ORİJİNAL MAKALE / ORIGINAL ARTICLE

Sağlık Bilimlerinde Değer / Sağlık Bil Değer
Value in Health Sciences / Value Health Sci
ISSN: 2792-0542 sabd@duzce.edu.tr 2023; 13(2): 222-226
doi: https://dx.doi.org/10.33631/sabd.1199501

Estimation of Birth Weight from HbA1c and Glucose Levels in Diabetic Pregnancies

Kamuran SUMAN [1], Ebru GÖK [2], Zafer BÜTÜN [3], Pınar BÜTÜN [3], Musa BÜYÜK [4], Murat SUMAN [5]

ABSTRACT

Aim: The aim of this study was to investigate the sensitivity of baby birth weight estimation in relation to HbA1c levels of pregnant women diagnosed with pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM).

Material and Methods: 105 patients who met the criteria agreed to participate in our study, of whom 7 were type 1 DM and 32 were type 2 DM. The pregnancy history of the patients who agreed to participate was obtained with a lot of demographic information as well as weight gains during pregnancy, HbA1c and fasting blood glucose levels.

Results: Fasting glucose values were measured at 28 and 32 weeks of gestation. The blood glucose values that we measured one hour after satiation and HbA1c were higher in the PDGM group than in the GDM group. There was no significant difference between weight gain and BMI values. We used ROC curve analysis to test the predictive power of fasting and postprandial blood glucose levels or weight gain during pregnancy in our patients with GDM for LGA babies(LGA) (AUC: 0.663, %95 CI [0.526, 0.800], AUC: 0.678, %95 CI [0.540, 0.816], AUC: 0.677, %95 CI [0.548, 0.805], respectively).In addition, ROC analysis was used in evaluating fasting blood glucose measurements, 1-hour postprandial blood glucose measurements, and HbA1c levels to predict LGA.(AUC: 0.889, %95 CI [0.782, 0.996], AUC: 0.893, %95 CI [0.737, 1.000], AUC:0.931, %95 CI [0.807, 1.000], respectively).

Conclusion: In both healthy people and pregnant women, it is important to keep blood glucose levels within normal limits. In pregnant women diagnosed with PDGM or GDM, this is even more important as the welfare of the baby is considered. LGA deliveries can be avoided in pregnant women with PDGM by close monitoring of postprandial blood glucose and HbA1c levels. Close monitoring of GWG is also beneficial in the follow-up of pregnant women diagnosed with GDM.

Keywords: HbA1c; fasting glucose level; postprandial glucose level; birth weight.

Diyabetik Gebelerde HbA1c ve Glukoz Düzeylerinin Doğum Ağırlığı Tahmininde Kullanılması

ÖZ

Amaç: Bu çalışmanın amacı, pregestasyonel diyabet mellitus (PGDM) ve gestasyonel diyabet mellitus (GDM) tanısı konan hamilelerin HbA1c düzeyleri ile ilişkili olarak bebek doğum ağırlığı tahmininin duyarlılığını araştırmaktır.

Gereç ve Yöntemler: Kriterleri karşılayan 105 hasta çalışmamya dahil edildi. Hastaların 7'si tip 1 DM ve 32'si tip 2 DM idi. Katılmayı kabul eden hastaların gebelik öyküleri, demografik bilgilerinin yanı sıra gebelik süresince kilo alımları, HbA1c ve açlık kan şekeri düzeyleri de dahil olmak üzere kayıt edildi.

Bulgular: Açlık glukoz değerleri, gebeliğin 28 ve 32. haftalarında ölçüldü. Tokluk sonrası bir saatte ölçtüğümüz kan glukoz değerleri ve HbA1c, PDGM grubunda GDM grubuna göre daha yüksekti. Kilo alımı ve BMI değerleri arasında anlamlı bir fark yoktu. GDM'li hastalarımızda açlık ve tokluk sonrası kan glukoz seviyeleri veya gebelik sırasında kilo alımının LGA bebekleri (LGA) öngörmedeki tahmin gücünü test etmek için ROC eğrisi analizi kullandık (sırasıyla AUC: 0.663, %95 CI [0.526, 0.800], AUC: 0.678, %95 CI [0.540, 0.816], AUC: 0.677, %95 CI [0.548, 0.805]). Ayrıca, LGA'yı öngörmek için açlık kan glukoz ölçümleri, 1 saatlik tokluk sonrası kan glukoz ölçümleri ve HbA1c düzeylerini değerlendirmede ROC analizi kullanıldı (sırasıyla AUC: 0.889, %95 CI [0.782, 0.996], AUC: 0.893, %95 CI [0.737, 1.000], AUC: 0.931, %95 CI [0.807, 1.000]).

Sonuç: Sağlıklı insanlarda ve gebelerde kan glukoz seviyelerinin normal sınırlar içinde tutulması önemlidir. PDGM veya GDM tanısı konan gebelerde ise bebek sağlığı göz önünde bulundurularak bu daha da önemlidir. PDGM'li gebelerde tokluk sonrası kan glukoz ve HbA1c seviyelerinin yakın takibiyle LGA doğumları önlenebilir. GDM tanısı konan gebelerin takibinde de GWG'nin yakın takibi faydalıdır.

1 Afyonkarahisar State Hospital, Departmant of Perinatology, Ayyonkarahisar, Turkey
2 Erciyes University,Department of Pediatrics, Kayseri, Turkey
3 Eskisehir City Hospital, Department of Pediatrics, Kayseri, Turkey
4 Cay State Hospital, Department of Gynecology and Obstetrics, Afyonkarahisar, Turkey.
5 Cay State Hospital, Department of Pediatrics, Afyonkarahisar, Turkey.

Sorumlu Yazar / Corresponding Author: Murat Suman, e-mail: muratsuman@hotmail.com

Geliş Tarihi / Received:04.11.2022 Kabul Tarihi / Accepted:31.03.2022

Anahtar Kelimeler: HbA1c; açlık glukoz düzeyi; doğum ağırlığı, tokluk glikozu.

INTRODUCTION

Diabetes mellitus (DM), which affects a significant portion of women of reproductive age, is defined as an increase in blood glucose level due to insufficient insulin production or the ineffectiveness of insulin. Hyperglycemia in pregnancy (HIP) is a metabolic disorder and may lead to gestational diabetes mellitus (GDM) or pregestational diabetes mellitus (PGDM) (1). HIP has been reported as 15.8% globally (2). PGDM refers to type 1 DM and type 2 DM diagnosed before pregnancy. While PGDM accounts for approximately 13-21% of DM in pregnancy, GDM accounts for the remaining proportion. Maternal, fetal and neonatal sequelae including polyhydramnios, high gestational age (LGA), fetal growth restriction (FGR), stillbirth and neonatal hypoglycemia, polycythemia, hyperbilirubinemia and respiratory distress are increased in DM (3). The main cause of these risks is hyperglycemia (4). Fetal hyperinsulinemia due to maternal hyperglycemia leads to fetal weight gain. Insulin is one of the most important factors in fetal growth and has a mitogenic effect by stimulating food intake in insulin-sensitive tissues. High birth weight , which is common in neonates of diabetic pregnant women, may cause birth trauma such as shoulder dystocia and also increases the cesarean delivery (5). The aim of this study was to investigate the sensitivity of baby birth weight estimation in relation to HbA1c levels of pregnant women diagnosed with pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM).

MATERIAL AND METHODS

In our clinic, a two-step approach is used in the diagnosis of GDM(6). American College of Obstetricians and Gynecologists recommends an oral 100-g glucose tolerance test (OGTT) performed one hour after the 50-g glucose challenge test (GCT) in pregnant women whose serum glucose is 140 mg/dl or more (24 to 28 weeks) (7). Carpenter and Coustan criterias are used for GDM diagnosis. OGTT is performed in pregnant women is 100 g after at least eight hours fasting (8). For fasting 95 mg/dl, for one hour 180 mg/dl, 155 mg/dl for two hours, and for three hours 140 mg/dl, at least two values above these thresholds diagnose the GDM (9). Conditions such as fetal anomalies diagnosed with maternal systemic disease or maternal smoking that could prevent us from obtaining healthy outcomes were our exclusion criteria. In addition, multiple pregnancies, which we thought might affect outcomes, were also excluded from the study. 105 pregnant women who met the criteria were included in our study. Of these 105 patients, 39 had PDGM and 66 had GDM. In this population, which formed our study group, The demographies of the patients were meticulously recorded. In addition, values such as weeks of gestation, fasting blood glucose and first hour postprandial blood glucose, week of gestation at delivery, HbA1c level, body mass index (BMI), and pregnancy weight gain (GWG) were used in our records. We also used our records such as first and fifth-minute Apgar score, newborn weight, and percentiles of our babies. Birth weight greater than 90th percentile leads to the definition of LGA and warns us to watch for possible complications (10). Data from this multicenter study were obtained by our colleagues by performing file scans over a 6-month period between March and August 2021. The study was conducted with the consent of other centers of the city hospital, which is one of the centers included in our study, after obtaining the approvals of the local Ethics Committee (Ethics Committee num.17-22-E3).

Statistical Analysis

The sample size was calculated using G Power software (version 3.1; Franz Foul, Kiel College of Applied Sciences, Kiel, Germany). The effect size was 0.80 (large) for the sample size, the p-value was 0.05, and the power was 95%. It was planned to include at least 74 patients, 37 cases for each group. Statistical analyzes were performed with SPSS 26 software (SPSS, Inc., Chicago, IL, United States). Despirctive statistics such as mean, standard deviation, median, descriptive frequency, percentage, and interquartile ranges (IQR) are expressed the quantitative data. The normal distribution of variables was tested using the Kolmogorov-Smirnov test. Statistical comparisons between groups were performed with independent t-test for normally distributed variables. For variables that did not have a normal distribution, the Mann-Whitney U test was used. The chi-square test and Fisher's exact test were used to compare categorical data. Receiver operating characteristic (ROC) curve analysis was used to predict neonatal birth weight. The p-value < 0.05 was considered statistically significant.

RESULTS

Sociodemographic and clinical characteristics, biochemical data, and perinatal outcomes are listed in Table 1-2;with a close look at the tables HbA1c, Fasting glucose (mg/dl) and 1st-hour p.glucose (mg/dl) results show statistically significance. When we compared the groups in terms of LGA frequency, we found that 25 neonates were in the GDM group and 18 neonates were in the PGDM group. We have tried to summarize these results in Tables 3 and 4, there was no significance with GDM mother results in table 3 but when it comes to the results of PGDM mothers in table 4 there is an obvious significance as shown in the table.

Table 1. Sociodermographic results of mothers

	GDM	Mean+ SD	PGDM	Mean+ SD	p value
Age (years)	33	±6	31	±5	0.085*
Gravidity	3	±1	3	±1	0.364*
Parity	1	±1	1	±1	0.245*
Gestational age (Weeks)	30.6	±1.4	30.2	±1.8	0.687*
Pre-preg.BMI (kg/m^2)	29.1	±4.8	28.4	±3.7	0.074*
GWG (kg)	9	±3	10	±4	0.452*
HbA1c (%)	5.8	±0.7	6.9	±1.5	<0.001*
Fasting glucose (mg/dl)	85	±16.5	99.2	±25	<0.001*
1st-h p.glucose (mg/dl)	138.1	±28.9	145	±45	<0.001*
GA at delivery (weeks)	37	±2	37	±2	0 .775*

* Independent t-test

Table 2. Birth characteristics and results of newborn

	GDM Mean+SD	PGDM Mean+SD	P val.
Birth weight (grams)	3157 ±590	3422 ±656	0.087*
Birth weight (percentile)	69.3 ±25.6	75 ±23.3	0.154*
LGA	25 (37.9%)	18 (46.2%)	0.405†
1st minute APGAR score	7 (7-8)	7 (7-8)	0.645‡
5th minute APGAR score	9 (9-10)	9 (9-9)	0.795‡

* Independent t-test
† Chi-square test
‡ Mann Whitney U tes

Table 3. GDM pregnancies and LGA& AGA results

	LGA (n=25)	Median IQR*	AGA (n=41)	Median IQR*	p val.
HbA1c (%)	7.6	(7.2-8.7)	5.7	(5.1-6.3)	0.327‡
Fasting glu.(mg/dl)	114	(94-126)	88	(78-93)	0.027‡
1st-hour p.glu. (mg/dl)	167	(157-212)	114	(111-127)	0.016‡
Pre-preg.BMI (kg/m²)	28.4	(27.7-32.2)	28.3	(26.9-30.4)	0.247‡
GWG (kg)	10	(9-12)	9	(8-10)	0.015‡

*(IQR (Inter Quartile Range))
‡ Mann Whitney U test

Table 4 . PGDM pregnancies and LGA& AGA results

	LGA (n=18)	Median IQR*	AGA (n=21)	Median IQR*	p val.
HbA1c (%)	7.6	(7.1-8.9)	5.8	(5.3-6.7)	<.001‡
Fasting glu.(mg/dl)	114	(94-126)	88	(78-93)	<.001‡
1st-hour p.glu. (mg/dl)	167	(157-212)	114	(111-127)	<.001‡
Pre-preg.BMI (kg/m²)	27.6	(25.2-29.7)	27.7	(26.5-30.4)	0.364‡
GWG (kg)	11	(8-12)	12	(8-12)	0.813‡

*(IQR (Inter Quartile Range))
‡ Mann Whitney U test

We used ROC curves to estimate LGA in groups and tried to summarize them in Figures 1 and 2. We examined values such as fasting and postprandial glucose levels and GWG for our LGA estimates in pregnant women with GDM using ROC analysis. (AUC: 0.663, %95 CI [0.526, 0.800], AUC: 0.678, %95 CI [0.540, 0.816], AUC: 0.677, %95 CI [0.548, 0.805], respectively). ROC curve analysis was also used to determine fasting glucose, first-hour postprandial glucose, and HbA1c to predict LGA in the PGDM group (AUC: 0.889, %95 CI [0.782, 0.996], AUC: 0.893, %95 CI [0.737,1.000], AUC: 0.931, %95 CI [0.807, 1.000], respectively).

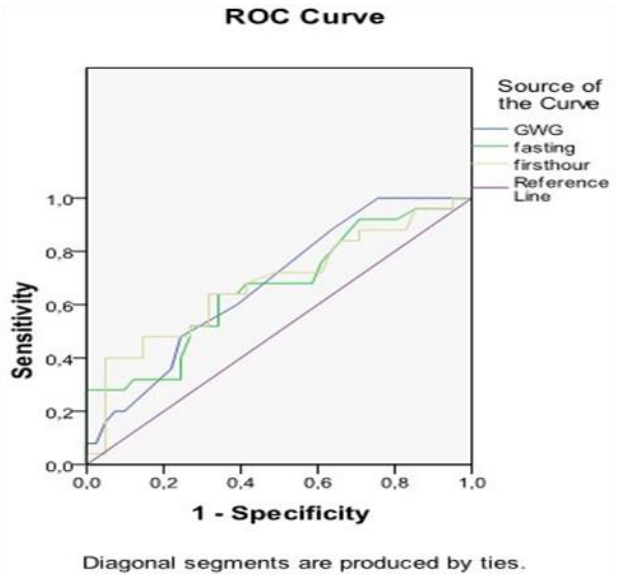

Figure 1. GDM group's Fasting glucose, 1st-hour postprandial glucose, and GWG estimating the LGA

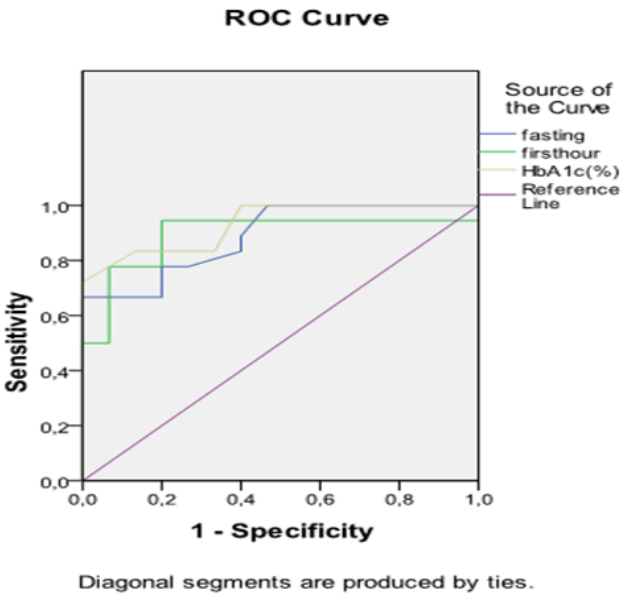

Figure 2. PGDM group's Fasting glucose, 1st-hour postprandial glucose, and GWG estimating the LGA

DISCUSSION

The present study showed that, first-hour postprandial glucose,fasting glucose and HbA1c levels were higher in the PGDM group than in the GDM group, whereas GWG and BMI levels before pregnancy were similar. In addition, HbA1c, blood glucose in the first hour, and fasting blood glucose to predict LGA were higher in the PGDM group. First-hour postprandial glucose, GWG, and fasting glucose ability to predict LGA were higher in the GDM group. Glucose tests are inexpensive and easy to use. They also reflect immediate changes in blood glucose levels. One study comparing type 1 DM with a control group found that levels of postprandial glucose measured in the third trimester were the strongest predictor of macrosomia (11). Other studies have similarly demonstrated the importance of postprandial blood glucose levels. The present study showed that for the predictive power of LGA of first-hour postprandial glucose, a sensitivity of 64% and a specificity of 68% were achieved with a cut-off value of 140.5 mg/dl in the GDM group. Moreover, for the predictive power of LGA of first-hour postprandial glucose, a sensitivity of 94% and a specificity of 80% were achieved with a cut-off value of 128.5 mg/dl in the PGDM group. In contrast, a sensitivity of 78% and a specificity of 80% at a cut-off value of 93.5 mg/dl in the PGDM group were achieved for fasting glucose. Our study showed that postprandial blood glucose significantly predicted LGA, especially in PGDM compared with the GDM group. We also showed that postprandial blood glucose significantly predicted LGA compared with fasting blood glucose in the PGDM group. HbA1c is a commonly used test for chronic glycemic control that reflects the average blood glucose level over the past one to two months, especially in pregnant women with PGDM. Because of increased hemodilution and the rate of erythrocyte destruction during pregnancy, levels of HbA1c are lower in pregnant women than in non-pregnant. The use of the HbA1c test, performed every 4-5 weeks in pregnant women with GDM, has not been shown to be useful as a parameter for glycemic control. Birth weight correlated significantly with HbA1c level measured at different time points in the PGDM group. For example, in a prospective study, HbA1c measured in the third trimester was the strongest predictor of macrosomia in 289 pregnant women with type 1 DM (12). Abnormalities in serum glucose levels less occur in the GDM group than in the PGDM group. For this reason, the evidence for an association between HbA1c and birth weight is weaker in the GDM group. Many studies have examined HbA1c levels at the time of OGTT (13). There is no clear association between HbA1c levels and infant birth weight in the early period. However, the association between HbA1c levels and macrosomia has been more clearly demonstrated. Therefore, the HbA1c level just before birth can be measured to predict birth weight in the GDM group. Similarly, in our study, HbA1c strongly predicted LGA in the PGDM group (14). The present study showed that the predictive power of HbA1c for LGA at a cut-off value of 6.55 in PGDM had a sensitivity of 93% and a specificity of 87%. Because the HbA1c level has weak predictive power for LGA in the GDM group, measurement of the HbA1c level can be planned just before delivery, especially in the GDM group. The risk of GDM is increased, especially in overweight or obese women before pregnancy, and GWG should be carefully monitored (15). In studies, excessive GWG has been associated with cesarean section, hypertension, LGA, inability to lose weight gained after delivery, and increased risk of diabetes. The present study showed that the predictive power of GWG for LGA,which is sensitivity of 60% and specificity of 61% was performed at a cut-off weight of 11.5 kg for GDM. In contrast, fasting glucose had a sensitivity of 64% and specificity of 66% at a cut-off value of 84.5 mg/dl for GDM. Our study demonstrated that GWG is more valuable than fasting glucose and HbA1c for predicting LGA in pregnant women with GDM. In addition, glycemic control and GWG should be closely monitored.

One of the study's limitations is its design which is retrospective and the calculation of the BMI of the pregnant women before pregnancy based on their self-reported body weight. In addition, maternal blood glucose markers were measured only once and there were no repeated measurements. In addition, the number of pregnant women with type 1 DM in the study was very small (n=7).

CONCLUSION

Glycemic control is critical in pregnant women with PGDM and GDM. The risk of LGA may diminish by monitoring of HbA1c better and postprandial glucose in PGDM and GWG in GDM. Better control of fetal overgrowth may have a positive impact on the risk of childhood obesity and related metabolic syndrome. This positive impact may develop in the long term, and improve the cardiometabolic profile. For this reason, the parameters that can predict LGA in the early stages of pregnancy are very valuable.

Authors's Contributions: Idea/Concept: K.S., E.G., M.S.; Design: K.S., E.G., M.B., M.S.; Data Collection and/or Processing: H.S., K.A., M.B.; Analysis and/or Interpretation: Z.B., P.B., M.B.; Literature Review: Z.B., P.B.; Writing the Article: K.S., E.G., M.S.; Critical Review: Z.B., P.B.

REFERENCES

1. Kansu-Celik H, Ozgu-Erdinc AS, Kisa B, Eldem S, Hancerliogullari N, Engin-Ustun Y. Maternal serum glycosylated hemoglobin and fasting plasma glucose predicts gestational diabetes at the first trimester in Turkish women with a low-risk pregnancy and its relationship with fetal birth weight; a retrospective cohort study. The Journal of Maternal-Fetal & Neonatal Medicine. 2021; 34(12): 1970-7.
2. Immanuel J, Simmons D, Desoye G, Corcoy R, Adelantado JM, Devlieger R, et al. Performance of early pregnancy HbA1c for predicting gestational diabetes mellitus and adverse pregnancy outcomes in obese European women. Diabetes research and clinical practice. 2020; 168: 108378.
3. Abdelsttar MM, Omarah MA, Abdelgaied AM, El-Sharkawy MA. Role of glycosylated hemoglobin in prediction of birth weight and amniotic volume in gestational diabetes. Menoufia Medical Journal. 2018; 31(4): 1258.
4. Fayez Mohamed Fathi M, Mohammed Moustafa T, Ramadan Alsawy Rady I. The role of umbilical cord thickness and glycated hemoglobin (hba1c) levels for prediction of fetal macrosomia in patients with gestational diabetes mellitus. Al-Azhar Medical Journal. 2020; 49(4): 1741-52.
5. Kumar N, Kumar P, Harris N, Monga R, Sampath V. Impact of maternal HbA1c Levels≤ 6% and race in nondiabetic pregnancies on birthweight and early neonatal hypoglycemia. The Journal of pediatrics. 2020; 227: 121-7. e3.
6. Belay DM, Bayih WA, Alemu AY, Sinshaw AE, Mekonen DK, Ayele AS, et al. Macrosomia and its predictors in pregnant women with diabetes in Ethiopia. Tropical Medicine & International Health. 2021;26(12):1539-52.
7. Wojtyla C, Stanirowski P, Gutaj P, Ciebiera M, Wojtyla A. Perinatal outcomes in a population of diabetic and obese pregnant women-the results of the polish national survey. International Journal of Environmental Research and Public Health. 2021; 18(2): 560.
8. Abolfathi M, Ashtarian H, Eskandari S, Irandoost SF, NeJhaddadgar N, Mirzaei N. Evaluation of quality of life in diabetic pregnant women. Primary Care Diabetes. 2022; 16(1): 84-8.
9. Lorusso L, Kato DMP, Dalla Costa NRA, Araujo Junior E, Bruns RF. Performance of local reference curve on the diagnosis of large for gestational age fetuses in diabetic pregnant women. The Journal of Maternal-Fetal & Neonatal Medicine. 2022; 35(10): 1899-906.
10. Hong JGS, Fadzleeyanna MYN, Omar SZ, Tan PC. HbA1c at term delivery and adverse pregnancy outcome. BMC pregnancy and childbirth. 2022; 22(1): 1-9.
11. Mañé L, Flores-Le Roux JA, Pedro-Botet J, Gortazar L, Chillarón JJ, Llaurado G, et al. Is fasting plasma glucose in early pregnancy a better predictor of adverse obstetric outcomes than glycated haemoglobin? European Journal of Obstetrics & Gynecology and Reproductive Biology. 2019; 234: 79-84.
12. Zhang X, Xiao Y, Fan Y. Investigating the reliability of HbA1c monitoring for blood glucose control during late pregnancy in patients with gestational diabetes mellitus (GDM) with and without β-thalassemia minor. Diabetes Therapy. 2018; 9(6): 2305-13.
13. Kaur N, Goel P, Mehra R, Kaur J. Correlation of HbA1c levels in late pregnancy with maternal and perinatal outcome in patients with gestational diabetes mellitus. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2019; 8(9): 3664-71.
14. Mendes N, Alves M, Andrade R, Ribeiro RT, Papoila AL, Serrano F. Association between glycated haemoglobin, glycated albumin and fructosamine with neonatal birthweight and large-for-date status infants in gestational diabetes mellitus: a prospective cohort study. Journal of Obstetrics and Gynaecology. 2019; 39(6): 768-73.
15. Bozkurt L, Göbl CS, Leitner K, Pacini G, Kautzky-Willer A. HbA1c during early pregnancy reflects beta-cell dysfunction in women developing GDM. BMJ Open Diabetes Research and Care. 2020; 8(2): e001751.