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Ultrasonographic evaluation of Caval Aortic Index in gestational and pregestational diabetes: a predictor of perinatal outcomes?

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ABSTRACT

Aims: Diabetes mellitus (DM), including gestational (GDM) and pregestational diabetes (pre-GDM), adversely affects maternal and fetal outcomes due to hyperglycemia and vascular changes. The Caval Aortic Index, a non-invasive measure of blood volume, could provide insights into these complications. In our study, we aimed to determine the functional changes in inferior vena cava (IVC) and aorta (Ao) diameters as well as the importance of caval aortic index in predicting perinatal outcomes in diabetic pregnant women.

Methods: This prospective case-control study included 120 DM patients and 100 controls. DM patients were divided into pre-GDM, diet-regulated GDM, and insulin-regulated GDM groups. Ultrasound measurements of inferior vena cava and aortic diameters were performed, alongside Doppler evaluations. Statistical analyses were conducted to assess the association of these parameters with adverse perinatal outcomes.

Results: Although the IVC and aortic diameters of the pregnant women with DM were higher compared to the control group and a statistically significant difference ($p<0.001$) was found between the groups, the Caval-Aortic Index was similar between the groups. Adverse outcomes (APGAR 5 min <7, need for mechanical ventilation, need for continued positive airway pressure, respiratory distress syndrome, transient tachypnea of the newborn and neonatal intensive care unit admission and neonatal low cord blood pH) were higher in DM groups but showed no direct correlation with IVC or aortic parameters. IVC diameter was the most predictive parameter in DM patients and the cut-off was >3.81 mm (AUC: 0.674).

Conclusion: Ultrasonographic IVC and aortic diameters reflect vascular adaptations in diabetic pregnancies but lack predictive value for adverse outcomes. While the Caval Aortic Index provides limited prognostic utility, integrating these measurements into comprehensive models may enhance perinatal risk assessment.

Keywords: Gestational diabetes, pregestational diabetes, Caval Aortic Index, perinatal outcomes, ultrasonography, vascular adaptations

INTRODUCTION

A collection of illnesses known as diabetes mellitus (DM) are typified by hyperglycemia brought on by an issue with the secretion and/or action of insulin.[1] Gestational diabetes mellitus (GDM) is the term for glucose intolerance that first appears in the second or third part of pregnancy, whereas pregestational diabetes mellitus (pre-GDM) is the term for glucose intolerance that already exists before pregnancy or is identified in the first trimester.[2,3] On average, 1.3% of pregnancies are affected with pre-GDM, whereas 7-11% are affected by GDM. As maternal age and obesity rise, this rate also rises.[2,4] Macrosomia, congenital abnormalities, perinatal mortality, hypertrophic cardiomyopathy, fetal growth restriction (FGR), preterm birth, respiratory distress syndrome (RDS), and newborn hypoglycemia are all more common in pregnancies affected by diabetes mellitus. Among the long-term consequences of diabetes mellitus are obesity, type 2 diabetes, and an increased risk of cardiovascular disease.[5-7]

As pregnancy goes on, maternal insulin resistance rises as a result of elevated levels of estrogen, progesterone, cortisol, and human placental lactogen acting as counter-regulatory hormones to insulin and influencing glucose homeostasis.[8] As a result, maternal carbohydrate metabolism changes during

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pregnancy.[9,10] Through the fetoplacental circulation, elevated maternal glucose is passed to the fetus, resulting in reactive hyperinsulinemia and hyperglycemia. Moreover, elevated oxidative stress is linked to a hyperglycemic setting.[9] Vascular abnormalities in fetuses of diabetes moms can be caused by endothelial dysfunction brought on by elevated fetal oxidative stress and the production of inflammatory cytokines. Furthermore, around one-third of fetuses born to pregnant mothers with diabetes may develop hypertrophy of the aortic and pulmonary trunk muscle layers, which may change the volume of blood in circulation.[11,12]

Venous blood is transported from the lower body to the right atrial chamber by the inferior vena cava (IVC). Variations in circulating blood volume and central venous pressure affect the IVC's size.[13] Originally used to evaluate the body's fluid state, the caval aortic index is a non-invasive technique that is calculated as the ratio of the diameter of the descending aorta to the diameter of the inferior vena cava (IVA/Ao).[14,15]

Along with functional alterations in IVC and Ao diameters in pregnant women with diabetes, our study sought to determine the relevance of Caval Aortic Index in predicting perinatal outcome.

METHODS

The Ankara Etlik City Hospital Clinical Researches Ethics Committee gave its permission to the study protocol (Date: 18.10.2023, Decision No: AESH-EK1-2023-621). Every participant provided written consent after being told about the study. The Declaration of Helsinki's guiding principles were followed when conducting the study. This prospective case-control study was carried out in the Ankara Etlik City Hospital's Perinatology Clinic from November 2023 to August 2024. The study population was divided into four groups: group 1: 40 patients diagnosed with pre-GDM, group 2: 40 patients with diet-regulated gestational diabetes (DR-GDM), group 3: 40 patients with insulin-regulated gestational diabetes mellitus (IR-GDM) and group 4: 100 healthy control patients.

GDM was diagnosed based on the American College of Obstetricians and Gynecologists' (ACOG) Committee's criteria.[2,3] Our clinic used a two-stage oral glucose tolerance test (OGTT), which was advised for all pregnant women between weeks 24 and 28. Following 50 grams of oral glucose solution, a 1-hour glucose measurement was first carried out in the vein. Patients whose 1-hour glucose result was greater than 140 mg/dl were next subjected to a diagnostic OGTT using 100 grams. GDM was identified in women who had two or more abnormal 3-hour OGTT results. In the OGTT, abnormal values were defined as fasting glucose ≥95 mg/dl, first-hour glucose ≥180 mg/dl, second-hour glucose ≥155 mg/ dl, and third-hour glucose ≥140 mg/dl. Pre-GDM was identified if the random fasting plasma glucose level was ≥126 mg/dl, the 2-hour glucose value in the 75-g-OGTT surpassed ≥200 mg/dl, or the glycosylated hemoglobin (HbA1c) was ≥6.5 before to pregnancy or during the first trimester.[1] When necessary, diet or treatment was started for patients with diabetes mellitus. Patients who began insulin treatment were placed in the IR-GDM group, while those who maintained their pregnancy on diet were placed in the DR-GDM group. Based on the first day of the last menstrual cycle, the study participants' weeks of gestation were determined. The crown-rump length, which was obtained during the first trimester ultrasound examination, was used to calculate the gestational age in patients who were unaware of their most recent menstruation. The study involved women who were 28-41 weeks pregnant. The control patients were selected on the basis of their gestational age. Patients who discontinued follow-up, patients with smoking, alcohol consumption, congenital anomalies, multiple pregnancies, chronic maternal diseases (such as hypothyroidism, hypertension) and patients with obstetric complications other than DM diagnosis (such as isolated FGR, intrahepatic cholestasis in pregnancy) were excluded from the study. All of the study's patients had their demographic data, including their body-mass index (BMI), weight gain during pregnancy, and maternal age, gathered. Maternal venous blood was used to calculate the HbA1c value.

The patients were examined by transabdominal sonography using the Voluson S10 Expert sonography device (GE Healthcare, Milwaukee, Wisconsin, USA) by the same perinatology specialist (GK) under the supervision of an experienced supervisor (ZVY). The patient was positioned supine or semi-recumbent at 15° to 30° for Doppler exams, with the head and chest slightly raised to avoid caval compression. Pulsatility Index (PI) of the umbilical artery (UA) and systolic/diastolic ratio (S/D), PI of the middle cerebral artery (MCA), peak systolic velocity (PSV) and S/D values, and S/D and PI values of the uterine artery (UtA) were recorded for the Doppler evaluation. Every measurement was carried out in compliance with the International Society of Ultrasound in Obstetrics and Gynecology's (ISUOG) guidelines. The UA waveform was measured and recorded from the free-floating portion of the cord in the absence of minimal fetal activity and fetal respiration. The circle of Willis was seen using the color Doppler in the axial portion of the fetal head while the MCA Doppler was being inspected. The insonation angle was consistently near 0° during the measurement, which took place in the proximal third of the MCA, which is derived from the circle of Willis. A sagittal cut of the uterus was produced to locate the cervical canal in order to do the Doppler measurement of the uterine artery. The measurement was taken prior to the uterine artery giving off the arcuate branch.[16] The diameter of the IVC was measured from inner edge to inner edge in the parasagittal section and in the bicaval view. The anteroposterior diameter of the IVC increases during expiration and decreases during inspiration. Therefore, the measurement was repeated and averaged for 3 respiratory cycles to account for the changes during breathing. The aortic diameter was examined on the descending aorta at the end of systole. The Ao diameter in the fetus's coronal section was measured from inner edge to inner edge, which represents the upper and lower ends of the iliac and renal arteries, respectively. At least three measurements were made, and the mean of them was used (**Figure 1**).[13]

In our clinic, decisions on the follow-up care and delivery of patients diagnosed with DM are made according to the criteria

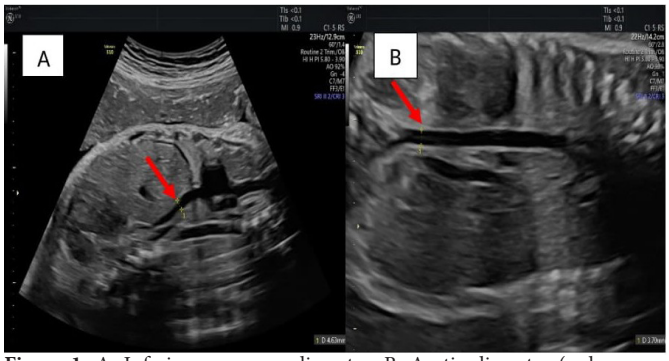

Figure 1. A: Inferior vena cava diameter, B: Aortic diameter (red arrows: inner wall to inner wall vessel diameter measurement)

of the American College of Obstetricians and Gynecologists (ACOG) committee.[2,17] In patients with pre-GDM and IR-GDM, delivery was decided at 36^{+0}-38^{+6} weeks in the case of a complicated pregnancy and at 39^{+0}-39^{+6} weeks in the case of an uncomplicated pregnancy. In DR-GDM patients, expectant management was applied until 40^{+6} weeks of gestation. If the estimated fetal weight was ≥4500 g, a decision for cesarean section was made. Patients' birth information, birth weight, APGAR 1/APGAR 5 scores and neonatal morbidities were recorded. Composite adverse perinatal outcome (CAPO) was defined as at least one of the following: APGAR 5 min <7, need for mechanical ventilation (MV), need for continued positive airway pressure (CPAP), RDS, transient tachypnea of the newborn (TTN), admission to the neonatal intensive care unit (NICU), and low cord blood pH.

Statistical Analysis

IBM Corporation SPSS version 22.0 (IBM Corporation, Armonk, NY, USA) was used to conduct the statistical analysis. The conformance to the normal distribution was examined using the Kolmogorov-Smirnov test. For continuous variables with a normal distribution, descriptive statistics are displayed as "mean±standard deviation". and for those who don't, as the "median (interquartile range)". When comparing more than two groups, the Analysis of Variance (ANOVA) test was employed. The number of groups was taken into consideration while determining the ANOVA test's statistical significance. Fisher's exact test or the chi-squared test were used to compare categorical variables. The independent sample T test and the Mann-Whitney U test were used to compare continuous variables that were and were not regularly distributed. The optimal cutoff values based on the Youden Index were found by calculating and comparing the areas under the curve (AUC) using the ROC curve. For all tests, a p-value of less than 0.05 was considered statistically significant.

The number of people to be included in the study was determined using the G-Power 3.1.9.7 software (University of Dusseldorf, Dusseldorf, Germany). When calculating the estimated sample size, the Caval-Aorta Index was used as the primary variable; the sample size was calculated using the student's paired test with 80% power, a probability of error of α=0.05 and the Cohen effect size as 'medium'. Accordingly, it was considered appropriate to conduct the study with at least one hundred and eighty patients, ensuring the robustness of the study's findings.

RESULTS

One hundred control participants and 120 DM patients participated in this study. The maternal features and ultrasonography results of the DM and control patients are displayed in **Table 1**. The pre-GDM group had a greater maternal age than the control group, which was a significant difference (p<0.001). Gravida of the pre-GDM group was higher than that of the DR-GDM, IR-GDM and control groups (p=0.037). All four groups had similar parity and gestational weeks at evaluation (p=0.537, p=0.142). The control group and the pre-

Table 1. Comparison of maternal characteristics and ultrasound parameters of the groups

	Pre-GDM n=40	DR-GDM n=40	IR-GDM n=40	Control n=100	p-value
Maternal age (year)	32.9±5	30.9±6	31.1±6	28.2±5.1	<0.001[a]
Gravida	3 (2)	2 (2)	2 (3)	2 (2)	0.037[b]
Parity	1 (1)	1 (2)	1 (2)	1 (2)	0.142[b]
BMI (kg/m²)	32.4±4.2	31.7±6.2	33.2±5.2	29.4±4.9	<0.001[a]
Gestational week at examination	34 (4)	34 (4)	33 (4)	34 (3)	0.537[b]
UA S/D	2.58 (0.76)	2.33 (0.76)	2.34 (0.54)	2.50 (0.63)	0.240[b]
UA PI	0.92 (0.28)	0.85 (0.31)	0.81 (0.21)	0.89 (0.25)	0.335[b]
UtA S/D	1.98 (0.45)	1.94 (0.59)	2.05 (1.12)	1.94 (0.70)	0.379[b]
UtA PI	0.75 (0.30)	0.73 (0.35)	0.83 (0.50)	0.75 (0.37)	0.577[b]
MCA PSV	47.19 (10.36)	43.13 (15.08)	49.39 (11.67)	47.80 (16.29)	0.522[b]
MCA S/D	5.10 (2.17)	4.38 (2.19)	4.55 (1.34)	4.96 (2.33)	0.305[b]
MCA PI	1.68±0.33	1.55±0.41	1.61±0.31	1.60±0.35	0.428[a]
SDVP (mm)	65 (30)	66 (43)	64 (24)	50 (15)	<0.001[b]
IVC diameter (mm)	3.98 (0.77)	4.12 (1.35)	3.97 (0.80)	3.53 (0.84)	<0.001[b]
IVC diameter (z-score)	-0.01±0.83	0.07±1.34	-0.20±0.98	-0.75±1.06	<0.001[a]
Aortic diameter (mm)	4.70±0.91	4.86±0.75	4.91±0.76	4.51±0.69	0.012[a]
Aortic diameter (z-score)	-1.28±1.15	-1.28±1.31	-1.29±1.19	-1.9±1.19	0.003[a]
IVC/Ao index (mm)	0.85±0.16	0.86±0.23	0.82±0.14	0.80±0.17	0.240[b]
IVC/Ao index (z-score)	0.15±0.97	-0.65±8.88	0.25±2.05	0.74±1.71	0.337

[a]: Analysis of variance with Bonferroni test, [b]: Kruskal-Wallis test, Pre-GDM: Pregestational diabetes mellitus, DR-GDM: Diet regulated gestational diabetes mellitus, IR-GDM: Insulin regulated gestational diabetes mellitus, BMI: Body-mass index, UA: Umbilical artery, S/D: Systolic/diastolic ratio, PI: Pulsatility Index, UtA: Uterine artery, MCA: Middle cerebral artery, PSV: Peak systolic velocity, SDVP: Single deepest vertical pocket, IVC: Inferior vena cava, Ao: Aorta, Data are expressed as mean±standard deviation or median (interquartile range) where appropriate

GDM and IR-GDM groups had significantly different BMIs (p=0.012 and p=0.001, respectively). UA S/D, UA PI, MCA S/D, PI, PSV, UtA S/D, and PI were comparable among groups on ultrasonographic evaluation (p=0.240, p=0.335, p=0.305, p=0.428, p=0.522, p=0.379, p=0.577, respectively). In the single deepest vertical pocket (SDVP), there was a substantial correlation between control and pre-GDM, DR-GDM, and IR-GDM (p<0.001, p<0.001, and p=0.001, respectively). The control and DR-GDM groups differed considerably in IVC diameter, with the DR-GDM group showing a thicker IVC diameter (p<0.001). Between the control and IR-GDM groups, there was a significant difference in the aortic diameter, with the IR-GDM group's Ao diameter being thicker (p=0.012). The Z-score evaluation revealed a significant difference between the control group and the pre-GDM, DR-GDM, and IR-GDM groups in terms of the Z-score of the IVC (p=0.002, p<0.001, and p=0.005, respectively). The aortic Z-score of the pre-GDM, DR-GDM, and IR-GDM groups differed significantly from that of the control group (p=0.006, p<0.001, and p=0.008, respectively). All four groups' IVC/Ao index (mm) and IVC/Ao index (Z-score) values did not differ significantly (p=0.240 and p=0.337, respectively).

Table 2 displays the birth characteristics and perinatal outcomes of the study participants. According to gestational week, there was a significant difference between control and pre-GDM, DR-GDM, and IR-GDM (p<0.001, p=0.001, and p<0.001, respectively). Fetal distress, birth weight, and the APGAR score at one minute were comparable among groups (p=0.604, p=0.294 and p=0.104, respectively). Significant differences were observed between the groups in terms of neonatal hypoglycemia, APGAR 5. minute, prematurity, cesarean section rate, NICU admission, TTN, antenatal corticosteroid use, RDS, CPAP, MV need, and phototherapy need (p=0.023, p=0.018, p=0.005, p=0.004, p<0.001, p=0.001, p=0.012, p=0.002, p=0.008, p=0.002, p=0.004).

Table 3 compares IVC/Ao index, IVC and aortic diameter (mm, Z-score), birth characteristics and perinatal outcomes of newborns between patients with pre-GDM or GDM and control patients. Both the IVC and Ao diameters (mm) were significantly different between the two groups, and the DM group's diameters increased (p<0.001, p=0.002) (Figure 2). Additionally, there were substantial differences in both groups' IVC and Ao Z-scores (p<0.001, p<0.001). Both groups' IVC/Ao indexes (mm) and Z-scores were similar (p=0.078, p=0.136). he rates of fetal distress and the need for phototherapy were comparable in both groups when comparing the neonatal outcomes (p=0.147, p=0.515). However, the DM group had significantly higher rates of cesarean section, prematurity, NICU admission, neonatal hypoglycemia, TTN, RDS, CPAP, and MV needs (p=0.011, p=0.001, p<0.001, p=0.033, p=0.004, p=0.001, p=0.006, and p=0.004, respectively).

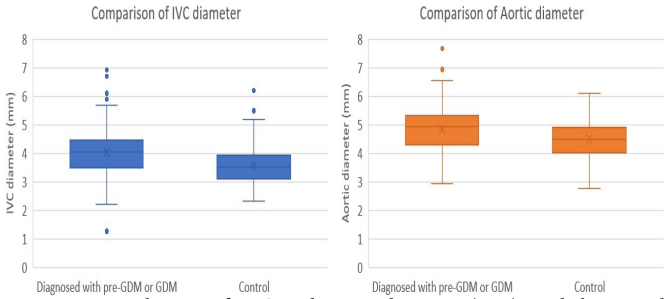

Figure 2. Distribution of IVC and aortic diameter (mm) in diabetes and control groups

IVC: Inferior vena cava

Table 4 compares the Doppler measurements of the groups in DM that had and did not have CAPO. IVC diameter (mm), IVC diameter (Z-score), Ao diameter (mm), Ao diameter (Z-score), IVC/Ao index (mm), and IVC/Ao index (Z-score) did not significantly differ across the groups (p=0.504, p=0.473, p=0.986, p=0.066, p=0.510, p=0.526, respectively).

Table 2. Birth characteristics and perinatal outcomes of the newborns

	Pre-GDM n=40	DR-GDM n=40	IR-GDM n=40	Control n=100	p-value
Gestational age at delivery (week)	37 (2.4)	37 (1.35)	37 (2.5)	39 (1.55)	<0.001[a]
Prematurity (<37 weeks)	14 (35%)	9 (22.5%)	12 (30%)	11 (11%)	0.005[b]
Cesarean section	35 (87.5%)	24 (60%)	30 (75%)	58 (58%)	0.004[b]
Birth weight (gram)	3287±511	3219±575	3238±537	3124±447	0.294[c]
Apgar score at 1st minute	9 (1)	9 (1)	9 (1)	9 (0)	0.104[a]
Apgar score at 5th minute	10 (1)	10 (1)	10 (1)	10 (0)	0.018[a]
NICU admission	20 (50%)	11 (27.5%)	10 (25%)	9 (9%)	<0.001[b]
Umbilical cord pH	7.37 (0.07)	7.36 (0.15)	7.38 (0.16)	7.42 (0.07)	0.247[a]
Transient tachypnea of the newborn	8 (20%)	9 (22.5%)	2 (5%)	4 (4%)	0.001[b]
Antenatal corticosteroid	12 (30%)	7 (17.5%)	11 (27.5%)	10 (10%)	0.012[b]
Fetal distress	2 (5%)	1 (2.5%)	1 (2.5%)	8 (8%)	0.604[b]
Respiratory distress syndrome	6 (15%)	4 (10%)	5 (12.5%)	1 (1%)	0.002[b]
Continues positive airway pressure	8 (20%)	10 (25%)	4 (10%)	6 (6%)	0.008[b]
Mechanical ventilation	7 (17.5%)	3 (7.5%)	2 (5%)	1 (1%)	0.002[b]
Phototherapy for neonates	6 (15%)	0 (0%)	0 (0%)	3 (3%)	0.004[b]
Neonatal hypoglycemia	3 (7.5%)	1 (2.5%)	2 (5%)	0 (0%)	0.023[b]

[a]: Kruskal-Wallis test, [b]: Pearson chi-square, [c]: Analysis of variance with Bonferroni test, Pre-GDM: Pregestational diabetes mellitus, DR-GDM: Diet regulated gestational diabetes mellitus, IR-GDM: Insulin regulated gestational diabetes mellitus, NICU: Neonatal intensive care unit

Table 3. Comparison of IVC/Ao index, IVC and aortic diameter (mm, z-score), birth characteristics and neonatal outcomes of newborns according to patients diagnosed with pre-GDM or GDM

	Diabetes mellitus (Pre-GDM+DR-GDM+IR-DM) n=120 (54.5%)	Control n=100 (45.5%)	p-value
IVC diameter (mm)	4.03±0.90	3.57±0.68	<0.001[a]
IVC diameter (z-score)	-0.5±1.07	-0.74±1.06	<0.001[a]
Aortic diameter (mm)	4.82±0.81	4.51±0.69	0.002[a]
Aortic diameter (z-score)	-1.28±1.21	-1.90±1.19	<0.001[a]
IVC/Ao index (mm)	0.84±0.17	0.80±0.16	0.078
IVC/Ao index (z-score)	-0.08±5.26	0.74±1.71	0.136[a]
Cesarean section	89 (74.2%)	58 (58%)	0.011[b]
Fetal distress	4 (3.3%)	8 (8%)	0.147[c]
Prematurity (<37 weeks)	35 (29.2%)	11 (11%)	0.001[b]
NICU admission	41 (24.2%)	9 (9%)	<0.001[b]
Neonatal hypoglycemia	6 (5%)	0 (0%)	0.033[c]
Transient tachypnea of the newborn	19 (15.8%)	4 (4%)	0.004[c]
Respiratory distress syndrome	15 (12.5%)	1 (1%)	0.001[c]
Continues positive airway pressure	22 (18.3%)	6 (6%)	0.006[b]
Mechanical ventilation	12 (10%)	1 (1%)	0.004[c]
Phototherapy for neonates	6 (5%)	3 (3%)	0.515[c]

[a]: Student T test, [b]: Pearson chi-square, [c]: Fisher's exact test, Pre-GDM: Pregestational diabetes mellitus, DR-GDM: Diet regulated gestational diabetes mellitus, IR-GDM: Insulin regulated gestational diabetes mellitus, IVC: Inferior vena cava, Ao: Aorta, NICU: Neonatal intensive care unit, A p-value of <0.05 indicates a significant difference and statistically significant p-values are in bold

Table 4. Comparison of Doppler measurements of groups with and without composite adverse perinatal outcomes in DM

	With CAPO n=51 (23.1%)	Without CAPO n=169 (76.9%)	p-value
IVC diameter (mm)	0.81±0.19	0.83±0.17	0.504[a]
IVC diameter (z score)	-0.27±1.19	-0.39±1.1	0.473[a]
Aortic diameter (mm)	4.69±0.87	4.69±0.75	0.986[a]
Aortic diameter (z score)	-1.28±1.32	-1.65±1.2	0.066[a]
IVC/Ao index (mm)	3.76±0.93	3.85±0.82	0.510[a]
IVC/Ao index (z score)	0.61±2.23	0.20±4.47	0.526[a]

[a]: Student T test, IVC: Inferior vena cava, Ao: Aorta, CAPO: Composite adverse perinatal outcomes, APGAR 5 min <7, need for mechanical ventilation, need for continued positive airway pressure, respiratory distress syndrome, transient tachypnea of the newborn and neonatal intensive care unit admission and neonatal low cord blood pH, data are expressed as mean±standard deivation or median (inter quartile range) where appropriate

The evaluation of the IVC/Ao index, IVC and aortic diameter (mm, Z-score) in the diabetes and control groups using the ROC analysis is shown in Table 5. The value of the IVC/Ao index (Z-score) (AUC: 0.590, cut-off: <0.28 p=0.022) shows limited significance for the diagnosis of DM. The IVC diameter (mm) cut-off value was found to be >3.81, which led to a 60% sensitivity and a 60.8% specificity (AUC: 0.674, p<0.001). With a sensitivity of 61.7% and a specificity of 64% (AUC: 0.679, p<0.001), the determined cut-off value for IVC diameter (Z-score) was >-0.35. The Ao diameter (mm) cut-off value was >4.63, which produced a 62.5% sensitivity and a 58% specificity (AUC: 0.623, p=0.002). With a sensitivity of 60% and a specificity of 59% (AUC: 0.632, p<0.001), the computed cut-off value for Ao diameter (Z-score) was >-1.64 (Figure 3).

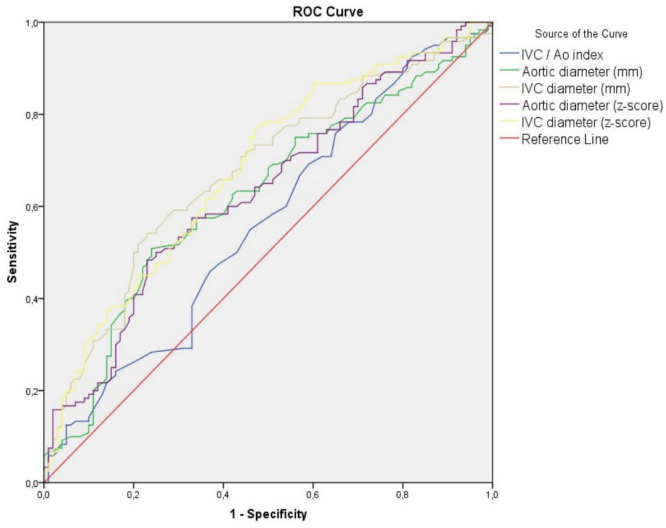

Figure 3. ROC analysis of IVC/Ao index, IVC and aortic diameter (mm, Z-score) by ROC analysis in diabetes and control groups

ROC: Receiver operating characteristic, IVC: Inferior vena cava

Table 5. Evaluation of IVC/Ao index, IVC and aortic diameter (mm, Z-score) in diabetes and control groups by ROC analysis

	LR+	LR-	Cut-off*	Sensitivity	Specificity	AUC	95% CI	p-value
IVC/Ao index (Z-score)	1.32	0.77	<0.28	55%	58.3%	0.590	0.515-0.665	0.022
IVC diameter (mm)	1.88	0.59	>3.81	60%	60.8%	0.674	0.60-0.75	<0.001
IVC diameter (z score)	1.71	0.60	>-0.35	61.7%	64%	0.679	0.61-0.75	<0.001
Aortic diameter (mm)	1.49	0.65	>4.63	62.5%	58%	0.623	0.55-0.70	0.002
Aortic diameter (z score)	1.46	0.68	>-1.64	60%	59%	0.632	0.56-0.71	0.001

*Cut-off values were found according to Youden Index. IVC: Inferior vena cava, ROC: Receiver operating characteristic, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio, AUC: Area under the curve, CI: Confidence interval, Ao: Aorta

The comparison of IVC and aortic diameter (Z-score) of the DM-diagnosed group and the control group by week of gestation is shown in Table 6. There were 29 patients diagnosed with DM at 32 weeks' gestation and 14 control patients. Before 32 weeks, the IVC diameter (Z-score) of the DM group was 0.02±1.25, while that of the control group was -0.25±0.99. There was no noticeable difference between the two groups (p=0.480). Between 32 and 37 weeks, 72 individuals were diagnosed with diabetes mellitus, while 73 patients served as controls. Between 32 and 37 weeks, the DM group's IVC diameter (Z-score) was -0.01±0.95, while the control group's was -0.75±1.06; the two groups' differences were statistically significant (p<0.001). Thirteen patients in the control group and 19 in the DM group were older than 37 weeks. There was a significant difference between the two groups (p=0.026), with the IVC diameter (Z-score) in the DM patients after 37 weeks being -0.30±1.24 and in the control group being -1.27±1. There was no significant difference between the two groups (p=0.114), with the Ao diameter (Z-score) in the DM patients under 32 weeks being -0.86±1.29 and in the control group being -1.46±0.69. Between 32 and 37 weeks, the DM group's Ao diameter (Z-score) was -1.31±1.17, whereas the control group's was -1.89±1.22. The two groups' differences were statistically significant (p=0.004). The DM group's Ao diameter (Z-score) was -1.8±1.02 over 37 weeks, whereas the control group's was -2.37±1.3. There was no significant difference between the two groups (p=0.172).

Table 6. Comparison of IVC and aortic diameter (Z-score) of the group diagnosed with pre-GDM or GDM and the control group according to gestational week

		Diagnosed with pre-GDM or GDM n=120 (54.5%)		Control n=100 (45.5%)		
		z score	n	z score	n	p-value
IVC diameter (z score)	<32 week	0.02±1.25	29	-0.25±0.99	14	0.480[a]
	32-37 week	-0.01±0.95	72	-0.75±1.06	73	<0.001[a]
	>37 week	-0.30±1.24	19	-1.27±1	13	0.026[a]
Aortic diameter (z score)	<32 week	-0.86±1.29	29	-1.46±0.69	14	0.114[a]
	32-37 week	-1.31±1.17	72	-1.89±1.22	73	0.004[a]
	>37 week	-1.8±1.02	19	-2.37±1.3	13	0.172[a]

[a]: Student T test, pre-GDM: Pregestational diabetes mellitus, IVC: Inferior vena cava, GDM: Gestational diabetes mellitus

DISCUSSION

This study demonstrated that the IVC and Ao diameters are impacted by gestational diabetes. The DM group had higher IVC diameter (mm, Z-score) and Ao diameter (mm, Z-score) than the control group, but the IVC/Ao index (Z-score) was lower. The IVC diameter was the most important parameter in the DM patients compared to the control patients. The determined cut-off value for IVC diameter (mm) was >3.81 and resulted in a sensitivity of 60% and a specificity of 60.8% (AUC: 0.674, p<0.001). The identified cut-off value for IVC diameter (Z-score) was >-0.35, which corresponds to a sensitivity of 61.7% and a specificity of 64% (AUC: 0.679, p<0.001). No correlation was found between IVC diameter (mm, Z-score), Ao diameter (mm, Z-score) and IVC/Ao index and CAPO. To our knowledge, our study is the first to investigate the effects of changes in IVC and aortic wall diameter on maternal and fetal circulation in diabetic pregnancies.

The first known study on fetal aortic diameter was conducted by Tonge et al.[18] This study showed that the aortic diameter increased with the increase in fetal blood volume over the course of the gestational week. Following a stillbirth, Szpinda et al.[19] carried out an autopsy investigation to provide reference values for the descending aorta's diameters at various weeks of gestation. This study showed that the fetal gender had no influence on the assessment of the aortic diameter, the aortic thickness was similar in both sexes and the aortic thickness increased with gestational week. Skilton et al.[20] compared aortic thickness in patient groups. This study was based on the measurement of aortic wall thickness by ultrasound in 25 FGR newborns and 25 normal birth weight infants. Maximum aortic diameter was significantly higher in infants with FGR (810 µm) than in infants without FGR (743 µm, p=0.02), and a significant increase in aortic diameter was observed in neonates with FGR. This suggests that prenatal events may favor a later cardiovascular risk. Aortic diameter was also considerably greater in FGR patients than in control patients, according to Cosmi et al.'s[21] research of FGR patients. This difference was observed both intrauterine (1.9 mm vs. 1.15 mm; p<0.001) and postnatally (2.4 mm vs. 1.03 mm; p<0.001). The IVC transports venous blood to the right atrium of the heart from the abdominal cavity and lower limbs.[22] According to Çilingir et al.[23] the IVC width was smaller in FGR patients than in control patients and varied with gestational age. The reason for this was attributed to decreased blood flow from the placenta, kidneys, lower extremities and peripheral organs such as the pelvis. They argued that the thickness of the IVC changes with the relative influence of blood flow to the IVC. The IVC/Ao-index was used for the first time in 2014 for the assessment of vascular fluid and is a non-invasive, objective assessment method.[14] The change in IVC/Ao index with intravascular volume in healthy volunteers was investigated by Bilgin et al.[24] In this study, changes in IVC/Ao index and IVC diameter due to blood loss were observed. In this investigation, the highest IVC diameter was 17.3±0.3 mm, and after 500 ml of blood loss, a 6% change was noted. Denizli et al.[13] used this index to assess the thickness change that may occur in FGR patients with endothelial dysfunction. The IVC/Ao index was comparable in both groups, despite the fact that the IVC and aortic diameter values were substantially lower in FGR patients than in the control group. IVC/Ao (Z-score), Ao diameter, and IVC diameter were all greater in our study than in the control group. Nevertheless, CAPO was not linked to these factors. Increased IVC and aortic diameters in diabetic pregnancies could be related to vascular adaptations and endothelial dysfunction. Fetal and maternal hyperglycemia triggers oxidative stress and inflammatory processes that can lead to changes in vessel wall thickness. The IVC diameter in particular is the most important parameter in diabetic pregnant women. Although long-term vascular complications develop in DM patients due to inflammation and endothelial dysfunction, these are not present in every patient. The ability to measure vessel wall thickness in fetuses using a non-invasive technique such as ultrasound may be an early sign of

atherosclerosis. This could be an important step in predicting the long-term effects after birth. Larger studies are needed for CAPO and long-term complications.

Maternal and fetal hyperglycemia causes hemodynamic changes in DM patients through vascular changes and high oxidative stress effects.[25] As a result, the uteroplacental blood flow may decrease. A brain-protective effect occurs when prenatal adaptation redirects blood flow from the peripheral to the brain rather than the internal organs. The development of the brain-protective effect can manifest itself in a decrease in MCA S/D, PI and an increase in UA S/D, PI. Doppler ultrasonography measures can be used to identify these hemodynamic alterations.[26] Rane et al.[27] analyzed a total of 10 prospective and 5 retrospective studies in a review. The predictive accuracy of Doppler ultrasonography data in forecasting adverse perinatal outcomes in DM pregnancies was examined in this study. UA Doppler measurements showed significant prognostic value for neonatal hypoglycemia, hyperbilluribinemia, NICU admission, RDS, and preterm labor. In their investigation of 138 GDM patients, Leung et al.[28] discovered no association between CAPO and UA and MCA Doppler measures, despite the fact that the CAPO rate was 27.5%. This situation shows that Doppler parameters will not play a role in every patient diagnosed with DM. Similarly, another meta-analysis that examined 151 publications found that pregnancies with diabetes had significantly greater UtA PI and S/D ratios than pregnancies without diabetes, but that there was no difference in UA PI, UA S/D ratio, MCA PI, and MCA S/D ratio.[26] The control and DM groups in our study had comparable values for UA PI, S/D, UtA PI, UtA S/D, MCA PI, MCA S/D, and MCA PSV. In pregnant women diagnosed with DM, the rates of cesarean section, need for MV, TTN, RDS, need for CPAP, neonatal hypoglycemia, NICU admission, and preterm delivery were significantly higher in the DM group than in the control group. However, no correlation was found between CAPO and these Doppler parameters.

Limitations

There are limitations on the study. The results' generalizability may be limited by the fact that it was only carried out at one location. In addition, the low prognostic value of the IVC/Ao index suggests that this parameter alone is not a sufficient tool. To validate these findings, larger patient groups and various centers should be the focus of future research. It is also advised to conduct research on how alterations in IVC and aortic diameter affect long-term perinatal outcomes.

The fact that this study was carried out in a broad patient group using a prospective strategy is one of its main advantages. The opportunity to examine the distinctions between pregestational and gestational diabetes was given by four distinct groups, which included individuals with both illnesses.

CONCLUSION

The present study examined the predictive power of alterations in IVC, aortic diameter, and Caval-Aortic Index in perinatal outcomes in pregnancies complicated by diabetes. Our results showed significant differences in IVC and aortic diameter between diabetic and non-diabetic pregnancies, suggesting that these parameters reflect the effects of diabetes on maternal and fetal circulation. However, the limited prognostic value of the Caval-Aortic Index shows that this parameter alone is not sufficient for risk assessment. Although an increased IVC and aortic diameter was observed in diabetic pregnancies, no direct correlation between these changes and an adverse perinatal outcome could be established. However, integrating these parameters into a comprehensive risk assessment model can provide additional information on maternal and fetal health. In conclusion, this study highlights the impact of gestational and pregestational diabetes on ultrasonographic vascular parameters, suggesting potential vascular adaptations during pregnancy. Given the long-term cardiovascular risks associated with diabetes, future research should focus on postnatal follow-up studies assessing both maternal and neonatal vascular health. A longitudinal approach may provide deeper insights into the implications of these vascular changes beyond the perinatal period.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ankara Etlik City Hospital Clinical Researches Ethics Committee (Date: 18.10.2023, Decision No: AESH-EK1-2023-621).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. American Diabetes Association. 2. classification and diagnosis of diabetes: standards of medical care in diabetes-2019. *Diabetes Care*. 2019;42(Suppl 1):S13-S28. doi:10.2337/dc19-S002
2. American College of Obstetricians and Gynecologists' committee on practice bulletins-obstetrics. ACOG practice bulletin no. 201: pregestational diabetes mellitus. *Obstet Gynecol*. 2018;132(6):e228-e248. doi:10.1097/AOG.0000000000002960
3. ACOG Practice Bulletin No. 190: Gestational Diabetes...: Obstetrics & Gynecology. Accessed December 27, 2024. https://journals.lww.com/greenjournal/abstract/2018/02000/acog_practice_bulletin_no__190__gestational.37.aspx
4. Duygulu D, Mutlu Sütcüoğlu B, Turgut E, Özdemir H, Karçaaltıncaba D. Prospective evaluation of ultrasonographic fetal cardiac morphometry and functions in the third trimester of pregnancies with gestational diabetes mellitus. *J Clin Ultrasound*. 2024;52(9):1265-1272. doi:10.1002/jcu.23776

5. Mitanchez D, Yzydorczyk C, Siddeek B, Boubred F, Benahmed M, Simeoni U. The offspring of the diabetic mother-short- and long-term implications. *Best Pract Res Clin Obstet Gynaecol*. 2015;29(2):256-269. doi:10.1016/j.bpobgyn.2014.08.004
6. Rubarth LB. Infants of diabetic mothers. *Neonatal Netw NN*. 2013;32(6): 416-418. doi:10.1891/0730-0832.32.6.416
7. Bayraktar B, Balıkoğlu M, Kanmaz AG. Pregnancy outcomes of women with hypoglycemia in the oral glucose tolerance test. *J Gynecol Obstet Hum Reprod*. 2020;49(4):101703. doi:10.1016/j.jogoh.2020.101703
8. Bayraktar B, Balıkoğlu M, Bayraktar MG, Kanmaz AG. Number of relationships between abnormal values in oral glucose tolerance test and adverse pregnancy outcome. *Indian J Med Spec*. 2021;12(4):211-215. doi:10.4103/injms.injms_29_21
9. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. *Int J Mol Sci*. 2018; 19(11):3342. doi:10.3390/ijms19113342
10. Di Cianni G, Miccoli R, Volpe L, Lencioni C, Del Prato S. Intermediate metabolism in normal pregnancy and in gestational diabetes. *Diabetes Metab Res Rev*. 2003;19(4):259-270. doi:10.1002/dmrr.390
11. Chen ZY, Mao SF, Guo LH, Qin J, Yang LX, Liu Y. Effect of maternal pregestational diabetes mellitus on congenital heart diseases. *World J Pediatr WJP*. 2023;19(4):303-314. doi:10.1007/s12519-022-00582-w
12. Codazzi AC, Ippolito R, Novara C, Tondina E, Cerbo RM, Tzialla C. Hypertrophic cardiomyopathy in infant newborns of diabetic mother: a heterogeneous condition, the importance of anamnesis, physical examination and follow-up. *Ital J Pediatr*. 2021;47(1):197. doi:10.1186/s13052-021-01145-x
13. Denizli R, Tanaçan A, Sakcak B, et al. Evaluation of the Caval Aortic Index in fetal growth restriction: a case-control study in a tertiary center. *Int J Gynecol Obstet*. 2023;163(1):186-193. doi:10.1002/ijgo.14808
14. Durajska K, Januszkiewicz E, Szmygel Ł, Kosiak W. Inferior vena cava/aorta diameter index in the assessment of the body fluid status-a comparative study of measurements performed by experienced and inexperienced examiners in a group of young adults. *J Ultrason*. 2014; 14(58):273-279. doi:10.15557/JoU.2014.0027
15. Miller JB, Sen A, Strote SR, et al. Inferior vena cava assessment in the bedside diagnosis of acute heart failure. *Am J Emerg Med*. 2012;30(5):778-783. doi:10.1016/j.ajem.2011.04.008
16. Bhide A, Acharya G, Baschat A, et al. ISUOG Practice Guidelines (updated): use of Doppler velocimetry in obstetrics. *Ultrasound Obstet Gynecol J Int Soc Ultrasound Obstet Gynecol*. 2021;58(2):331-339. doi:10.1002/uog.23698
17. Tsakiridis I, Mamopoulos A, Athanasiadis A, Kourtis A, Dagklis T. Management of pregestational diabetes mellitus: a comparison of guidelines. *J Matern Fetal Neonatal Med*. 2022;35(3):423-432. doi:10.1080/14767058.2020.1719481
18. Tonge HM, Struyk PC, Custers P, Wladimiroff JW. Vascular dynamics in the descending aorta of the human fetus in normal late pregnancy. *Early Hum Dev*. 1983;9(1):21-26. doi:10.1016/0378-3782(83)90098-1
19. Szpinda M, Szpinda A, Woźniak A, Mila-Kierzenkowska C, Kosiński A, Grzybiak M. Quantitative anatomy of the growing abdominal aorta in human fetuses: an anatomical, digital and statistical study. *Med Sci Monit Int Med J Exp Clin Res*. 2012;18(10):BR419-426. doi:10.12659/msm.883483
20. Skilton MR, Evans N, Griffiths KA, Harmer JA, Celermajer DS. Aortic wall thickness in newborns with intrauterine growth restriction. *Lancet*. 2005;365(9469):1484-1486. doi:10.1016/S0140-6736(05)66419-7
21. Cosmi E, Visentin S, Fanelli T, Mautone AJ, Zanardo V. Aortic intima media thickness in fetuses and children with intrauterine growth restriction. *Obstet Gynecol*. 2009;114(5):1109-1114. doi:10.1097/AOG.0b013e3181bb23d3
22. Rizzo G, Arduini D, Romanini C. Inferior vena cava flow velocity waveforms in appropriate- and small-for-gestational-age fetuses. *Am J Obstet Gynecol*. 1992;166(4):1271-1280. doi:10.1016/s0002-9378(11)90621-8
23. Uzun Çilingir I, Sayın C, Sutcu H, İnan C, Erzincan S, Varol F. Evaluation of inferior and superior vena cava and the vena cava ratio in growth restricted fetuses. *J Ultrasound Med*. 2023;42(11):2653-2659. doi:10.1002/jum.16300
24. Bilgin S, Topal FE, Yamanoğlu A, et al. Effect of changes in intravascular volume on inferior vena cava and aorta diameters and the Caval Aorta Index in healthy volunteers. *J Ultrasound Med*. 2020;39(2):231-238. doi:10.1002/jum.15093
25. Ornoy A, Becker M, Weinstein-Fudim L, Ergaz Z. Diabetes during pregnancy: a maternal disease complicating the course of pregnancy with long-term deleterious effects on the offspring. a clinical review. *Int J Mol Sci*. 2021;22(6):2965. doi:10.3390/ijms22062965
26. Perkovic-Kepeci S, Cirkovic A, Milic N, et al. Doppler indices of the uterine, umbilical and fetal middle cerebral artery in diabetic versus non-diabetic pregnancy: systematic review and meta-analysis. *Med Kaunas Lith*. 2023;59(8):1502. doi:10.3390/medicina59081502
27. Rane BM, Malau-Aduli BS, Alele F, O'Brien C. Prognostic accuracy of antenatal doppler ultrasound measures in predicting adverse perinatal outcomes for pregnancies complicated by diabetes: a systematic review. *AJOG Glob Rep*. 2023;3(3):100241. doi:10.1016/j.xagr.2023.100241
28. Leung WC, Lam H, Lee CP, Lao TT. Doppler study of the umbilical and fetal middle cerebral arteries in women with gestational diabetes mellitus. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol*. 2004;24(5):534-537. doi:10.1002/uog.1730