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Amylin for diagnosis of gestational diabetes mellitus and its association with advers obstetric-neonatal outcomes

Gestasyonel diyabetes mellitus tanısında amilin ve amilinin olumsuz obstetrik ve yenidoğan sonuçları ile ilişkisi

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ABSTRACT

Aim: The aim of the study was to measure serum amylin levels in pregnant women who applied for oral glucose tolerance test(OGTT) between 24-28 weeks,to compare the diagnostic use of amylin in pregnant women with and without a diagnosis of gestational diabetes mellitus(GDM),and to evaluate the relationship between amylin values and obstetric-neonatal outcomes.

Material and Methods: The study includes 86 patients selected among 430 pregnant women who applied to the antenatal outpatient clinic for OGTT. 43 of the pregnants whose 50-gr OGTT results were within normal limits; 43 pregnant women who underwent 100-gr OGTT test because their 50-gr OGTT was above 140 mg/dl and diagnosed with GDM because 2 values were defective were determined as the study group.Serum amylin levels were evaluated by matching the control and study groups according to body mass index (BMI).

Results: In the study,serum amylin levels were found to be 73.7 in the GDM group and 76.1 in the control group, and there was no significance between the groups (p>0.05). Amylin levels were negatively correlated with age, BMI, gravida,parity in the GDM group,and positively correlated with weight gained and gestational week.There was no statistically significant difference between the groups in terms of obstetric (birth week, birth weight,delivery type,birth trauma) and newborn(NEDCU need) outcomes (p>0.05).

Conclusion: Serum amylin concentrations measured before the OGTT do not have a predictive value for the diagnosis of GDM, and serum amylin levels do not predict adverse obstetric and neonatal outcomes.

Keywords: Amylin; diabetes, gestational; glucose tolerance test

ÖZ

Amaç: Çalışmanın amacı, 24-28. haftalar arasında oral glukoz tolerans testi (OGTT) için başvuran gebelerde serum amilin düzeylerini ölçmek, gestasyonel diabetes mellitus (GDM) tanısı almış ve almamış gebelerde amilinin tanısal kullanımını karşılaştırmak ve amilin değerleri ile obstetrik-neonatal sonuçlar arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntemler: Çalışmaya OGTT için antenatal polikliniğe başvuran 430 gebe arasından 86 hasta dahil edildi. 50 gr OGTT sonuçları normal sınırlarda olan gebelerden 43'ü; 50 gr OGTT'si 140 mg/dl'nin üzerinde olduğu için 100 gr OGTT testi yapılan ve 2 değeri bozuk olduğu için GDM tanısı konulan 43 gebe çalışma grubu olarak belirlendi. Serum amilin düzeyleri, kontrol ve çalışma grupları vücut kitle indeksine (VKİ) göre eşleştirilerek değerlendirildi.

Sonuçlar: Çalışmada serum amilin düzeyleri GDM grubunda 73,7, kontrol grubunda ise 76,1 olarak bulundu ve gruplar arasında anlamlı farklılık yoktu (p>0,05). Amilin düzeyleri GDM grubunda yaş, BKİ, gravida, parite ile negatif, kazanılan kilo ve gebelik haftası ile pozitif korelasyon gösterdi. Gruplar arasında obstetrik (doğum haftası, doğum ağırlığı, doğum şekli, doğum travması) ve yenidoğan (NEDCU ihtiyacı) sonuçları açısından istatistiksel olarak anlamlı bir fark yoktu (p>0,05).

Sonuç: OGTT'den önce ölçülen serum amilin konsantrasyonları GDM tanısı için öngörücü bir değere sahip değildir ve serum amilin düzeyleri olumsuz obstetrik ve neonatal sonuçları öngörmez.

Anahtar Kelimeler: Amilin; diyabet, gebelik; glukoz tolerans testi

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INTRODUCTION

GDM is carbohydrate intolerance developing during pregnancy and is the most common medical complication of pregnancy (1). The main reason is the insufficient insulin secretion to meet up the demand of building blood glucose in the body during pregnancy. GDM adversely affects the mother and baby, congenital anomalies (2), preeclampsia and cesarean delivery rates are higher in pregnant women diagnosed with GDM (3). With obesity, advanced maternal age, and a sedentary lifestyle, the prevalence of GDM is increasing in women of reproductive age all over the World(4).The prevalence of GDM in the United States is approximately 8.2%(5). The prevalence also differs according to which screening test is used and according to which diagnostic criteria (4). Therefore, if GDM is diagnosed in time and blood sugar regulation can be achieved, it is possible to avoid most of these complications like obesity, Type 2 diabetes mellitus, chronic cardiovascular disease, for this purpose recommended that screening for GDM between 24-28 weeks in patients without additional risk factors.

Therefore, it is unclear which test will screen for early GDM or Type 2 diabetes(T2DM). The American College of Obstetricians and Gynecologists(ACOG) recommends a two-step approach for screening and diagnosis. Similarly, the National Institutes of Health(NIH) (6) argues that there is insufficient evidence to adopt the single- step approach. A two-step screening approach is used in antenatal clinics, mostly starting with 50-gr OGTT(7). In this case, the specificity-sensitivity of the method is discussed by discussing the cut-off values(8). Although a one-step approach was recommended by the International Association of Diabetes and Pregnancy Study Groups(IADPSG) Consensus Panel for GDM screening(9), a consensus could not be reached.

There is a need for a new method that will provide early diagnosis for GDM and perhaps even be used for preconception screening. For this purpose, many new biomarker studies are carried out (10). Searches for new diagnostic markers for GDM shows that amylin may be a good candidate, a hormone associated with diabetes, is a peptide that has functions related to energy metabolism by being released from pancreatic beta cells together with insulin (11). It has been shown that amylin is secreted together with insulin at a rate of approximately 15:1(insulin: amylin)(12), reduces body fat, reduces fat storage in the body, and plays a role in weight control by increasing energy consumption (13). Amylin is deficient in Type 1 diabetes (T1DM) and T2DM (14). Amylin cytotoxicity causes -cell dysfunction and death, which lowers insulin secretion and lowers glucose tolerance. A study by Wareham et al. found an association between gestational diabetes mellitus and elevated serum levels of amylin (15). There may be a connection between the effect of amylin cytotoxicity and the emergence of GDM; however, there is currently insufficient data to support this notion. The lack of data and the need for new diagnostic markers for GDM have made amylin potentially associated with diabetogenic conditions.

Preconceptional diagnosis of GDM may eliminate maternal and especially fetal complications of GDM by providing normoglycemia throughout pregnancy (16). Based on this idea, the study aims to investigate whether amylin has a marker potential in the screening and diagnosing of GDM and to create a new alternative or supportive method to OGTT. In our study, amylin measurement will be performed in pregnant women with GDM who have not received treatment to make the diagnosis of GDM easier with physiological evaluations and to investigate whether amylin levels could predict neonatal and obstetric outcomes.

MATERIAL AND METHODS

The study included 86 people selected among 430 pregnant women who visited to the antenatal outpatient clinic between 1 November 2018 and 31 January 2019 for OGTT. Of the 430 actively literate patients who had fasted for at least 8 hours between 08.30 and 10:00 in the morning, 43 were included in the control group, and 43 were included in the study group, randomly. Voluntary consent was obtained by interviewing the patients face to face.

The following patients were excluded from the study: with chronic disease, overt diabetes diagnosis, endocrine disease(Cushing's disease, hyperthyroidism, hypothyroidism, Addison's disease, pituitary insufficiency, acromegaly, etc.), multiple pregnancies, pregnant with ovulation induction or IVF cycles, patients who were diagnosed with a congenital anomaly in the anomaly screening performed during pregnancy, who did not have a fasting state of at least 8 hours when they came for blood donation, who was planning to give birth in another hospital, who were younger than 18 years old, morbid obeses, and who did not want to participate in the study were excluded from the study.

The following were questioned in all patients: demographic characteristics(age, height, weight), BMI (kg/height squared(kg/m2)), gravida (pregnancy number), parity(live births), number of abortions, gestational week by last menstrual period, previous delivery types(standard vaginal delivery/cesarean section), whether there is a history of GDM, large baby or birth trauma in previous pregnancies, whether the baby has an additional congenital anomaly in previous pregnancies, and whether there is a need for hospitalization in the neonatal intensive care unit after delivery.

Reference values for the 50-gr OGTT test are variable. Threshold values of 130 mg/dl, 135 mg/dl, and 140 mg/dl are used. While we accepted the 50-gr OGTT test as standard, we accepted 130 mg/dl as the upper value to avoid conflict. Among the patients who underwent 50-gr OGTT, with 1st-hour plasma glucose below 130 mg/dl were included in the control group. Patients with 1st-hour plasma glucose above 140 mg/dl at a 50-gr OGTT were called for the 100-gr OGTT test at least three days after the interval for the second step. The results of the 100-gr OGTT test were evaluated according to the Carpenter and Coustan reference intervals, and the diagnosis of GDM was made in patients with two or more abnormal values in the test. For the amylin evaluations, serum of the morning fasting blood of the patients who came to the 100 g-OGTT test was used.

After waiting for 10-20 minutes(min) at room temperature, the blood samples taken from the patients were centrifuged at 3000 rpm for 20 minutes, and the serums were stored at -80°C until the study day. Serum amylin levels were studied by the ELISA kit protocol(ELISA Kit: Catalog no:201-12-0017, Shanghai Sunred(SRB) Technology Co., Ltd, Baoshan District, Shanghai, China).

Statistical Analysis

Statistical Package for Social Sciences (SPSS) for Windows version 22.0 software was used to analyze the data obtained in the study. The normal distribution was checked with the Shapiro-Wilk test. Data were presented as mean±standard deviation and median (25th and 75th percentiles) or number (percent). For variables that showed normal distribution, two independent group comparisons were made with Student t-test. For variables that did not show normal distribution, two independent group comparisons were made with Mann-Whitney U. ANOVA Test was used to more two independent groups for normally data and, Kruskal-Wallis test was used to compare non-normally distributed data between more two independent groups. Tukey Test was used for post-hoc comperation for ANOVA results. Dunn Test was used for post-hoc comperation for Kruscal-Wallis results. Categorical data were presented as numbers and percentages and compared with the Chi-square test. Spearman's correlation analysis determined the relationship between amylin and other continuous variables. The statistical significance level was accepted as $p<0.05$.

RESULTS

Serum samples were obtained from 430 patients, of whom 44(10.2%) were diagnosed with GDM. After excluding a patient with a BMI of 43 kg/m^2 (morbidly obese) diagnosed with GDM, the remaining 43 patients constituted the study group. Among the remaining pregnant women whose 50 g OGTT result was below 130 mg/dl, 43 patients whose age and BMI matched were included in the control group.

Groups were evaluated according to age distribution, BMI, gestational week, gravida, parity, number of abortions, and delivery type, and there was no statistical significance between the study group and the control group ($p>0.05$). However, it was observed that pregnant women with a diagnosis of GDM gained more weight ($p<0.05$). In addition, fasting plasma glucose values were higher in the GDM group ($p<0.001$). As a result of the statistical analysis performed according to the 1st-hour plasma glucose values of the patients after 50-gr OGTT, fasting plasma glucose values were higher in the GDM group ($p<0.001$).

Table 1. Comparison of obstetric, demographic and amylin values between groups.

Variables \ Groups	Control (n=43)	GDM (n=43)	p
Fasting plasma glucose	85 (69-94)	93 (73-119)	**<0.001***
50 gr OGTT 1. hour (mg/dl)	108 (69-129)	165 (141-209)	**<0.001***
Amylin (ng/l)	76.1 (53.8-2787.4)	73.7 (51.6-2722.8)	0.959
Age (year)	29.2±4.7	31.3±5.7	0.068
BMI (kg/m^2)	29.4±3.7	30.9±4.5	0.086
Gestational week	25 (24-28)	26 (24-28)	0.079
Gravida	3 (1-6)	3 (1-7)	0.704
Parity	1.2±0.9	1.2±0.9	0.711
Alive	1.1±0.9	1.1±0.9	0.849
Abortus	0 (0-3)	0 (0-1)	0.726
Weight gain (kg)	6.6±2.9	8.1±3.4	0.040
Type of birth C/S	17 (39.5)	19 (44.2)	0.662
NVD	26 (60.5)	24 (55.8)	

Mean and standard deviation values are given for normally distributed data, median, Q1 and Q3 values are given for non-normally distributed data. $p<0.05$ was considered statistically significant.

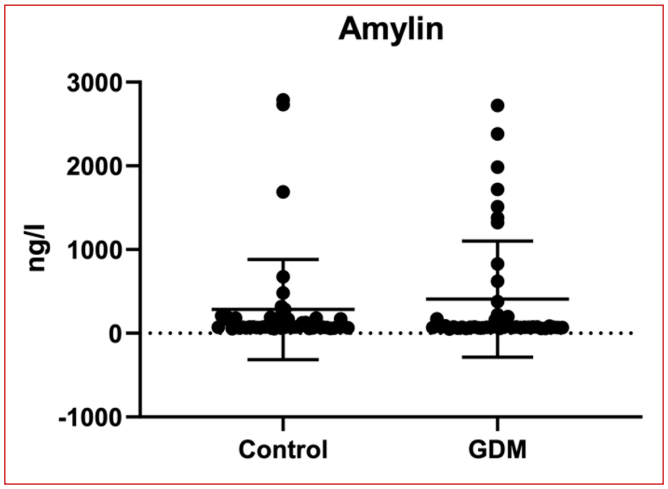

Figure 1. Serum amylin levels between groups.

No significant difference was observed between the groups according to the analysis results performed according to the Amylin values of the patients (p>0.05, Table 1, Figure 1).

Obstetric, Demographic and Amylin Results According to Obesity and Diabetes Status

There was no significant difference between the groups regarding amylin levels in the comparison by dividing them into four subgroups obese GDM, non-obese GDM, obese control, and non-obese control (p=0.312). In the subgroup comparison, there was no statistically significant difference between the groups regarding age, BMI, weight gain, blood collection week, gravida, parity, birth week, and birth weight. While forming the groups, patients were selected by matching in terms of these parameters (p>0.05) (Table 2, Figure 2).

Table 2. Comparison of obstetric. demographic and amylin values according to obesity and diabetes status of the patients obesity≥30.0 kg/m^2

Groups / Variables	Obese Control (n=20)	Non-obese Control (n=23)	Obese GDM (n=25)	Non-obese GDM (n=18)	p
Fasting blood glucose	84.4±7.5	85.0±6.1	94.1±10.2	89.4±9.5	**<0.001***
50 gr OGTT 1st hour (mg/dl)	107.9±16.8	104.9±17.0	167.8±19.4	165.2±18.1	**<0.001***
Amylin (ng/l)	150.35 (53-2787.3)	74.48 (57.7-1689.8)	70.74 (51.6-2722.8)	75.57 (64.4-2380.3)	0.312
Age (year)	27.9±5.5	30.3±3.5	31.4±6.2	31.2±5.1	0.093
Weight gain	6.8±3.6	6.5±2.3	8.0±4.0	8.1±2.4	0.217
Gestational week	25.6±1.0	25.1±1.2	26.0±1.6	26.0±1.7	0.194
Gravida	2 (1-6)	2.5 (0-4)	3 (1-5)	3 (1-7)	0.731
Parity	1 (0-3)	1 (0-3)	1 (0-3)	1.5 (0-3)	0.635
Birth week	38.1±1.8	38.4±1.7	38.2±1.3	38.2±1.8	0.822
Birth weight(gr)	3148.3±439.2	3198.5±466.4	3336.6±459.3	3272±529.7	0.614

Mean and standard deviation values are given for normally distributed data, median, Q1 and Q3 values are given for non-normally distributed data. p<0.05 was considered statistically significant.

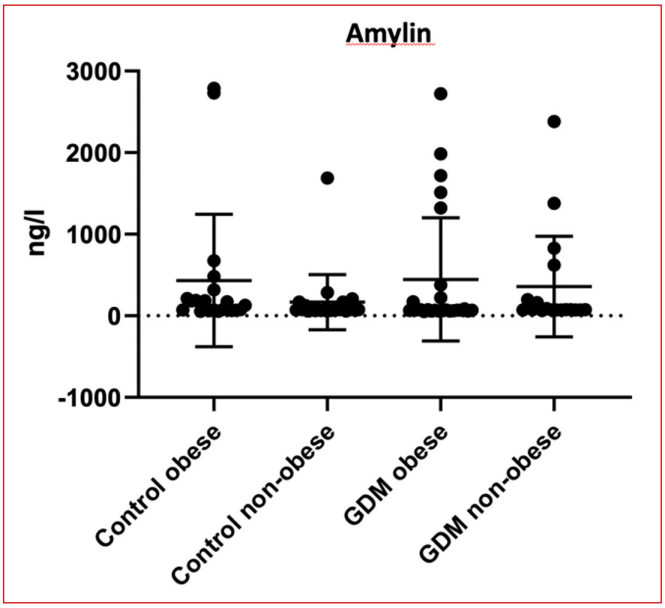

Figure 2. Serum amylin levels between subgroups.

Neonatal Outcomes

As a result of the statistical analysis performed according to the Apgar scores of the newborns showed that the 1st minute Apgar score was significantly lower in the GDM group(p<0,05).

According to the 5th min APGAR score, no significant difference was observed between the groups in terms of the need for the Neonatal Intensive Care Unit(NICU), length of stay in the NICU, week of birth, and newborn gender (p>0.05).

The groups were examined in terms of birth trauma, one birth trauma(parieto-occipital linear fracture) was found, and it was in the control group.

Obstetric and Neonatal Data from Previous Pregnancies

There was no significant difference between the groups according to the results of the analysis performed according to the delivery type of the patients in their previous pregnancies, the NICU needs

Table 3. Comparison of neonatal outcomes between groups. p<0.05 was considered statistically significant.

Variables \ Groups	Control (n=43)	GDM (n=43)	p
APGAR 1st minute score	8(5-8)	7(6-8)	**0.021***
APGAR 5th minute score	10 (7-10)	9 (8-10)	0.086
NICU time (day)	0 (0-3)	0 (0-4)	0.183
Need for NICU	4(9.3)	1 (2.3)	0.167
Birth week	38.2±1.7	38.2±1.5	0.866
Birth weight (gr)	3200 (2020-4040)	3350 (2445-4245)	0.186
Gender			
Girl	18 (41.9)	24(55.8)	0.196
Boy	25 (58.1)	19(44.2)	
Birth trauma	1 (2.3)	0	0.314

Mean and standard deviation values are given for normally distributed data, median, Q1 and Q3 values are given for non-normally distributed data. p<0.05 was considered statistically significant.

Table 4. Obstetric and neonatal data of patients in previous pregnancies.

Variables \ Groups	Control	GDM	p
Previous birth type			
C/S	17 (39.5)	12 (27.9)	0.254
NVD	26 (60.5)	31(72.1)	
Need for NICU	5 (11.6)	4(9.3)	0.725
Big baby	2 (4.7)	8(18.6)	0.044
GDM	2 (4.7)	6 (14)	0.138

Data are presented as numbers (percentage). Fischer used the exact or chi-square test. p<0.05 is statistically significant.

of the newborns, the history of giving birth to a large baby, and whether they were diagnosed with GDM (p>0.05).

Relationship Between Amylin and Other Parameters

The relationship between the amylin values and the parameters measured between the groups was examined, and it was observed that there was a correlation with age, BMI, weight gained, gestational week, gravida, and parity (Table 5).

Table 5. Correlation table of amylin and other variables.

Group / Variables	Control		GDM		Total	
	r	p	r	p	r	p
Fasting plasma glucose	0.047	0.764	-0.066	0.674	-0.001	0.996
1st hour plasma glucose after 50 g OGTT	0.266	0.085	0.028	0.856	0.061	0.577
Age	-0.336	0.028	-0.387	0.010	-0.375	<0.001*
BMI	0.282	0.067	-0.315	0.040	-0.037	0.736
Gestational week	-0.166	0.289	0.335	0.028	0.097	0.374
Gravida	-0.380	0.012	-0.558	<0.001	-0.474	<0.001*
Parity	-0.263	0.088	-0.569	<0.001	0.439	<0.001*
Abortus	0.344	0.024	-0.139	0.373	-0.230	0.033*
Weight gain	0.028	0.860	0.438	0.003	0.240	0.026*
Gravida	-0.380	0.012	-0.558	<0.001	-0.474	<0.001*
Parity	-0.263	0.088	-0.569	<0.001	0.439	<0.001*
Abortus	0.344	0.024	-0.139	0.373	-0.230	0.033*
100 gr 1. Saat PG	-	-	0.058	0.713	-	-
100 gr 2. Saat PG	-	-	-0.144	0.357	-	-
100 gr 3. Saat PG	-	-	0.213	0.171	-	-
Birth week	-0.027	0.864	-0.013	0.932	-0.036	0.741
Birth weight	0.171	0.274	-0.085	0.586	0.018	0.866
APGAR 1st minute score	0.048	0.762	-0.064	0.682	-0.015	0.891
APGAR 5th minute score	-0.102	0.515	-0.030	0.850	-0.069	0.526

Spearman correlation analysis. r: Spearman's correlation coefficient.* p<0.05 is statistically significant.

The relationship between amylin and other parameters was examined, and a negative correlation was observed between amylin and age (r=-0.387, p=0.010) and BMI (r=-0.315, p=0.040) in the GDM group (p<0.05). In the GDM group, a positive correlation was observed between amylin and the weight gained by the patients (r=0.438, p=0.003) (p<0.05). A positive correlation was observed between amylin and the gestational week (r=0.335, p=0.028) in the GDM group (p<0.05). It was observed that amylin values decreased as gravida (r=- 0.558, p<0.001) and parity (r=-0.569, p<0.001) increased in the GDM group.

DISCUSSION

According to the results of our study, there was no significant difference in serum amylin levels between the study and control groups and between these obese and non-obese subgroups. In the GDM group, amylin showed a negative correlation with age, BMI, gravida, and parity and a positive correlation with weight gained and gestational week. The 5th-minute APGAR score was low in infants of mothers with GDM, independent of the amylin.

Amylin release occurs at picomolar values in satiety at concentrations sufficient to produce glycemic effects in healthy people (14). However, in individuals with diabetes mellitus characterized by long-term hyperglycemia, amylin secretion becomes unregulated due to impaired insulin signaling. Although plasma amylin values decrease in T1DM in line with the pancreatic beta cell source of amylin (17), the situation in T2DM varies according to the progression stages of diabetes. At the beginning of T2DM, hyperamylinemia is observed in parallel with hyperinsulinemia, and amylin levels decrease due to the decrease in beta cell reserve as the disease progresses(18). In the literature, there are studies investigating the role of amylin and its biomarker value in GDM. For example, in a study comparing control and GDM patients formed from similar BMI, no difference was observed in serum amylin concentrations at 30 and 90 minutes after fasting and glucose loading. However, increased serum amylin values were observed in 120 minutes of GDM patients. Emphasizing that the amylin has the potential for diagnosing GDM, showing higher values of total amylin in GDM patients at every stage of the OGTT, they mentioned that the evaluation of the total amylin is a more sensitive measurement than the evaluation of the unmodified amylin(19). In another study, no difference was found in fasting serum islet amyloid pancreatic protein values between controls and those with GDM. However, a significant increase was found in patients with GDM compared to controls from the 30th minute of OGTT(20). One study found no difference in serum amylin levels between controls and those with GDM at fasting and during OGTT(21). In our study, similar to the results of Wareham et al., Kautzky-Willer et al. Furthermore, according to Grigorakis et al., fasting amylin values in patients with GDM do not differ from controls regardless of obese or non-obese. In this case, measuring fasting serum amylin does not provide an approach to diagnosing GDM. However, considering previous studies, since the release of amylin shows a parallel pattern with insulin (22), it was found that it increased after the 2nd hour of OGTT. In this situation, an increase in amylin should be expected to be observed 2 hours after the induction of insulin secretion by glucose in the OGTT. In our study, in 8-hour fasting, in the morning fasting blood sugars-the period when the blood level of insulin is the lowest, amylin is also low(23). Therefore, amylin can be used to strengthen diagnostic criteria in addition to blood glucose assessment in OGTT only after further clinical studies have shown that hourly changes of amylin are taken into account.

The amylin hormone released by insulin from pancreatic beta cells reduces body weight by modulating energy intake and nutrient use (24). Insulin resistance increases in parallel with weight gain during pregnancy, and the amount of amylin secreted by increasing insulin also increases (25). On the other hand, since patients with more diabetogenic effects of pregnancy and whose gestational week is advanced, amylin levels are expected to be higher. In this case, it is usual to observe a positive correlation between amylin and weight gain and gestational week. Besides, we concluded that amylin levels were negatively correlated with age. Progressive beta cell loss and insulin secretion decrease with age, gravida, and parity (26). The decrease in amylin and insulin secretion is inversely correlated with increasing age, and those who have experienced more pregnancies (gravida and parity) confirm our results.

Increasing satiety and reducing food intake are one of the most studied effects of amylin. Lutz (27) and Young (28) showed that plasma amylin levels increase in obese patients, while amylin receptor antagonists increase body adiposity. They reported that when amylin levels in the brain increased, body weight and obesity decreased. Pieber et al. (29) showed that basal serum amylin levels were higher in obese rats than in lean rats. Boyle et al. (30,31) showed that basal amylin levels were higher in rats fed high-fat content than in lean rats. Many studies (32-38) suggested that amylin levels increase in obese people. Beglinger et al. (39) showed that amylin levels increase in fasting compared to obese and non-obese adolescents. They noted that the increase in amylin following food intake was much more significant in obese subjects than in controls. In our study, we found a negative correlation between amylin and BMI. This correlation is also related to serum intake time. If we had evaluated amylin during the 2nd hour of the OGTT, we could have obtained similar results with other investigators. Although it has been suggested that amylin levels are higher in

obese subjects in the first studies (31), it is not fully known whether postprandial amylin secretion is affected by high-fat food intake and whether the postprandial secretion (synthesis and release) pattern is different in obese and non-obese subjects (40).

In order to provide the groundwork for multi-parameter screening methods, several research has evaluated the relationship between specific biomarkers and adverse neonatal and obstetric outcomes. For this purpose, many markers such as slit-2 (41), glycated albumin, fructosamine, HbA1c (42), visfatin (43) have been studied. In the study where we investigated whether amylin can predict obstetric and neonatal outcomes, amylin did not predict poor neonatal and obstetric outcomes. These may explain the low number of newborns with poor neonatal processes: a small number of patients, weekly control of the GDM group in our hospital until delivery after diagnosis, adjusting the diet and exercise program according to the results, and providing optimal glycemic control by adjusting the insulin doses. Regardless of the amylin, our study results determined that the 5th-minute APGAR score of the children of mothers with GDM was low. We know that women with GDM are at high risk of pregnancy complications, including low Apgar scores and cesarean delivery (44).

Our limitation is that repeated serum samplings of amylin before OGTT were not performed. Therefore, we could not check the reproducibility of the serum amylin levels. The study finding also needs more generalizability, further research should focus on multicenter studies.

CONCLUSION

Amylin still has the potential to be a biomarker for the diagnosis of GDM, although no significant results were obtained in our study. Further clinical and experimental studies considering the production and release pattern of amylin may contribute to the diagnosis and treatment processes of diabetes.

Conflict of Interest: Authors declared that there is no conflict of interest.

Data Availiability Statement: All data is availability if requested.

Author Contribution: Idea: Ş.Ç.; S.M., A.T. Design:A.T.; Ş.Ç. Literature investigation: S.M.; H.Ç. Laboratory study : S.M.; H.Ç. Statistical analysis: Ş.Ç.; S.M., A.T. Writing: A.T.; H.Ç., S.M.

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