg/dL and HbA1c ≤7%. Glycemic status was examined under the titles normoglycemic, prediabetes and diabetes mellitus. Prediabetes criteria: fasting glucose 100-125 mg/dL and glucose challenge test (GCT) 2nd hour plasma glucose <140 mg/dL; <100 mg/dL and 140-199 mg/dL, 100-125 mg/dL and 140-199 mg/dL are defined for isolated impaired fasting glucose, impaired glucose tolerance and combined impaired fasting glucose and glucose tolerance, respectively. All these patients were gathered up in a prediabetes title. Diabetes diagnostic criteria are fasting glucose ≥126 mg/dL, GCT 2nd hour plasma glucose ≥200 mg/dL, random plasma glucose ≥200 mg/dL and HbA1c ≥6.5%. Patients' medications and 5th year diagnoses were also assessed.

Statistical Analysis

The distribution of variables was measured by Shapiro-Wilk's test. Wilcoxon test was used to analyze dependent data, also chi-square test and Mann-Whitney U test used for independent data comparison. A p value <0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences 24.0 program.

Results

In total 1124 adult patients with and 3256 without gestational diabetes who are eligible for inclusion criteria were recruited, 152 with gestational diabetes and 202 healthy women with sufficient data were included.

In patient characteristics, mean age and gestational week and infant birth weight of GDM patient were 28.10±4.62 years old [minimum-maximum (min-max): 19-35], 37.71±2.32 week (min-max: 29-41), 3481.77±687.33 gr (min-max: 1800-5100) and of healthy persons were 27.89±4.86 (min-max: 19-35), 39.93±1.53 (min-max: 35-42), 3446.73±330.70 (min-max: 2690-4100) respectively (p=0.350, p=0.000, p=0.252). Primary cesarean section deliveries were common in the GDM group (48.68%) vs. control group (11.88%) (p=0.000).

In GDM patient indexed pregnancy vs 5th year follow-up mean fasting glucose, postprandial glucose, HbA1c and ALT, AST, urea, creatine, TSH were 110.23±54.54 vs 142.70±77.57 mg/dL (min-max: 46-374 vs min-max: 69-455), 161.43±68.86 vs 189.15±103.78 mg/dL (min-max: 59-506 vs min-max: 66-600), 5.82±1.60 vs 6.60±2.17% (min-max: 3.80-16.90 vs min-max: 4-14.80) and 20.69±43.26 vs 31.03±66.58 IU/L (min-max: 5-508 vs min-max: 6-679), 22,19±31,79 vs 27,35±41,03 IU/L (min-max: 9-386 vs min-max: 9-401), 18.94±6.60 vs 23.51±8.90 mg/dL (min-max: 6-44 vs min-max: 10-78), 0.64±0.36 vs 0.85±0.62 mg/dL (min-max: 0.33-4.70 vs min-max: 0.5-6.00), 2.36±6.08 vs 2.73±7.09 uIU/L (min-max: 0,03-75 vs min-max: 0.03-87.00) respectively. Other than urine glucose and protein, indexed GDM complicated pregnancies' analysis were found significantly increased in 5th year follow-up (p<0.05) (Supplement 1). Urine glucose and protein did not differ but ketone was found significantly decreased in follow-up of GDM patients (p<0.05). In the control group-indexed pregancy vs 5th year follow-up mean fasting glucose, postprandial glucose, HbA1c and ALT, AST, urea, creatine, TSH were 84.72±7.87 vs 87.87±10.29 mg/dL (min-max: 64-100 vs min-max: 66-126), 89.81±10.63 vs 93.98±13.11 mg/dL (min-max: 60-128 vs min-max: 64-145), 4.64±0.55 vs 4.75±0.70% (min-max: 3.60-5.90 vs min-max: 3.70-6.20) and 15.22±7.10 vs 15.51±11.53 IU/L (min-max: 4-59 vs min-max: 4-112), 17.25±4.32 vs 17.78±7.37 IU/L (min-max: 9-35 vs min-max: 8-63), 19.28±5.98 vs 19.64±5.58 mg/dL (min-max: 6-35 vs min-max: 7-32), 0.71±0.10 vs 0.72±0.09 mg/dL (min-max: 0.40-1.06 vs min-max: 0.46-1.00), 2.25±2.02 vs 2.24±2.30 uIU/L (min-max: 0.17-18.25 vs min-max: 0.37-19.34) respectively. In the control group fasting glucose, postprandial glucose, HbA1c were also significantly higher in 5th year (p<0.05) but other variables and urine analyse were did not differ from indexed pregnancy (Supplement 1).

Follow-up GDM vs control's total cholesterol, HDL, LDL, triglyceride median (25p-75p) (mean±SD) rates were; 193.5 (162-224.5) [197.40±45.46 (min-max: 110-337)] vs 173.5 (150-199) [175.58±36.06 mg/dL (min-max: 112-308)] (p=0.000), 47 (40-56) [47.84±11.32 (min-max: 20-77)] vs 48 (42-55) [49.47±11,04 mg/dL (min-max: 28-101)] (p=0,270), 110 (88.25-143.75) [117.30±38.23 (min-max: 44-262)] vs 105.80 (82.8-124.8) (105.92±30.29 mg/dL (min-max: 50.40-201.80)] (p=0.012), 151.5 (95.25-222.75) [187.59±177.94 (min-max: 43-1416)] vs 89 (63-128) [108.16±75.55 mg/dL (min-max: 17-507)] (p=0.000) respectively. In 5th year follow-up fasting glucose, postprandial glucose, HbA1c, ALT, AST, urea, creatine, total cholesterol, LDL, triglyceride was significantly higher in patients GDM compared to the control group (p<0.05) (Table 1).

We observed 80.92% (n=123) of pregnant women could not reach and only 19.07% (n=29) of them could meet the target glucose and HbA1c values in GDM patients in pregnancy;

however, all control patients were achieved glycemic targets (p=0.000). In 5th year follow-up we found 53.94% (n=82) GDM patients and 5.93% (n=12) control patient progressed into diabetes (p=0,000). 23.68% (n=26) of GDM patients were using oral antidiabetics, 9.21% (n=14) of them were using insulin and 14.47% (n=22) of them were having combined

Table 1. Index pregnancy vs postpartum follow-up profiles

	Index pregnancy Median (25p-75p)		**p**	**5th year follow-up Median (25p-75p)**		**p**
	Control (n=202)	**GDM patient (n=152)**		**Control (n=202)**	**GDM patient (n=152)**	
Fasting plasma glucose (mg/dL)	85.00 (78.00-91.00)	94.00 (79.00-118.75)	**0.000**	87.00 (80.00-92.00)	108.00 (93.00-172.75)	**0.000**
Postprandial plasma glucose (mg/dL)	90.00 (83.00-96.00)	147.50 (122.5-177.00)	**0.000**	91.00 (86.00-98.25)	144.50 (114.00-255.25)	**0.000**
HbA1c (%)	5.00 (4.00-5.00)	5.40 (4.92-6.22)	**0.000**	4.90 (4.00-5.00)	5.80 (5.10-7.20)	**0.000**
Urea (mg/dL)	19.00 (15.00-23.00)	18.00 (15.00-23.00)	0.400	19.00 (15.00-24.00)	22.00 (17.00-29.00)	**0.000**
Creatine (mg/dL)	0.70 (0.62-0.80)	0.80 (0.70-0.80)	**0.000**	0.71 (0.66-0.80)	1.51 (0.97-2.39)	**0.002**
ALT (IU/L)	14.00 (11.00-17.00)	13.00 (10.00-18.00)	0.207	14.00 (19.00-17.00)	16.00 (12.00-25.00)	**0.000**
AST (IU/L)	16.00 (15.00-20.00)	17.00 (14.00-21.00)	0.194	17.00 (14.00-19.00)	19.00 (15.00-23.00)	**0.000**
TSH (uIU/mL)	1.86 (1.30-2.46)	1.51 (0.97-2.39)	**0.036**	1.77 (1.21-2.49)	1.85 (1.27-2.70)	0.515
	Index pregnancy N (%)			**5th year follow-up N (%)**		
	Control (n=202)	**GDM patient (n=152)**		**Control (n=202)**	**GDM patient (n=152)**	
Urine glucose						
Neg	202 (100.00)	128 (84.21)		202 (100.00)	124 (81.57)	
Trace	0 (0.00)	1 (0.65)		0 (0.00)	0 (0.00)	
+	0 (0.00)	8 (5.26)	**0.000***	0 (0.00)	11 (7.23)	
++	0 (0.00)	4 (2.63)		0 (0.00)	5 (3.28)	**0.000***
+++	0 (0.00)	6 (3.94)		0 (0.00)	7 (4.60)	
++++	0 (0.00)	4 (2.63)		0 (0.00)	5 (3.28)	
+++++	0 (0.00)	1 (0.65)		0 (0.00)	0 (0.00)	
Urine keton						
Neg	199 (98.51)	128 (84.21)		201 (99.50)	137 (90.13)	
Trace	0 (0.00)	3 (1.97)		0 (0.00)	0 (0.00)	
+	3 (1.48)	15 (9.86)	**0.000***	1 (0.49)	13 (8.55)	
++	0 (0.00)	5 (3.28)		0 (0.00)	1 (0.65)	**0.000***
+++	0 (0.00)	0 (0.00)		0 (0.00)	1 (0.65)	
++++	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	
+++++	0 (0.00)	1 (0.65)		0 (0.00)	0 (0.00)	
Urine protein						
Neg	186 (92.07)	116 (75.31)		194 (96.03)	123 (80.92)	
Trace	12 (5.94)	0 (0.00)		5 (2.47)	11 (7.23)	
+	4 (1.98)	19 (12.50)	**0.000***	3 (1.48)	10 (6.57)	
++	0 (0.00)	8 (5.26)		0 (0.00)	2 (1.31)	**0.000***
+++	0 (0.00)	8 (5.26)		0 (0.00)	6 (3.94)	
++++	0 (0.00)	1 (0.65)		0 (0.00)	0 (0.00)	
+++++	0 (0.00)	0 (0.00)		0 (0.00)	0 (0.00)	

Mann-Whitney U test. *Chi-square test

antidiabetic therapy (Table 2). Only 30.26% (n=46) of GDM patients while 86.63% (n=175) of the control group were normoglycemic in 5th year follow up (p=0,000).

Our data shown most common diagnoses in 5th year follow up in GDM patients were insulin independent DM 36.85% (n=56). Then other diagnoses percentage patients compared to controls were angina pectoris 19.07% vs 1.48%, insulin dependent DM 17.04% vs 0.49%, hypertension 17.04% vs 4.45%, hyperlipidemia 13.81% vs 3.96%, obesity 8.55% vs 0.49%, cardiac arrhythmia 7.23% vs 7.42%, coronary artery disease 5.92% vs 1,48%. Also, cerebrovascular disease 3.28%, embolism/thrombosis 1.97% and chronic renal disease 0.65% were found in GDM patients in follow-up. While cardiac arrhythmia, embolism/thrombosis and chronic renal disease were found indifferent, all other diagnoses were found significantly higher (p<0.05) (Table 2).

Prescribed medications other than anti-diabetics recruited in 5th year GDM compared to the control group were ace-inhibitors 9.86% vs 1.98%; hypolipidemic agents 8.55% vs 0%, anti-platelets 5.26% vs 0%, angiotensin II receptor blocker 3.94% vs 0.49%, beta blockers 3.28% vs 2.47%, calcium channel blockers 2.63% vs 0.49%, anticoagulants 1.31% vs 0%. Only ace inhibitors, angiotensin II receptor blockers, hypolipidemic and anti-platelet agents were used significantly higher in GDM patients (p<0.05) (Table 2).

Discussion

Our results on the infant birth weights were significantly higher in the GDM patients and it was expected to find vaginal birth rates are lower compared to healthy pregnant[8]. The high cesarean rate in GDM patients in our study could be related to our hospital rates, which is perinatal center in our region and high overall rates in Turkey as well as GDM complications and adverse outcomes[9].

There are contradictory results about AST and ALT levels; while Tan et al.[10] could not relate GDM to high levels, yet another study found only higher ALT levels related to GDM[11]. Our data shown while healthy pregnant' ALT, AST values did not differ in their follow-up but GDM patients

Table 2. 5th year follow-up diagnose and medications

		Control n (%)	GDM patient n (%)	p
Diagnose	Insulin-independent diabetes mellitus	11 (5.44)	56 (36.84)	**0.000**
	Angina pectoris	3 (1.48)	29 (19.07)	**0.000**
	Insulin-dependent diabetes mellitus	1 (0.49)	26 (17.10)	**0.000**
	Hypertension	9 (4.45)	26 (17.10)	**0.000**
	Hyperlipidemia	8 (3.96)	21 (13.81)	**0.002**
	Obesity	1 (0.49)	13 (8.55)	**0.000**
	Cardiac arrhythmia	15 (7.42)	11 (7.23)	1.000
	Coronary artery disease	3 (1.48)	9 (5.92)	**0.047**
	Cerebrovascular disease	0 (0.00)	5 (3.28)	**0.014**
	Embolism/thrombosis	0 (0.00)	3 (1.97)	0.078
	Chronic renal disease	0 (0.00)	1 (0.65)	0.429
Medications	Anti-diabetic agents			
	Oral anti-diabetics	8 (3.96)	36 (23.68)	**0.000**
	Insulin	0 (0.00)	14 (9.21)	
	Combined therapy	0 (0.00)	22 (14.47)	
	Ace Inhibitors	4 (1.98)	15 (9.86)	**0.003**
	Hypolipidemic agents	0 (0.00)	13 (8.55)	**0.000**
	Antiplatelet agents	0 (0.00)	8 (5.26)	**0.001**
	Angiotensin II receptor blockers	1 (0.49)	6 (3.94)	**0.045**
	Beta blockers	5 (2.47)	5 (3.28)	0.750
	Calcium channel blockers	1 (0.49)	4 (2.63)	0.169
	Anticoagulant agents	0 (0.00)	2 (1.31)	0.184

Chi-square test.

were significantly higher compared to indexed pregnancy. Furthermore, we observed increased AST and ALT levels in postpartum follow-up statistically significant in GDM cases compared to the control groups We also showed that urea, creatine values increased in GDM patients' follow-up. Current results -similar to our results- have presented postpartum tubular failure findings are related to GDM[12]. However, Pinto et al.[13] observed conflicting data with lower urea and creatine levels after the diagnosis. GDM patients' follow-up urine analyze findings (urine glucose, protein and ketone) were significantly higher compared to controls. But our urine analyzes data have shown there was no significant difference between indexed pregnancy and 5th year in any group. Maternal diabetes, glycosuria and pregnancy-related results are inconsistent. Because some levels of glycosuria from increased glomerular filtration is common[14]. Our considerable results in 5th year ketonuria and proteinuria increase in GDM patients parallel with other findings[15]. Studies have shown this postpartum proteinuria or microalbuminuria may be related to early stage renal failure in long-term follow-up[16]. Limited data are focused on postpartum AST, ALT, urea, creatine and urine analyze long-term follow-up. Our study will be a new perspective in few works.

The prevalence of thyroid dysfunction in gestational diabetes follow-ups are significantly higher from indexed pregnancy also correlated with our findings[17]. We found significant TSH difference between GDM and control pregnant in indexed pregnancy. However, compared to healthy pregnant in follow-ups there was no difference. It is contradictory result to current data[18]. But in a cohort study, Agarwal et al.[19] found no difference between thyroid function tests but adding anti-thyroid peroxidase antibodies to tests they concluded there is a higher risk of abnormal thyroid function. So our insignificant results could be related that we recruited only TSH findings.

We observed a fourfold of GDM patients could not meet the glycemic targets in the pregnancy, which could be a sign of insufficient screenings or treatments for pregnant women. Furthermore, in our analysis in GDM patients 5th year fasting glucose, postprandial glucose and HbA1C values increased in follow-ups also compared to the control group considerably. Our results are supported by several studies, but there are various findings. Type 2 diabetes risk odds with previous GDM history may vary four times to eleven times higher; mostly depending on glycemic status, genetics, ethnicity[20,21]. Our study data shown seven times higher number of post-GDM patients were diagnosed with type 2 diabetes and half of the GDM patients were found using anti-diabetics in follow-up. Diabetes rates similar to our own findings were shown in ATLANTIC DIP's study[22]. But in this study, postpartum follow-up type 2 diabetes progression rates -3 months to 2.6 years were as low as 2.3%; twenty-fold difference can be explained by our study's long-term cumulative risk increase. Progression rates can vary 2.6% in six weeks to 70% in 26 years[20]. But in 5th year cumulative incidence remarkably higher than reached plateau after 10 years[23].

Dyslipidemia was found to be significantly higher in post-GDM results as expected. Overall results submitted that GDM patients appeared to have worse cardiometabolic risk profile than healthy pregnant[24]. Our study results also correlated with adverse outcomes, especially focused on 5th year lipid parameters and diagnoses of cardiovascular morbidities. Supposedly no difference was observed between patients and healthy controls in several studies[25]. New studies have attempted to lighten up the association between GDM and cardiovascular diseases.

GDM, type 2 DM and obesity share similar mechanisms such as metabolic dysregulation, decreased insulin sensitivity and additionally inappropriate insulin response[26]. Accordingly, high obesity rates in 5th year diagnoses are also associated with type 2 DM rates increase[26]. Thus, metabolic syndrome incident also higher in these individuals[27]. Our results shown GDM patients were much probably diagnosed with hypertension, hyperlipidemia, obesity, coronary artery and cerebrovascular disease in their follow-ups. Compatible with our data, Daly et al.[28] stated that GDM complicated postpartum cases show elevated risk of cardiovascular risk factors. Related to all these findings, our study found higher anti-hypertensive and antilipidemic and anti-platelet agents prescribed in post-GDM patients.

Although opposing studies, postpartum early lifestyle changes are considered to have a protective effect on outcomes. Outcomes can be improved by dietary modifications, physical activities and medications for insulin resistance[29]. Our retrospective study based on clinical data excluded lifestyle change approaches yet medications were recruited. Those results reinforce evidence. Thus, protocols for follow-up should focus on prevention for type 2 diabetes and recognize prediabetes diagnose alerts. Changing the course of events early before overt diseases may decrease outcomes, micro- and macrovascular complications of associated diseases and final costs.

There is still no certain postpartum screening protocol agreed on. Insufficient screenings could be associated with undetermined protocols and guidelines, their own challenges of screening tests, communication deficits between physicians and health professionals assuming screenings are not priority in post-GDM patients[30]. In the ACOG report, 75% of clinicians stated performing postpartum screenings, still other studies reported 35% of women with a history of GDM were tested[4].

Study Limitations

The current study was limited by the given the small sample size due to missing data considering the long term of the study's focus and fails of computer-based systems, caution must be exercised while interpreting the evidence.

Conclusion

In conclusion, although the guidelines do not suggest a common protocol in postpartum follow-up of women with a history of GDM, it is vitally based on comprehensive data. Patients are at an increased risk of type 2 diabetes, prediabetes and related diseases. Healthcare professionals -to protect the population and decrease the cost- need to establish frequent postpartum screening and provide preventive treatments if necessary for this particular population. Postpartum GDM follow-ups should include ALT, AST, urea, creatine, urine analysis in addition to well-documented tests as fasting glucose, postprandial glucose, HbA1c and lipid screenings. There is a need for further studies.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of İzmir Tepecik Education and Research Hospital (decision no: 2019/6-12, date: 10.04.2019).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.İ., H.İ., C.A., Concept: A.İ., H.İ., C.A., U.G.B., Design: A.İ., H.İ., C.A., U.G.B., Data Collection or Processing: A.İ., H.İ., C.A., A.R.Ş., Analysis or Interpretation: A.İ., H.İ., C.A., Literature Search: A.İ., H.İ., C.A., A.R.Ş., Writing: A.İ., H.İ., C.A., A.R.Ş., U.G.B.

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Supplement 1. Index pregnancy and 5th year follow up changes

	Control			GDM patient		
	T0 Median (Q1-Q3)	T5 Median (Q1-Q3)	p	T0 Median (Q1-Q3)	T5 Median (Q1-Q3)	p
Fasting plasma glucose (ng/dL)	85 (78-91)	87 (80-92)	**0.000**	94 (79-118.75)	108 (93-172.75)	**0.000**
Plasma glucose - 2nd hour (mg/dL)	90 (83-96)	91 (86-98.25)	**0.000**	147.5 (122.5-177)	144.5 (114-255.25)	**0.022**
HbA1c (%)	5 (4-5)	4.9 (4-5)	**0.012**	5.4 (4.92-6.22)	5.8 (5.1-7.2)	**0.000**
Urea (mg/dL)	19 (15-23)	19 (15-24)	0.442	18 (15-23)	22 (17-29)	**0.000**
Creatin (mg/dL)	0.7 (0.62-0.80)	0.71 (0.66-0.80)	0.127	0.59 (0.51-0.70)	0.8 (0.7-0.7)	**0.000**
AST (IU/L)	16 (15-20)	17 (14-19)	0.844	17 (14-21)	19 (15-23)	**0.016**
ALT (IU/L)	14 (11-17)	14 (10-17)	0.172	13 (10-13)	16 (12-25)	**0.000**
TSH (uIU/mL)	1.86 (1.30-2.46)	1.77 (1.21-2.49)	0.340	1.51 (0.97-2.39)	1.85 (1.27-2.70)	**0.000**
Urine glucose	0 (0-0)	0 (0-0)	1.000	0 (0-0)	0 (0-0)	0.829
Urine ketone	0 (0-0)	0 (0-0)	0.317	0 (0-0)	0 (0-0)	**0.038**
Urine protein	0 (0-0)	0 (0-0)	0.082	0 (0-0)	0 (0-0)	0.519

Wilcoxon test. T0: Index pregnancy, T5: 5th year follow-up, Q: Quartile, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, TSH: Thyroid stimulating hormone