The effect of diabetes mellitus on fetal hemodynamic indices in late pregnancy and fetal birth weight

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The Effect of Diabetes Mellitus on Fetal Hemodynamic Indices in Late Pregnancy and Fetal Birth Weight

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Abstract

Background: One of the most prevalent adverse pregnancy outcomes is gestational diabetes mellitus (GDM). Different degrees of impaired glucose metabolism characterize GDM, typically diagnosed during pregnancy. Consistent economic growth, rising living standards, and introducing more stringent diagnostic criteria have all contributed to a rise in GDM morbidity in emerging nations in recent years.

Aim and objectives: The purpose of this study was to determine whether or not gestational diabetes has an impact on fetal hemodynamics, fetal growth indices, and birth weight.

Patients and methods: This cross-sectional prospective comparative study included 210 pregnant ladies between 36 and 40 weeks of gestation with their pregnancies complicated by GDM who attended Al Hussien Hospital and El Galaa Teaching Hospital till the finale of the study.

Results: There was a statistically significant difference among the studied groups as regards fetal parameters, fetal and birth weight, laboratory investigations, and neonatal outcome.

Conclusion: We suggest that clinicians can estimate a GDM's birth weight in late pregnancy using fetal Doppler hemodynamic indicators. There is a statically significant positive correlation between hemoglobin A 1c (HA1C) and biparietal diameter, head circumference, abdominal circumference, femur length, estimated fetal weight, birth weight, uterine artery resistance index (UARI), middle cerebral artery resistance index (MCARI), and a significant negative correlation between HA1C and UAPI, MCAPI, and middle cerebral artery/umbilical artery pulsatility index ratio.

Keywords: Fetal birth weight, Fetal hemodynamic indices, Gestational diabetes mellitus

1. Introduction

One of the most prevalent adverse pregnancy outcomes is gestational diabetes mellitus (GDM). Different degrees of impaired glucose metabolism characterize GDM, typically diagnosed during pregnancy. GDM morbidity has been rising over the past several years in emerging nations due to rising incomes, better living conditions, and the introduction of more precise diagnostic tools.[1]

Impaired glucose tolerance is one of the primary causes of maternal and fetal morbidity, and it affects 7.2% of all pregnancies in Egypt. This is a very concerning statistic.[2]

The most prevalent and potentially life-threatening newborn problem that is associated with GDM is macrosomia. A birth weight greater than 4000−4500 g and bigger than predicted for the gestational age, as well as a birth weight greater than the 90th percentile for population-specific and set-specific development curves, is considered to be a case of macrosomia. Macrosomia may also be defined as a birth weight greater than the 90th percentile for population-specific and set-specific growth curves.[3]

Because they are insulin-dependent tissues, the adipose tissues in the thighs, intrahepatic region, and abdominal area are more vulnerable fetal fat growth. This is especially true in the first trimester of pregnancy. There is a correlation between having an accumulation of fat in the truncal area and an increased risk of cephalopelvic disproportion, shoulder dystocia, and birth trauma. Additionally, having shoulders that are bigger than typical is associated with an increased risk of shoulder dystocia. Those who have been given a diagnosis of diabetic macrosomia have a significantly higher risk of developing type 2 diabetes.[4]

Ultrasound (US) is now the gold standard for determining fetal size by evaluating fetal growth indices. Biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) are all examples of such measurements. An ultrasonic device using Hadlock's formula to automatically determine the fetal weight. However, due to fetal asymmetric development features, US estimates of birth weight in GDM in late pregnancy are generally erroneous.[5]

The umbilical artery (UA) is the principal blood channel that carries blood and nutrients between the fetus and the placenta. It is also known as the umbilical vein. The fetus obtains oxygen and nutrients through the umbilical cord, and the systolic-to-diastolic ratio (S/D), the pulsatility index (PI), and the resistance index (RI) are all hemodynamic indicators of the fetoplacental circulation. The S/D, PI, and RI are the hemodynamic parameters of brain circulation that can be directly reflected by the fetal middle cerebral artery (MCA). The fetal middle cerebral artery is located in the center of the head. It is common for the renal artery (RA) to reflect the blood flow going to the embryonic kidney. The RA is an organ vulnerable to hypoxia and prone to developing endothelial dysfunction.[4,5]

2. Patients and methods

This cross-sectional prospective study involved 210 gravid women between 36 and 40 weeks of gestation with their pregnancies complicated by GMD who attended Al Hussien Hospital and El Galaa Teaching Hospital from May 2022 to June 2023 till the end of the study.

Group 1 contained 70 pregnant females with managed GD. Group 2 involved 70 pregnant females with uncontrolled GD and group 3 involved 70 pregnant females without either kind of diabetes.

All trial participants provided written informed permission after receiving counseling and having the benefits and unanticipated hazards of each surgery explained to them.

2.1. Inclusion criteria

In pregnancy with only one fetus, early US indicated a gestational age between 36 and 40 weeks from the mother's first day of last menstrual period. Mother's ages between 20 and 38, group 1 had an glycated haemoglobin (HbA1c) of less than 6.5% and a BMI between 20 and 34.9 kg/m^2; group 2 had an uncontrolled DM as measured by a fasting blood glucose concentration of 80—100 mg/dl; and group 3 had an uncontrolled DM as measured by fasting blood glucose concentration of more than or equal to 105 mg/dl and/or a serum glucose level of more than or equal to 140 mg/dl, 2 h after a 75 group 2: a previous diagnosis of uncontrolled diabetic mellitus. Counseling and clearance from the local ethics council of the Obstetrics and Gynecology Department at Al-Azhar University are required before patients may participate in the study.

2.2. Exclusion criteria

Gestational ages, BMI under 20 or over 34.9 kg/m^2, gestational age before 36 weeks or beyond 40 weeks. Previous diagnosis of gestational diabetes, intrauterine growth limitation, severe anemia, pregnancy-induced hypertension, and renal diseases are among other well-known conditions that reduce blood supply to the fetus. Patients who have had or are currently carrying a child with a birth defect, those who have a history of hyperlipidemia, those who smoke cigarettes, and those who refuse to participate in the study.

2.3. Methods

Every patient was given a comprehensive examination that included a review of their medical history, a physical exam, the usual laboratory tests, an US, and a Doppler US (Figs. 1 and 2).

2.4. Glycosylated hemoglobin

Whole blood was drawn according to protocol (1 cm). Anticoagulants like heparin or EDTA. At 2—8 °C, HbA1c remains steady for 7 days.[6,7]
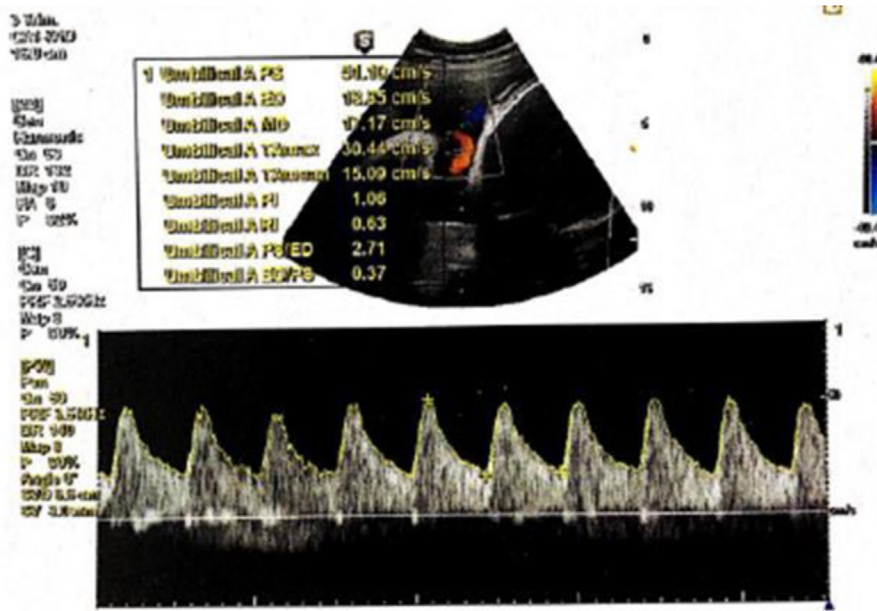
(a)

Figure 1. Doppler spectrum of ultrasound taken from the UA. UA, umbilical artery.
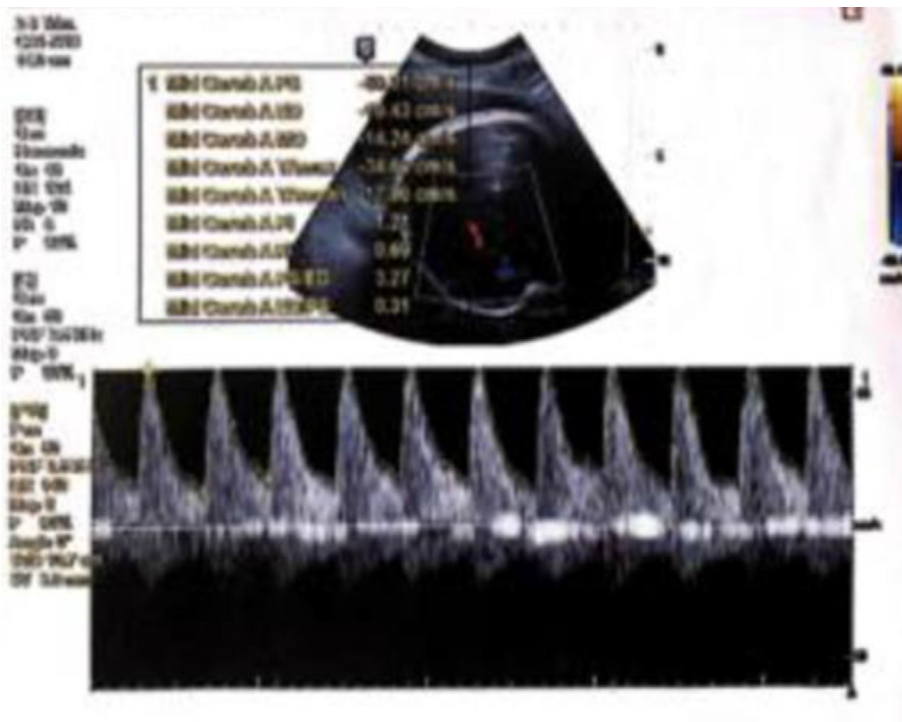
(b)

Figure 2. Doppler ultrasound of the middle cerebral artery; UA; MDC; S/D; PI; RI. PI, pulsatility index; RI, resistance index; S/D, systolic-to-diastolic ratio; UA, umbilical artery.

Principle of the method: during the process of making hemosylate, cation exchange resin is used to keep hemoglobins stable. Following the removal of the hemoglobin Aa+b portion, HbA1c is preferentially eluted, and its concentration is evaluated using direct photometric detection at 415 nm.

2.4.1. Procedure

Hemosylate preparation and labial fraction elimination. Column preparation. Separation and reading of HbACfraction. Reading of Hb total.

2.4.2. Additional equipment

Reference value: HbA1c 6.3%: very excellent glycemic control; HbA1c between 6.3 and 7.1%: good glycemic control; HbA1c between 7.1 and 9%: poor glycemic control; and HbA1c more than 9%: terrible glycemic control. Spectrophotometer or photometer with a 415 nm filter.

2.4.3. Statistical analysis design

The acquired data was evaluated and the coding was done by hand. The Statistic Package for the Social Sciences, Version 22 (IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA) for Windows, was used to do statistical analysis on these numerical codes.

2.4.4. Descriptive statistics

Quantitative data and qualitative data.

2.4.5. Analytical statistics

χ^2 analysis was used to compare the groups and one-way analysis of variance test.

We used a 95% confidence range for the coefficient. These P values were used to determine the significance level: P value less than 0.05.

3. Results

Table 1 showed that there is no statistically significant difference among the studied groups regarding GA, age, and BMI (Fig. 3).

Table 2 presented that fetal BPD, HC, AC, FL were statistically significant higher in the uncontrolled DM group than in the controlled DM and healthy group.

Table 3 showed that US Doppler parameters UAPI, MCAPI, and MCA/UA PI ratio have no statistically significant difference among controlled, uncontrolled DM, and healthy females.

Table 4 showed that FEW and birth weight were statistically significant higher in the uncontrolled DM group than controlled DM and healthy group.

According to the data shown in Table 5, the levels of hemoglobin A 1c (HA1C), FBG, and post prandial blood glucose (PBG) in the uncontrolled diabetes group were statistically significantly higher than those in the managed diabetes group and the healthy group.

Table 6 showed that there is statistically significant higher neonatal respiratory distress and NICU admission in the uncontrolled DM group than the controlled DM and healthy group.

4. Discussion

One of the main consequences of pregnancy is a condition known as GDM. During the gestational period, the first signs of gestational diabetes, which can manifest in varying degrees depending on their severity, are identified. The morbidity of GDM has gradually grown over the past several years in emerging nations due to ongoing economic growth, improvements in living conditions, and the use of new diagnostic criteria.[8]

The main results of this study were as follows:

GA, age, and BMI did not differ significantly across groups.

A previous study by Liu et al.[9] reported that 147 of 271 pregnant women had GDM and 124 did not. Both groups had similar maternal data ($P>0.05$).[9]

In an identical manner, Abd el Gawad and colleagues reported that a total of 180 females with GDM and 180 normal controls (NC) who presented between 38 and 40 weeks' gestation and had singleton pregnancies were recruited in this study.

Table 1. Clinical data of the studied population.

	Controlled DM		Uncontrolled DM		Healthy control		One-way ANOVA test	
	N=70		N=70		N=70			
	Mean	SD	Mean	SD	Mean	SD	F	P value
GA (weeks)	37.57	1.57	37.36	1.09	38.30	1.32	2.316	0.101
Age (years)	29.04	2.85	29.80	3.32	28.83	3.49	1.749	0.177
BMI	31.82	0.71	30.12	6.76	29.90	5.84	2.905	0.057

*Significant

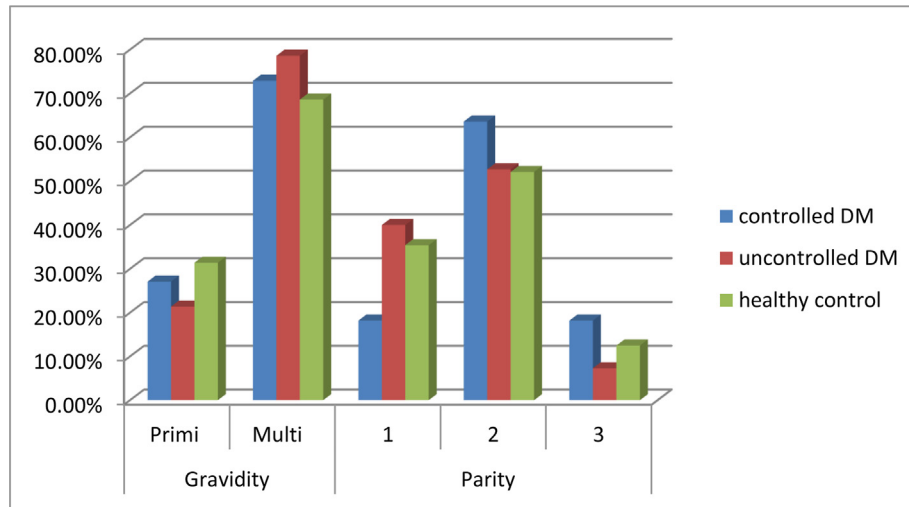ANOVA, analysis of variance; DM, diabetes mellitus.

Figure 3. Obstetric data of the studied population.

Table 2. Fetal parameters of the studied population.

	Controlled DM		Uncon-trolled DM		Healthy control		One-way ANOVA test	
	N=70		N=70		N=70			
	Mean	SD	Mean	SD	Mean	SD	F	P value
BPD	9.28	0.10	9.31	0.14	8.95	0.13	167.912	0.000*
HC	33.07	0.57	33.20	0.54	32.80	0.58	9.148	0.000*
AC	34.00	0.60	35.07	0.53	33.74	0.56	109.323	0.000*
FL	7.49	0.14	7.58	0.13	7.24	0.22	75.046	0.000*

AC, abdominal circumference; ANOVA, analysis of variance; BPD, biparietal diameter; DM, diabetes mellitus; FL, femur length; HC, head circumference.
  * Significant.

Table 3. Ultrasound Doppler parameters of the studied population.

	Controlled DM		Uncon-trolled DM		Healthy control		One-way ANOVA test	
	N=70		N=70		N=70			
	Mean	SD	Mean	SD	Mean	SD	F	P value
UAPI	0.82	0.07	0.83	0.08	0.82	0.04	1.628	0.199
UARI	0.56	0.06	0.57	0.08	0.56	0.08	1.281	0.280
MCAPI	1.37	0.03	1.38	0.07	138	0.07	1.963	0.143
MCARI	0.75	0.15	0.80	0.16	0.78	0.03	2.714	0.069
MCA/UA PI ratio	1.73	0.19	1.75	0.18	1.76	0.10	0.624	0.537

*Significant

ANOVA, analysis of variance; DM, diabetes mellitus; UARI, uterine artery resistance index; MCA, middle cerebral artery; RI, resistance index; MCARI, middle cerebral artery resistance index; PI, pulsatility index; UA, umbilical artery.

According to age, BMI, and gestational age, there was not a statistically significant difference between the two groups of females' clinical data ($P>0.05$).[10]

The findings of this study showed that there is no statistically significant difference among the groups that were investigated about the frequency of gravidity and parity.

Anness et al.'s[11] study included 141 pregnant women with GDM and 136 without diabetes and normal blood pressure. No group differed significantly in parity.

The results of this study exposed that uncontrolled diabetes was associated with significantly greater levels of fetal BPD, HC, AC, and FL compared to managed diabetes and the healthy group.

The findings of this study were backed up by a prior study conducted by Liu et al.,[9] who found that the BPD, HC, and AC of the fetus were all significantly increased in the GDM group in comparison to the NC group (all $P<0.05$).

In the study conducted by Abd el Gawad and colleagues, the independent samples t test showed that GDM had higher BPD, HC, AC, and FL than NC ($P<0.05$). GDM had a mean BPD of 9.29±0.23 mm, while NC had 9.08±0.32 mm. The mean HC was 33.14±0.67 mm in GDM and 32.56±0.84 mm in NC. The mean AC was 34.51±1.24 mm in GDM and 32.87±1.01 mm in NC. GDM had a mean FL of 7.56±0.21 mm, while NC had 7.20±0.28 mm.

The findings of this study indicate that the FEW and birth weight of infants born to women whose diabetes was not under control were considerably higher than those of children born to women whose diabetes was under control and healthy children.[10]

Consistent with these findings, Liu et al.[9] found that the birth weight of newborn to females with GDM was greater than that of infants born to females without GDM ($P<0.05$).

Table 4. Fetal and birth weight of the studied population.

	Controlled DM N=70		Uncontrolled DM N=70		Healthy control N=70		One-way ANOVA test	
	Mean	SD	Mean	SD	Mean	SD	F	P value
EFW	3437.86	74.91	3857.30	110.20	3359.53	88.54	66.784	0.000*
Birth weight	3627.00	102.47	4042.16	150.89	3352.96	125.17	518.042	0.000*

ANOVA, analysis of variance; DM, diabetes mellitus; EFW, estimated fetal weight.
* Significant.

Table 5. Laboratory investigations of the studied population.

	Controlled DM N=70		Uncontrolled DM N=70		Healthy control N=70		One-way ANOVA test	
	Mean	SD	Mean	SD	Mean	SD	F	P value
HA1C	5.93	0.30	10.02	1.29	5.11	0.52	672.62	0.000*
FBG	89.34	4.18	170.50	15.65	84.81	7.30	2375.49	0.000*
PBG	119.34	4.18	221.30	28.15	114.36	9.10	856.93	0.000*

ANOVA, analysis of variance; DM, diabetes mellitus; HA1C, hemoglobin A 1c; PBG, post prandial blood glucose.
* Significant.

Table 6. Neonatal outcome of the studied population.

	Controlled DM N=70 [n (%)]	Uncontrolled DM N=70 [n (%)]	Healthy control N=70 [n (%)]	χ^2 test	
				χ^2	P value
Outcome					
No complication	44 (62.9)	23 (32.9)	62 (88.6)	101.154	0.000*
TTN	16 (22.9)	27 (38.6)	2 (10)		
Need NICU	10 (14.3)	20 (28.6)	1 (1.4)		

DM, diabetes mellitus; NICU, neonatal intensive care unit; TTN, transient tachypnea of neonates.
* Significant.

In addition, the average birth weight of neonates in the GDM group was 3404 g, compared to 3243 g in the control group (P<0.01).[1]

Abd el Gawad et al.[10] found a highly statistically significant difference in the mean birth weights of neonates born to women with and without gestational diabetes, with the former having 3616.67±202.08 g and the latter having 3169.44±154.30 g.

The current study found that the risk of neonatal respiratory distress and NICU hospitalization was significantly greater in the uncontrolled DM group matched to the managed DM group and the healthy control group.

In agreement with the current study's finding, Li and colleagues conducted a meta-analysis showing that 24 papers were included from 23 total publications. Maternal diabetes was related to an amplified risk of newborn respiratory distress syndrome with an odds ratio of 1.47 [95% confidence interval (CI) 1.24−1.74], most notably in cohort studies (1.39, 95% CI 1.17−1.65). For women with GDM, the incidence of newborn respiratory distress syndrome was 1.57 (95% CI 1.28−1.93), and for women with PGDM the risk was 2.66 (95% CI 2.06−3.44).[12]

Positive correlations were found between HA1C and BPD, HC, AC, FL, estimated fetal weight, and birth weight, while negative correlations were found between HA1C and UAPI, MCAPI, and the MCA/ UA PI ratio in the current study.

In the Liu et al.[9] study, birth weight, BPD, HC, and AC were all negatively associated with UA hemodynamic markers (P<0.05). MCA (S/D, PI, and RI), birth weight, HC, and AC were negatively correlated in GDM (r=0.164, 0.206, 0.200, 0.226, 0.189, 0.179, 0.196, 0.177, and 0.172, respectively, P> 0.05), but not in NC. RA (S/D, PI, and RI) and birth weight were positively correlated in GDM (r=0.168, 0.207, and 0.184, respectively, P=0.05) but not in NC (P>0.05).

Quintero-Prado and colleagues conducted a study in 2014 on 169 women who were pregnant and had gestational diabetes. In this study, they compared the PI of the uterine artery to that of the UA, and they found that there was a significant negative connection between birthweight centiles and Z score values of the UA-PI. This study is consistent with its findings. In a second study conducted by Maruotti and colleagues on 106 pregnant women with GDM,[13] Doppler recordings of UA-PI were

acquired between the ages of 34 and 41 weeks of pregnancy. These recordings were associated with the birthweight of the neonate in the study. In keeping with the findings of the current study, linear regression analysis showed a statistically significant inverse connection between UA-PI and newborn birthweight centile.[14]

4.1. Conclusion

In conclusion, we suggest clinicians can better estimate the birth weight of GDM infants by using fetal Doppler hemodynamic indices in late pregnancy. There is a statically significant positive correlation between HA1C and BPD, HC, AC, FL, estimated fetal weight, birth weight, uterine artery resistance index (UARI), middle cerebral artery resistance index (MCARI). There is a significant negative correlation between HA1C and UAPI, MCAPI, and MCA/UA PI ratio.

Conflicts of interest

There are no conflicts of interest.

References

1. Jamal AS, Naemi M, Eslamian L, et al. The association between fetal renal artery indices in late pregnancy and birth weight in gestational diabetes mellitus: a cohort study. *Int J Reprod Biomed*. 2022;20:21.
2. El-Sherbiny HA, Awad Allah HI, El-Guindy AE-DA. The use of ultrasound in the prediction of fetal complications among diabetic patients in late pregnancy. *J Environ Sci*. 2020;49:21.
3. Fatihoglu E, Aydin S, Karavas E, Kantarci M. Gestational diabetes mellitus and early hemodynamic changes in fetus. *J Med Ultrasound*. 2021;29:270.
4. Lehtoranta L, Haapsamo M, Vuolteenaho O, Palo P, Ekholm E, Räsänen J. Fetal cardiovascular hemodynamics in type 1 diabetic pregnancies at near-term gestation. *Acta Obstet Gynecol Scand*. 2021;100:263—271.
5. Erkamp JS, Geurtsen ML, Duijts L , et al. Associations of maternal early-pregnancy glucose concentrations with placental hemodynamics, blood pressure, and gestational hypertensive disorders. *Am J Hypertens*. 2020;33:660.
6. American Diabetes Association. Classification and diagnosis of diabetes. *Diabetes Care*. 2015;38(suppl.1):s8—s16.
7. World Health Organization (WHO). *Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation*. Geneva: World Health Organization; 2011. PMID: 26158184. https://pubmed.ncbi.nlm.nih.gov/26158184/.
8. McIntyre HD, Fuglsang J, Kampmann U, Knorr S, Ovesen P. Hyperglycemia in pregnancy and women's health in the 21st century. *Int J Environ Res Public Health*. 2022;19:1—19.
9. Liu F, Liu Y, Lai YP, Gu XN, Liu DM, Yang M. Fetal hemodynamics and fetal growth indices by ultrasound in late pregnancy and birth weight in gestational diabetes mellitus. *Chin Med J*. 2016;129:2109—2114.
10. Abd el Gawad MMM, Moustafa MH, Farid LA, Abd El Aziz NEED. Assessment of the relation between fetal hemodynamic indices in late pregnancy and birth weight in gestational diabetic mellitus mothers: a correlational study. *Egypt J Hosp Med*. 2018;73:5856—5864.
11. Anness AR, Clark A, Melhuish K, et al. Maternal hemodynamics and neonatal birth weight in pregnancies complicated by gestational diabetes: new insights from novel causal inference analysis modeling. *Ultrasound Obstet Gynecol*. 2022;60:215—222.
12. Li Y, Wang W, Zhang D. Maternal diabetes mellitus and risk of neonatal respiratory distress syndrome: a meta-analysis. *Acta Diabetol*. 2019;56:729—740.
13. Quintero-Prado R, Bugatto F, Sánchez-Martín P, Fajardo-Expósito MA, Torrejón R, Bartha JL. The influence of placental perfusion on birthweight in women with gestational diabetes. *J Mater Fetal Neonat Med*. 2016;29:32—35.
14. Maruotti GM, Rizzo G, Sirico A, et al. Are there any relationships between umbilical artery pulsatility index and macrosomia in fetuses of type I diabetic mothers? *J Mater Fetal Neonat Med*. 2014;27:1776—1781.