Evaluation of Fetal Diaphragm Excursion and Thickness in Term Pregnancies Complicated with Pre-gestational and Gestational Diabetes Mellitus

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April 05, 2024

Abstract

Abstract Aim: Both pre-gestational (PGDM) and gestational diabetes mellitus (GDM) make pregnancy complicated. Moreover in literature GDM and PGDM have been accused for respiratory morbidity in newborns. Diaphragm ultrasound (DUS) is useful and noninvasive method that provides an opportunity to examination of the diaphragmatic morphology and function. This study examined quality of fetal diaphragmatic contractions in pregnant women complicated with GDM and PGDM. Materials and Methods: A total of 105 volunteers separated into 3 groups; (1) GDM group (n=35), (2) PGDM group (n=35), and (3) healthy non-diabetic control group (n=35). Thickness of fetal diaphragm (DT), diaphragmatic excursion (DE), diaphragm thickening fraction (DTF) and costodiaphragmatic angle (CDA) was measured on the video frame during inspiration and expiration phases of respiration. Results: Especially PGDM group represented adversely affected diaphragm measurement parameters. DT inspiration, DT expiration, DE, CDA inspiration and DTF values were significantly different between PGDM and control group. Conclusions: Quality of fetal diaphragm movements affected in pregnancies complicated with GDM and PGDM. Prolonged duration of diabetes may have additional adverse effects on diaphragm morphology and its function.

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Running Head: Fetal Diaphragm Evaluation in Diabetic Pregnancies

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Source of funding: None**Conflicts of interest:** The authors report no conflicts of interest. Grant Support & Financial Disclosures: None**Total number of tables: 3 Total number of figures: 2**

Keywords: Fetus, pre-gestational diabetes mellitus, gestational diabetes mellitus, diaphragm, ultrasound

CRediT Classification:

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Materials and Methods: A total of 105 volunteers separated into 3 groups; (1) GDM group (n=35), (2) PGDM group (n=35), and (3) healthy non-diabetic control group (n=35). Thickness of fetal diaphragm (DT), diaphragmatic excursion (DE), diaphragm thickening fraction (DTF) and costodiaphragmatic angle (CDA) was measured on the video frame during inspiration and expiration phases of respiration.

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Introduction

Pre-Gestational (PGDM) and gestational diabetes mellitus (GDM), are two frequent medical conditions that make pregnancy complicated due to high levels of blood glucose levels [1,2]. There are well-known medical complications which are related with PGDM and GDM include increased probability of cesarean, preterm labor, decreased levels of glucose (hypoglycemia), macrosomia, shoulder dystocia and fetal death[3]. Moreover both GDM and PGDM have been accused for respiratory morbidity in newborns[4-6]. Fetal hyperinsulinemia has been accused for delayed pulmonary maturation[7].

Diaphragm ultrasound (DUS) is useful and noninvasive method that provides an opportunity to examination of the diaphragmatic morphology and function and has attracted attention of the researchers. Diaphragm excursion (DE), diaphragm thickness (DT) and costo-diaphragmatic angels (CDA) can be evaluated via using DUS. The diaphragmatic thickening ratio reflects diaphragm's contractile capacity that is related with its strength[8]. Moreover efficiency of diaphragm contractions can be assessed via using DT and diaphragm thickness fraction (DTF) measurements which was obtained during expiratory and inspiratory phases of respiration[9]. Authors established that DUS technique supplies valuable information for severe diaphragm weakness in critically ill adult patients[10, 11].

According to our knowledge, authors did not clarify fetal diaphragmatic function in patients with GDM or PGDM in literature. This study is aimed to investigate the quality of fetal diaphragmatic contractions in pregnant women complicated with GDM and PGDM and compare these parameters with healthy pregnant volunteers.

Materials and methods

Both signed written informed consent from all participants and Ethical Committee approve from the Erciyes University School of Medicine was obtained (no: 2019/652). This study was performed at the perinatology clinic of the Erciyes University School of Medicine and classified as prospective, cross sectional and case-controlled. This study has not been published elsewhere.

Participants of the Study

All participants (n=105) of this study were followed up in our clinic after detection of heart beat to delivery time. Gestational week of study population were calculated via using last menstrual date. Gestational age was calculated according to first trimester ultrasound reports in patients who did not remember the date of their last menstrual period. All volunteers were delivered via scheduled caesarean section at the 39^{th} weeks of gestation with cephalic presentation due to previous caesarean section.

According to type of diabetes participants were separated into 3 groups; (1) GDM group (n=35), (2) PGDM group (n=35), and (3) healthy non-diabetic control group (n=35). All volunteers in GDM and healthy non-diabetic control group; were screened by 75 gr OGTT after 12 hours fasting between 24th and 28th weeks of gestation. Upper limits of fasting, first and second hour after 75 gr glucose administration were 92, 180 and 153 mg/dL, respectively[12]. Above this threshold, patients were diagnosed as GDM. All participants in GDM group received diet and exercise therapy. Then they re-evaluated for glucose levels both fasting and post-prandial second hour. Upper limits of fasting and post-prandial second hour were 95 mg/dl and 120 mg/dl respectively. We only included insulin required participants in GDM group. Patients in PGDM group received examinations by an ophthalmologist and a nephrologist for retinopathy and nephropathy at the end of second trimester (28th weeks of gestation) and 37th weeks of gestation. Moreover patients in PGDM group were classified according to Sacks and Metzger definition and all volunteers in this group were Type 1 insulin depended DM without vascular complications[13].

Exclusion Criteria

All participants were examined in detail for fetal abnormalities and received toxoplasma, rubella and cytomegalovirus tests at the 21th weeks of gestation. In the presence of any abnormality or positive test results, they were not accepted suitable for the study. Because fetal sex is a confounder, only volunteers with male fetuses were included to the study. Patients with maternal fever, retinopathy, nephropathy,labor pain, non- cephalic presentation, female fetuses, preeclampsia/eclampsia, intrauterine growth retardation, oligohydroamnios, membrane rupture, chronic systemic diseases, chromosomal or fetal anomaly, twin gestation or more, placenta accereata, increata and percreata, intrahepatic cholestasis of pregnancy were excluded from the study. Among volunteers who use steroid, narcotic, sedative, tobacco, alcohol or anti-psychotic were eliminated. Patients in PGDM group received examinations by an ophthalmologist and a nephrologist for retinopathy and nephropathy at the end of second trimester and 37th weeks of gestation. If diabetic volunteers complicated with retinopathy and nephropathy, these patients were not included into the study. Additionally volunteers who were not capable of achieving normal glucose levels with insulin therapy were not included to the study in patients with PGDM and GDM.

Methods of Diaphragmatic Evaluation and DUSG Timing

An obstetrician aimed to obtain horizontal views of the both left and right diaphragm and measure angle of costodiaphragmatic sinus during examination. Diaphragm consisting of three layers; two echogenic outher layers (pleura and peritoneum) and a non echogenic middle layer (central layer). Video records of diaphragmatic examinations both inspiration and expiration states were obtained from all volunteers by an obstetrician (FO) who was blinded to the diagnosis of the volunteers. Then measurements were performed by reviewing records frame by frame. We obtained thickness of fetal diaphragm (DT) at two time point of respiratory cycle (end-inspiration thickness and end-expiration thickness of fetal diaphragm). Both right and left diaphragm have different movement ability due to the position of liver thus all examinations were performed bilaterally and measurements were illustrated as mean values of both sides. In the presence of gasping or 'picket-fence'breathing of fetus FO did not evaluate that respiratory cycle. All volunteers with cephalic presentation were examined at 37 th weeks of gestation after ruling out nephropathy and retinopathy.

Measurement of other diaphragm parameters

During expiration and inspiration phases of respiratory cycle, diaphragm moves highest and lowest points in fetal chest. The average distances between highest and lowest points of diaphragm on two respiratory cycles were recorded and calculated. Distance between these two points illustrates the ability of diaphragmatic movement and it is called diaphragmatic excursion (DE). We evaluated another diaphragmatic function marker ''diaphragm thickening fraction (DTF)" by using a formula (end-inspiration thickness- end-expiration thickness/end-expiration thickness×100)[14]. Then costodiaphragmatic angle (CDA) was measured on the same video frame during inspiration and expiration phases of respiration.

Figure 1 Exhibition of CDA

Figure 2 Exhibition of Diaphragm Thickness

Other parameters

None of the volunteers had fetal distress and all volunteers underwent planned caesarean section at the 39th weeks of gestation with general anesthesia due to previous uterine scar. For determining fetal lactate, pH, oxygen and carbon dioxide (pO_2, pCO_2, sO_2), levels, arterial cord blood obtained after expulsion of the fetus. Apgar scores, fetal hypoxia, hypotonia, transient tachypnea, mild respiratory distress syndrome, NICU requirement, and other factors were evaluated by a pediatrician. An author (ES) collected required demographic and clinical data before USG examination.

Determining sample size and Statistical analysis

For calculating sample size means, standard deviations and reference values were taken from the article "Adverse fetal outcomes in patients with IUGR are related with fetal diaphragm evaluation parameters"[14]. We found 29 volunteers necessary when we assumed that power = 0,80 and alpha = 0,05. Because of possible data loss and dropouts, 36 volunteers were included in the study. We excluded 1 volunteer for each group.

To test the normality assumption of the data, Shapiro-Wilk test was used. Variance homogeneity assumption was tested with Levene test. Values are expressed as mean ± standard deviation, median (25th percentile-75th percentile) or n(%). One-Way ANOVA, Chi –Square and Kruskal–Wallis H test were performed for the comparison of differences between groups. Tukey, ZandMann-Whitney U test were used for the multiple comparisons. $p<0.05$ probability value was considered as statistically significant. All calculations were made via using PASW Statistics 18 software.

Results

Of the 105 pregnant women enrolled in the study, 35 were in the GDM group, 35 were in the pre-gestational DM group, and 35 were in the healthy controlgroup. Table 1 provides the demographic characteristics and fetal biometric measurements among groups.

Table 1. Demographic characteristics and fetal biometric measurements

Both PGDM and GDM volunteers are older than control group. Other parameters are homogenously distributed.

Table 2 provides the comparison fetal diaphragm measurement parameters among groups.

Table 2 . Comparisons of fetal diaphragm functional parameters among groups

Especially PGDM group represented adversely affected diaphragm measurement parameters. DT inspiration, DT expiration, DE, CDA inspiration and DTF values were significantly different between PGDM and control group.

Table 3 provides the comparison of delivery outcomes among groups.

Table 3 . Comparisons of delivery outcomes among groups

Babies who was born to both PGDM and GDM volunteers, showed significantly high NICU admission.

Discussion

Volunteers with GDM and PGDM antepartum surveillance of the patients usually begins at 32th weeks of gestation. We use biophysical profile two times per week until delivery and one of the important parameter for evaluation is fetal breath. Therefore this study opened a horizon about the quality of breathing efforts on fetuses complicated with GDM and pre-gestational DM.

In the presence of GDM and pre-gestational DM, diaphragm USG might be useful to understand quality of breathing efforts in newborns. Good quality diaphragm movements are an important sub-type of diaphragm movements.

Results of previous studies about DUSG, PGDM, GDM and their babies

DUSG has been used as a marker of well being in the intensive care unit (ICU) patients moreover it is purposive to determine suitable patients for liberation from mechanic ventilator[15, 16]. DE and DTF, which are DUSG components, exhibit breathing effort and active muscular contractions respectively[16].

Previously published studies illustrated and discussed the structure of diaphragm. Authors showed that lateral regions of both right and left diaphragm do not participate completely in the movement however medial and middle regions plays an important role[17]. Sonographic measurements showed that CDA at the end of expiration state were not different among groups however CDA during inspiration state was significantly affected in PGDM group. This situation may be related with ineffective diaphragmatic contractions. Moreover expiration state of respiratory cycles occurs passively within the relaxation of diaphragm muscles[18]. Thus we are of the opinion that CDA at the inspiration state of respiratory cycle is better indicator of diaphragmatic contractions. Other findings of study supported this situation and we found DE and DTF parameters were significantly affected in the PGDM group which showed movement ability and contraction capacity respectively[9, 14].

Clinical significance

Four of the fetuses (% 11) in GDM group, 6 of the fetuses (% 17) in PGDM group were admitted NICU, however none of the fetuses in control group were required NICU admission. Fetal weight, gestational age and umblical artery pH values were not different among groups.

In the present study we found that DT inspiration, DT expiration and DTF was significantly higher and DE and CDA inspiration was significantly lower in PGDM group than control group. In addition umblical artery blood gas PO_2, umblical artery blood gas PCO_2, and NICU admission rates were statistically different among groups. In literature GDM and pre-gestational DM have been accepted as a risk factor for neonatal respiratory morbidity[19-21]. Glucose imbalance and fetal hyperinsulinemia has been accused for delayed pulmonary maturation[22]. Moreover these complications presumably related to insufficient surfactant synthesis, due to maternal hyperglycemia[23, 24]. In literature authors examined the effect of insulin on surfactant protein A (SP-A) and surfactant protein B (SP-B) secretion. They found that insulin lowers both surfactant protein (protein A and protein B) productions in lung tissue[25,26]. Additionally reduced fluid clearance in the fetal lungs, augmented by increased cesarean delivery rates was another problem[27-29]. As far as we know this is the first study shows that GDM and pre-gestational DM have adverse effects on fetal diaphragm thickness and diaphragm function in term pregnancies. In this case, we can argue that diabetes has negative effect on diaphragm movements and diaphragm structure.

Our results indicated that not only surfactant synthesis but also quality of fetal diaphragm movements affected in pregnancies complicated with GDM and pre-gestational DM. Prolonged duration of diabetes may have adverse effect on diaphragm morphology and its function.

Study limitations

We can suggest that cephalic presentation, male gender, small sample size can be accepted limitations of study.

Disclosure

All authors have declared that they have no conflicts of interest associated with this study or its results.

Funding

This study did not receive grants from any funding source within the public, commercial, or not for profit sector.

Data Availability

The data used to support the findings of this study are available on request from the corresponding author.

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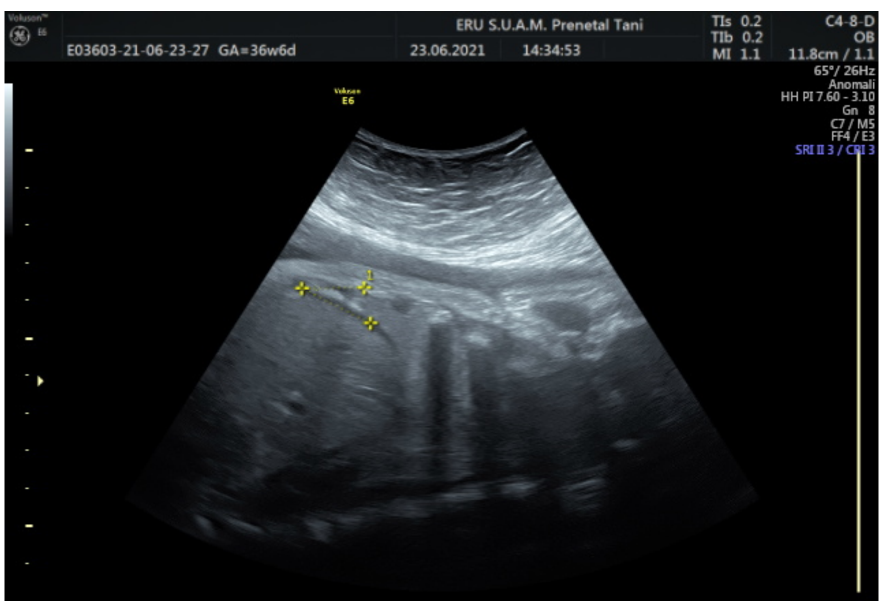

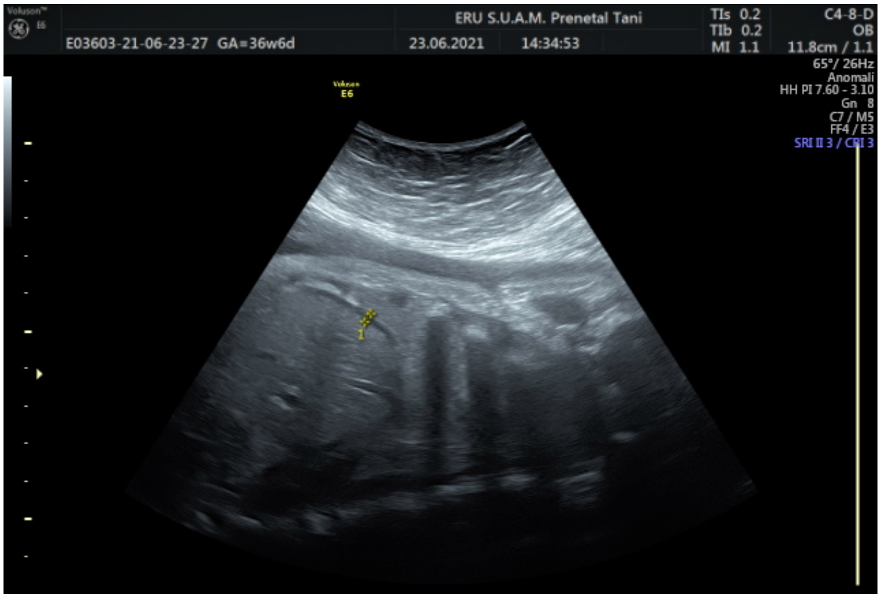
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