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ORIGINAL ARTICLE

Factors affecting insulin dosage in pregnant women with diabetes

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ABSTRACT

Objective: We aimed to explore the clinical indicators necessitating insulin therapy and the factors affecting the amount of insulin used by pregnant women with diabetes diagnosed either during or before pregnancy.

Material and Methods: We reviewed all diabetes-related prenatal clinic visits from January 2015 to December 2017. A keyword search of electronic medical data identified cases of gestational, pregestational, type 1, and type 2 diabetes. Pregnant diabetics treated with insulin were included. Age, parity, consanguineous marriage, birthweight of prior children, first-degree relatives with diabetes, BMI before pregnancy, weight gain during pregnancy, and exercise compliance were recorded. Total insulin dose, as well as short-, intermediate-, and long-acting insulin doses, were documented separately. Hyperemesis in the first trimester, dietary changes, and ketonuria were also noted. HbA1c readings were obtained when gestational diabetes mellitus was diagnosed and when pregestational diabetes mellitus patients first visited our institution. Plasma lipid profiles were measured in all cases. Third-trimester fetal biometry was calculated using three ultrasonographic measurements.

Results: A total of 202 diabetic patients were included in the study. The prevalence of pregestational diabetes mellitus was 52.5%, while diabetes diagnosed during pregnancy accounted for 47.5%. The combined effect of age and the discrepancy between the last menstrual period and abdominal circumference was found to be statistically significant in predicting insulin dosage. Specifically, total insulin requirements increased by 1.903 units for every additional year of age, and by 4.390 units for every unit increase in the Last Menstrual Period/Abdominal Circumference discrepancy.

Conclusion: The global rise in diabetes prevalence has led to an increase in pregnancies complicated by diabetes. Our objective is to manage this condition optimally, enabling patients to continue therapy with minimal adverse effects and achieving the best possible outcomes for both mother and baby.

Keywords: Diabetes, insulin, pregnancy.

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INTRODUCTION

As diabetes prevalence increases and the average age of onset decreases, the fertility and pregnancy rates of the young population rise. Consequently, pregnancy and diabetes co-occur more frequently.[1]

Diabetes complicates pregnancy, as is well known. Diabetes should be well-recognized, its treatment should be managed, and patients' desire to cooperate with treatment should be improved to achieve favorable pregnancy outcomes for both mother and baby.[2]

Pregnancy is a physiological process in which insulin resistance arises.[3] When there are additional risk factors, therapy becomes necessary. Insulin treatment is the gold standard when diabetes complicates the pregnancy. Insulin has been used throughout pregnancy for decades, and when blood sugar management is maintained, results for both mother and baby are comparable to those of a normal pregnant woman.[4]

Insulin treatment is now personalized. Each pregnant woman's blood sugar profile must be determined by self-monitoring, and an insulin regimen must be tailored to her profile. BMI, age, lifestyle, prior pregnancy history, fetal ultrasonographic abnormalities, and concurrent conditions may result in changes in insulin dosage, regimen, and type.[5]

Based on this data, we wanted to study the findings necessitating insulin therapy as well as the factors influencing the quantity of insulin used by pregnant women who had previously been diagnosed with diabetes or who were diagnosed with diabetes during pregnancy.

MATERIAL AND METHODS

We retrospectively reviewed all pregnancies with diabetes followed up in the antenatal clinic at Zeynep Kamil Women and Children's Diseases Training and Research Hospital from January 2015 to December 2017. A keyword (gestational diabetes, pregestational diabetes, type 1 diabetes, and type 2 diabetes) search of electronic medical records identified cases. Diabetic pregnant women treated with insulin were included.

The diagnosis of gestational diabetes mellitus (GDM) was made based on any single plasma glucose value exceeding the threshold during the 75-gram oral glucose tolerance test (OGTT) (fasting value=92 mg/dL; 1-hour value=180 mg/dL; 2-hour value=153 mg/dL) or two values exceeding the threshold during the 100-gram OGTT (fasting value=95 mg/dL; 1-hour value=180 mg/dL; 2-hour value=155 mg/dL; 3-hour value=140 mg/dL).[6] If diabetes diagnosis was made in the first or early second trimester per American Diabetes Association (ADA) criteria, it was considered pregestational diabetes mellitus (DM).[7] Insulin treatment protocol was commenced if fasting plasma glucose values consistently exceeded 95 mg/dL or 1-hour levels exceeded 140 mg/dL, in spite of diet and exercise. The protocol generally is a multi-dose regimen of 0.6–1.0 U/kg, divided into intermediate- and short-acting insulin.

Maternal data—age, parity, consanguineous marriage, birthweight of any previous children, presence of diabetes mellitus in first-degree relatives, body mass index (BMI) before pregnancy, weight gain during pregnancy, gestational age (GA) at diagnosis, and exercise compliance—were recorded. Gestational age was determined based on the last menstrual period (LMP) and dating by first-trimester crown–rump length (CRL) if there was discrepancy or the date of LMP was unknown. The total insulin dose needed and short-, intermediate-, and long-acting insulin doses separately were recorded. The presence of hyperemesis in the first trimester, the number of visits for diet adjustments (the number of diet lists prepared by the dietician based on the patient's weight gain rate), and ketonuria at any time of pregnancy (from +1 to +4 urine dipstick test) were recorded. Hemoglobin A1c (HbA1c) values were obtained at the time of GDM diagnosis and at our institution's first visit for preGDM patients. Glycemic control was assessed by self-monitoring. Plasma triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) values of all cases were recorded (measurements by COBAS Integra 800–Roche Diagnostics, Mannheim, Germany).

Daily exercise compliance was questioned for all participants enrolled following the initiation of insulin treatment. Walking briskly for 15–20 minutes in a straight line after each meal was deemed sufficient exercise.

Biometry of the fetus in the third trimester was obtained by means of three ultrasonographic measurements. The diagnosis of macrosomia was made if the abdominal circumference (AC) and/or estimated fetal weight (EFW) were greater than the 90th percentile for GA.[8]

Polyhydramnios was diagnosed if the amniotic fluid index (AFI) was >24 cm.

Preeclampsia accompanied by diabetes, nephropathy, cardiopathy, retinopathy, and other disorders was taken into consideration while assessing extra disease. These were disorders identified either before or during pregnancy.

The primary outcome measure was factors associated with the dosage of insulin treatment. Additional outcomes were a comparison of obstetric outcomes in GDM and preGDM.

The study was approved by the Institutional Review Board (Zeynep Kamil Women and Children's Diseases Training and Research Hospital) (Decision-Nr.:132/2017). This study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Mean and standard deviation were used in descriptive statistics for continuous data; categorical variables were reported as numbers and proportions. Using the Chi-square test, the significance of the difference between groups for categorical variables was determined. In multiple groups, the Mann–Whitney U test was employed for pairwise comparisons, and it was calculated using the Kruskal–Wallis test and Bonferroni adjustment. The data were analyzed using version 23.0 of SPSS for Windows. A p-value<0.05 was considered statistically significant.

RESULTS

A total of 202 patients with DM were analyzed. One hundred and six (52.5%) were pregestational DM, whereas 96 (47.5%) were GDM. Among pregestational DM cases, 22 (20.7%) were diagnosed with Type 1 DM and 84 (79.2%) with Type 2 DM.

Table 1: Demographic and clinical characteristics of the study cohort	
Age (years)	33.5±5.9
Gravida	
Primigravid	60 (29.7%)
Multipara	142 (70.3%)
Birthweight in the previous pregnancy (g)*	3574.9±878
Diabetes mellitus in a first-degree relative	132 (66%)
BMI (kg/m^2)	
Pre-pregnancy	29.7±5.3
Before insulin treatment	31.4±5.2
At the time of delivery	33.6±5.5
Weight gain during pregnancy (kg)	10.3±4.8
HbA1c	6.77±1.58
Type of diabetes	
Type 1 DM	22 (10.9%)
Type 2 DM	84 (41.6%)
Gestational DM	96 (47.5%)
Age at the time of diagnosis (years)**	28.2±9
Gestational age at the time of diagnosis (weeks)***	27.1±3.3
Multiple pregnancy	7 (3.5%)
Hyperemesis gravidarum	77 (38.1%)

Data represented as mean±standard deviation or n (percentage). *: If applicable; **: For pregestational diabetes; BMI: Body mass index; HbA1c: Hemoglobin A1c; DM: Diabetes mellitus.

Demographic and clinical characteristics of the cases are shown in Table 1. The mean BMI of the patients before pregnancy was 29.7±5.3 kg/m². The mean BMI just before the initiation of insulin treatment was 31.4±5.2 kg/m², and right before birth was 33.6±5.5 kg/m². The mean weight gain during pregnancy was 10.3±4.8 kg. The mean HbA1c level was 6.77±1.58.

A total of 114 (56.4%) patients had a history of oral antidiabetic treatment or insulin resistance. Accompanying preeclampsia was reported in 29 (14.4%) women, nephropathy in 9 (4.5%), and retinopathy in 3 (1.5%). Seventy-seven patients (38.1%) reported a history of hyperemesis gravidarum in the first trimester.

Forty-two (20.8%) patients had polyhydramnios in the third-trimester growth scan.

Fetal AC measurements were consistent with GA in 131 (64.9%) patients; however, 14 (6.9%) were below the 10th and 57 (28.2%) were above the 90th centile.

Eighty-four (63.2%) of the patients were hospitalized at least once during pregnancy due to non-regulated glycemic control. The number of pregnant patients with ketonuria was 63 (31.2%), with 49 (77.8%) of them exhibiting first-degree ketonuria.

Mean serum triglyceride levels were 255.2±155.6 mg/dL, HDL levels were 55.1±15.9 mg/dL, and LDL levels were 127.6±38.5 mg/dL.

Except for minor meal modifications performed at our outpatient clinic, diet regulation under the supervision of a nutritionist was required at least once in 32.2% of patients, twice in 40.6%, and three times in 19.8%.

The computed mean short-acting insulin dosage for all cases was 30.6±16.7 units, the mean long-acting insulin dose was 23.2±14.3 units, and the mean total insulin dose was 45±31.6 units.

A comparison of laboratory and clinical characteristics between pregestational and gestational diabetes is shown in Table 2. GDM patients gained more weight during pregnancy than preGDM (p=0.001). Compared to Type 2 DM and GDM, the BMI of Type 1 DM patients was considerably lower (p<0.001) in both instances. GDM had a lower HbA1c level compared to preGDM (p<0.001).

There was no statistically significant difference between GDM and preGDM regarding the occurrence of pregnancy and diabetes-related complications (preeclampsia, nephropathy, cardiopathy, retinopathy) (p>0.05).

There were no statistically significant differences found between hyperemesis gravidarum in the first trimester, polyhydramnios, fetal AC below the 10th or above the 90th centile, and the type of DM (p>0.05).

Mean fasting plasma glucose levels were not significantly different between GDM and preGDM groups (89.6% vs. 93.4% were >95 mg/dL, p=0.33). The GDM group had lower postprandial levels (64.6% vs. 84.9% were >140 mg/dL, p=0.001) and spot blood glucose levels than the preGDM group (102±26 vs. 131±56, p<0.001).

The frequency of need for hospitalization, length of stay, and number of outpatient visits did not differ across types of diabetes (Table 2).

In the GDM group, short-acting, intermediate-acting, and total insulin dosages were found to be lower than in the other groups (p<0.001) (Table 2).

HbA1c and spot plasma glucose levels were positively correlated with the total dose of insulin (Pearson correlation coefficient=0.46 and 0.39 respectively, p<0.001). Total insulin dose was significantly lower in patients who reported regular exercise compared to those who did not (37.1±28.9 U vs. 50.4±32.3 U, p=0.004).

The medium–long-acting insulin dosage (p=0.009) and total insulin dose (p=0.026) were found to be greater in individuals with a history of insulin resistance/oral antidiabetic treatment compared to those without.

There was an increase in short-acting insulin dosage (p<0.001), medium–long-acting insulin dose (p=0.027), and total insulin dose (p<0.001) when fasting plasma glucose and postprandial plasma glucose levels increased.

There was no statistically significant association between polyhydramnios, the LMP/AC difference, and the short-acting, medium–long-acting, and total insulin dosages.

However, a regression analysis was conducted to identify the independent impacts of variables that may influence insulin levels. The multivariate regression analysis showed that the quantity of short-acting insulin was significant (p=0.013) when

Table 2: Comparison of laboratory and clinical characteristics between pregestational and gestational diabetes

	Pregestational diabetes	GDM	p*
BMI (kg/m^2)			
Pre-pregnancy	30.2±5.6	29.1±4.9	0.080
Before insulin treatment	31.3±5.6	31.5±4.9	0.921
At the time of delivery	33.7±6	33.5±5.1	0.578
Weight gain during pregnancy (kg)	9.4±4.7	11.3±4.8	0.001
HbA1c	7.22±1.83	6.28±1.06	<0.001
Need for hospitalization	40 (41.6%)	44 (41.5%)	0.362
Length of hospital stay (days)	10.7±7.9	11.5±9.9	0.850
Number of additional outpatient visits	14±5	13±6	0.089
Ketonuria*	28 (26.4%)	35 (36.5%)	0.124
Total dose of insulin (U)	58.8±32.3	29.7±22.4	<0.001
Type of insulin			
Intermediate acting (U)	27.9±15.2	17.6±10.9	<0.001
Short acting (U)	36±17.3	22.1±11.4	<0.001

*: At least once during pregnancy. Data presented as mean (standard deviation) and n (percentage). GDM: Gestational diabetes mellitus; BMI: Body mass index; HbA1c: Hemoglobin A1c.

age, pre-pregnancy BMI, previous birthweight, presence of DM in a first-degree relative, and LMP/AC difference were included in the analysis. Age and LMP/AC difference were independently associated with the dose of short-acting insulin (p=0.049 and B=0.607 for age; p=0.012 and B=2.195 for LMP/AC difference). It was discovered that the level of short-acting insulin rose by 0.607 units for each 1-year increase in age, and the dosage increased by 2.195 units for each 1-unit increase in the LMP/AC difference (Table 3).

When age, pre-pregnancy BMI, prior birthweight, presence of DM in a first-degree relative, and LMP/AC difference were included in the equation, the cumulative influence of these variables on the quantity of medium–long-acting insulin was shown to be statistically significant (p=0.001). Pre-pregnancy BMI and LMP/AC difference independently influenced the amount of medium–long-acting insulin (p=0.018 and B=0.351 for pre-pregnancy BMI; p=0.021 and B=1.705 for LMP/AC difference). It was found that the medium–long-acting insulin level increased by 0.351 units for each 1-unit rise in pre-pregnancy BMI and by 1.705 units for each 1-unit increase in the positive LMP/AC difference.

When age, pre-pregnancy BMI, prior birthweight, presence of diabetes in a first-degree relative, and LMP/AC difference were added to the equation, the cumulative influence of these variables on the total quantity of insulin was statistically significant (p=0.002). Age and LMP/AC difference independently influenced the total insulin level (p=0.038 and B=1.093 for age; p=0.005 and B=4.390 for LMP/AC difference). It was discovered that the total insulin level increased by 1.093 units for every 1-year increase in age and that the total insulin dosage increased by 4.390 units for every 1-unit rise in the positive LMP/AC difference.

Table 3: Prevalence of hyperemesis, LMP-AC difference, polyhydramnios, and insulin dosage

	Short acting insulin (U)	Intermediae-long acting insulin (U)	Total insulin dose (U)
Hyperemesis gravidarum			
No; (n=125)	30.3±17.8	22.7±14.2	43.8±32.2
Yes; (n=77)	31.1±14.9	24±14.5	47±30.7
p*	0.489	0.515	0.373
Polyhydramnios			
No; (n=160)	30.4±15.3	22.9±13.9	44.2±30.2
Yes; (n=42)	31.3±21.1	24.3±16.1	48±36.5
p*	0.646	0.766	0.722
Difference LMP/AC			
<0 2SD<; (n=14)	23.7±14.1	20.2±11.7	37.4±26.4
0 2SD; (n=131)	29.8±15.2	21.9±13.6	42.6±29.5
>0 2SD>; (n=57)	34±19.6	26.8±15.9	52.3±36.3
p**	0,200	0.095	0.180

*: Mann-Whitney U Test; **: Bonferroni-adjusted Kruskal-Wallis Test; LMP: Last menstrual period; AC: Abdominal circumference; SD: Standard deviation.

DISCUSSION

For the best results in a pregnancy complicated by diabetes, good glycemic management is essential. Blood glucose monitoring conducted by patients with calibrated instruments, self-monitoring, or the results of measurements taken by us with standardized devices is essential for altering insulin therapy.[4]

As important as hyperglycemia is, hypoglycemia in pregnant women is equally crucial for maintaining tight glycemic control and ensuring the health of both mother and baby. This situation is delicately balanced. Adjustments to the insulin dosage and regimen should be made with these factors in mind,[9] and immediate glycemic control should be accomplished.

The need for insulin fluctuates throughout the day. During the night, insulin levels in pregnant women are low. It peaks at sunrise and decreases progressively over the remainder of the day. It is crucial, based on this equilibrium, to adjust the insulin regimen without upsetting the endogenous insulin balance.[10] Pregnancy is generally associated with baseline insulin resistance. Insulin treatment is essential for optimal glucose control during pregnancy.[11]

Numerous variables influence insulin treatment. The effectiveness of the therapy depends on the dose and schedule of insulin chosen with these considerations in mind. Options for appropriate insulin treatment should be reviewed, evaluated, and selected.[10]

The body mass index is one of the most important factors influencing insulin levels. Although a high BMI is the most well-known risk factor for Type 2 DM and GDM, Type 1 DM develops independently of BMI and is more prevalent in individuals with a low BMI.[12] However, the quantity of insulin is unrelated to this circumstance. Given that it is estimated based on BMI, a positive association is anticipated. McDonald et al.,[13] in their investigation, discovered that as the BMI of pregnant women increases, glycemic management becomes more difficult and treatment dosages increase. In our study, similar to previous research, the patient's pre-pregnancy weight, weight at the time insulin was initiated, and weight at the time of birth all raised the insulin dosage. However, in the cases included in our analysis, weight gain during pregnancy was statistically significantly greater in individuals with GDM compared to those without the condition. This indicates that a rise in BMI in women without pregestational diabetes promotes gestational diabetes as a secondary result.

HbA1c readings are used to measure the degree of glycemic control and to determine therapy in individuals with diabetes mellitus.[7,12] In the literature, research indicates that elevated HbA1c levels are associated with high blood glucose levels and the requirement for higher insulin dosages. Sacks et al.[14] discovered that HbA1c values reflect blood glucose control during the past two months and that these findings can influence therapy. In our study, rising HbA1c levels led to a substantial rise in the doses of short-acting, medium–long-acting, and total insulin for all types of diabetes. These findings are consistent with the published literature.

Changes in glucose metabolism, including partial insulin resistance and islet cell failure, may be connected with the aging process.[15] Early-diagnosed individuals are more fortunate in terms of therapy and management of complications, but extended exposure to diabetes results in physiological deterioration and a greater demand for insülin.[16] The average age at which our patients were diagnosed was comparable to that reported in the literature. However, the average age at which pregestational diabetes patients were identified and the week of gestation at which gestational diabetic patients were diagnosed did not significantly affect the quantity of insulin administered. Parallel to this, we discovered that the short-acting insulin level increased by 0.607 units and the total insulin level increased by 1.903 units with increasing age.

In research, it has been demonstrated that the glucose levels of primiparous pregnant women are lower than those of multiparous pregnant women who have previously given birth. In particular, a difference in fasting plasma glucose levels has been noted. Multiparous diabetic pregnant women require more insulin than nulliparous diabetic pregnant women.[17] It is believed that pregnant women with a history of delivery have a greater incidence of abdominal adipose tissue than individuals who have never given birth.[18] Although not statistically significant, the medium–long-acting insulin levels used by patients were higher in multiparous individuals in our study, which is consistent with the literature. In terms of short-acting insulin levels, primiparous pregnant women required a lower insulin dosage. This raises the possibility of a counterargument related to postprandial plasma glucose levels. Nonetheless, this requires further research.

Numerous investigations into the frequency of glucose intolerance in twin pregnancies have stemmed from clinical interest in the association between placental size and the incidence of GDM. Even though hPL levels are higher in twin pregnancies, some studies have concluded—based on intravenous glucose tolerance test results—that twin gestation is not a risk factor for GDM.[19] Some researchers discovered that the incidence of diabetes did not rise with multiple pregnancies, nor did blood glucose levels or insulin consumption.[20] In our investigation, it was determined that the average doses of short-acting insulin, medium–long-acting insulin, and total insulin in singleton pregnancies were greater than in multiple pregnancies. The literature supports this distinction.

Among diabetes risk factors, family history is one of the most well-known.[12] Genetic mutation contributes to the progression of the disease, as does the similar lifestyle of family members. This is especially relevant for Type 2 DM and GDM. Although lifestyle may be associated with the emergence of Type 1 diabetes symptoms, the fundamental etiology of the disease is hereditary.[21] In our study, 60% of individuals with Type 2 diabetes and 62.8% of patients with GDM had a first-degree relative with diabetes. This was reflected in insulin dosage as follows: short-acting insulin dose and total insulin dose were lower in patients without a family history of diabetes, although medium–long-acting insulin dose was comparable. A finding consistent with previous research on this topic has been observed.[22]

Preeclampsia is one of the most dreaded pregnancy complications. It is believed that insulin resistance also contributes to the pathophysiology of preeclampsia. Compared to normotensive pregnant women, women with preeclampsia are more likely to develop diabetes and require insulin.[23] This effect is associated with numerous preeclampsia risk factors, including obesity, advanced maternal age, race, chronic hypertension, diabetes, and gestational diabetes.[24] This is partially explained by the fact that it is associated

with insulin resistance, which includes obesity, advanced maternal age, race, chronic hypertension, and diabetes. However, according to the studies of Hauth et al.,[25] pre-diagnosed diabetes or insulin resistance developing at 22–26 weeks of gestation, even after correcting for these common risk factors, is an independent risk factor for preeclampsia, and the need for insulin is greater in diabetes with concomitant preeclampsia. In our study, 14% of the cases were associated with preeclampsia. In all three groups, the insulin dose increased by 10, 13, and 23 units for the short-acting, medium–long-acting, and total insulin doses, respectively. Although this result was not statistically significant, it suggests that the control of blood sugar becomes more challenging when preeclampsia is present.

Retinopathy and nephropathy, which are among the additional illnesses or complications of diabetes, are also caused by vascular disease—one of the mechanisms behind the development of preeclampsia.[1] Various studies have also revealed an association between insulin use and the development of diabetic retinopathy.[26] Multiple studies have demonstrated that insulin usage increases the risk of diabetic retinopathy. There is a need for multicenter research with larger patient groups to determine whether this is associated with diabetes exposure severe enough to necessitate insulin administration or related to the insulin dosage itself.[27] In our investigation, individuals with concomitant retinopathy had a short-acting insulin dosage approximately 10 units higher than those without retinopathy, although this difference was not statistically significant. There was no increase in medium–long-acting insulin dosage.

In diabetic nephropathy, the decline in kidney function impacts the metabolism of carbohydrates and insulin, consequently altering insulin requirements. There is research indicating that some forms of insulin may require a dosage reduction, while others may require an increase. This scenario is dependent on the individual's renal function.[28] In our study, 4.5% of patients had concomitant nephropathy. There was no variation in short-acting insulin or total insulin doses among patients with nephropathy, and there was only a small, statistically insignificant rise in medium–long-acting insulin dosage.

Exercise is one of the most crucial lifestyle modifications for diabetic pregnant women. In our clinic, we advise all diabetic patients to walk briskly in a straight line for 15–20 minutes after each meal, prior to taking insulin. We encourage insulin-treated individuals to maintain this exercise routine. As reported by researchers, exercise compliance was observed in 40% of the patients examined. There was a substantial decrease in short-acting insulin dosage, medium–long-acting insulin dose, and total insulin dose in patients with exercise compliance compared to those without exercise compliance.[29]

Although nausea and vomiting occur in 50–90% of pregnancies, hyperemesis gravidarum occurs only in 0.3% to 2% of cases. The relationship between hyperemesis and gestational diabetes has been the subject of fewer studies than the association between hyperemesis and childhood diabetes.[30]

In our study, 50% of pregnant women with Type 1 diabetes had a history of hyperemesis. We believe that the association between Type 1 diabetes and biochemical pathways may explain this finding, as Type 1 diabetes was more prevalent than Type 2 DM and GDM in our cohort. The effect of hyperemesis on insulin levels was not observed. However, in pregestational diabetes types, it is important to note that vomiting during the first trimester may affect blood glucose homeostasis and necessitate a new insulin regimen.[31]

Inpatient requirements for diabetic pregnant women may be related to the inability to manage blood sugar, insulin-induced hypoglycemia crises, or the patient's inability to self-monitor insulin therapy. Among the subjects included in our analysis, the Type 1 DM group required hospitalization the most. However, even in this group, hospitalization was required three times or fewer at a rate of 88.9%. We believe this is due to care being provided in a disease-specific polyclinic, regular dietician oversight, and education by a diabetes nurse. Although not statistically significant, we found that the frequency of hospitalization and the total duration of hospital stay led to an increase of approximately 13 units in the total insulin dosage.

Ketonuria in diabetic individuals is caused by insulin deficiency. When the body lacks the insulin needed to utilize energy sources, it begins to produce and use ketones through the metabolism of adipose tissue.[12] In our study, ketonuria was rarely identified, especially among individuals with gestational diabetes. We found that individuals with ketonuria required lower insulin dosages than those without ketonuria. However, this difference was not statistically significant.

Pregnancy induces physiological modifications to lipid metabolism. This contributes to metabolic harmony between mother and child. When maternal metabolic demands are fulfilled with high triglyceride concentrations, glucose is preserved for the fetus. Elevated blood LDL cholesterol levels promote the production of steroids by the placenta. In summary, the second and third trimesters of pregnancy are characterized by fat deposition.[32]

Triglyceride readings are typically 60 mg/dL in healthy non-pregnant women, 75–100 mg/dL in early pregnancy, and 210 mg/dL in late pregnancy. Serum LDL cholesterol levels are 105 mg/dL in non-pregnant women, 100–125 mg/dL in early pregnancy, and 150 mg/dL in late pregnancy. Serum HDL cholesterol levels should be 55 mg/dL in non-pregnant women, 55–75 mg/dL in early pregnancy, and 65 mg/dL in later weeks of pregnancy.[33] The individuals in our research had mean values that were higher than predicted. We believe this condition is a result of the obesity and metabolic syndrome underpinning the diabetes process. This circumstance has a negligible influence on the amount of insulin used. Given that the amount of insulin is determined according to weight, a patient with a high lipid profile is likely to require a greater dose of insulin.

Insulin resistance was a prior condition for 39% of the research participants with GDM diagnoses. This demonstrates that gestational diabetes may be minimized with lifestyle modifications, counseling for women contemplating pregnancy, and weight control. Short-acting, medium–long-acting, and total insulin doses increased significantly among pregnant women with Type 2 diabetes and GDM. We believe that the increase in dosage is associated with the rise in insulin resistance and the increase in the BMI of the patients.

Our study also reveals a correlation between the type of diabetes and the amount of insulin administered. Even if the BMI is

higher, the quantity of insulin needed in pregestational diabetes is more than that used in gestational diabetes. Due to the physiology of gestational diabetes, there is no long-term insulin resistance; control may be obtained with much lower doses. This reduces the adverse effects of insulin (hypoglycemia, etc.) and enhances patient adherence to therapy.[34]

The most noticeable finding of our investigation is the correlation between the ultrasound-measured abdominal circumference of the fetus and the projected abdominal circumference based on gestational week, and the quantity of insulin. In the third-trimester ultrasound assessments, the difference between the fetal abdominal circumference measured by experienced obstetricians at our hospital and the expected fetal abdominal circumference based on gestational age represents a factor that influences insulin requirements independently of other variables. In our regression equation, a 1-week difference between LMP and AC results in an increase of 2.195 units for short-acting insulin, 1.705 units for medium–long-acting insulin, and 4.390 units for total insulin. As corroborated by the research of Gilmartin et al.,[35] these results indicate that blood glucose regulation is directly associated with prenatal macrosomia, and we should not hesitate to raise the insulin dose to avoid fetal macrosomia and its sequelae.

The greatest limitation of our study is that it was conducted at a single center using a retrospective methodology. However, one of its major strengths is that it includes a relatively large sample of 202 insulin-using pregnant women, encompassing Type 1 DM, Type 2 DM, and GDM groups. The rising incidence of diabetes globally increases the frequency of pregnancies complicated by diabetes. Our goal is to manage this condition optimally, to ensure patients continue therapy with minimal adverse effects, and to achieve favorable pregnancy outcomes for both mother and baby.

CONCLUSION

At Zeynep Kamil Training and Research Hospital, we continuously monitor patients enrolled in our Diabetic Pregnancy program to provide the best possible care for the growing population of pregnant women with diabetes. Through our dedicated outpatient follow-up department and perinatology polyclinic—and, when necessary, through hospitalization in the perinatology ward—we aim to ensure comprehensive management. By working as a multidisciplinary team with nutritionists and diabetes nurses, we can achieve better pregnancy outcomes with lower medication dosages.

Unquestionably, pre-pregnancy education and public awareness efforts must be expanded globally to reduce the prevalence of diabetes in pregnancy. To ensure these patients receive the care they require, our hospital must further expand outpatient services dedicated to this specific population. This is vital so that these pregnant women are not overlooked and can be monitored separately from other obstetric cases.

To gain a clearer understanding of the factors influencing insulin requirements, further multicenter studies involving larger and more precisely selected patient groups are needed.

Patient education and interdisciplinary teamwork will undoubtedly yield far more favorable outcomes.

Statement

Ethics Committee Approval: The University of Health Sciences, Turkey. Istanbul Zeynep Kamil Maternity and Children's Diseases Health Training and Research Center Ethics Committee granted approval for this study (date: 05.05.2017, number: 96).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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