Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. Maternal hyperglycemia leads to fetal hyperglycemia, which stimulates pancreatic islet cells and consequently fetal hyperinsulinemia. This state results in excessive fat tissue and total body size and the major reason for poor perinatal outcome is accelerated fetal growth and macrosomia [2,3]. Fetal macrosomia complicates 20–30% of pregnancies with gestational diabetes mellitus (GDM) [4]. The presence of hyperglycemia influences biochemical transformation processes in the fetus [5]. The birth of a macrosomic fetus has been associated with adverse outcomes for both mother and fetus. Shoulder dystocia during delivery and related permanent brachial plexus injury may be seen. Both neonatal mortality and morbidity are higher in macrosomic fetuses compared with normal weight fetuses [6]. Maternal complications such as postpartum hemorrhage, infections, as well as third or fourth-degree vaginal lacerations may occur because of operative delivery. Today, cesarean sections performed for fetal macrosomia are not rare at all. Birth weight of the fetus is an important factor in determining the mode of delivery, but pelvic assessment should not be ignored [7]. Ultrasound-based birth weight prediction is still insufficient. Investigators have attempted to improve ultrasound-based prediction of fetal macrosomia by various methods, such as the assessment of fat deposition at different locations. None of these methods have gained wide popularity because of the inability to accurately estimate fetal weight against conventional biometric formulas [8,9]. The umbilical cord is responsible for materno-fetal blood flow. Normally, it is composed of two arteries permeated with venous blood and a vein that transports arterial blood, cushioned by a special type...
of mucus connective tissue known as Wharton's jelly and by remnants of the allantois [10]. Ultrasonographic examination of umbilical cord is usually limited to Doppler blood flow and assessment of the number of vessels. Also, the effect of umbilical cord morphology on the fetus and neonates has not been adequately shown [11–13]. Studies that have assessed umbilical cord components to predict fetal weight have shown that there is a correlation between umbilical cord diameter, area and fetal biometric parameters [14]. In addition, some observers have suggested that combination of these two methods should give more reliable results for estimating macrosomic fetuses.

**Materials and Methods**

This prospective case–control study was carried out at Ain Shams University maternity hospital between April 2015 and October 2015 on 80 pregnant women.

They were divided into two groups:

40 pregnant women as case group with gestational diabetes mellitus and 40 non–diabetic pregnant women as control group after being approved by the local hospital ethics and research committee.

A verbal consent was taken from each patient.

Inclusion criteria were singleton gestation, gestational age over 27 weeks, intact membranes, normal umbilical morphology (two arteries and one vein) and Diagnosis of gestational diabetes.

Exclusion criteria were congenital anomalies, Multifetal pregnancy, maternal chronic diseases (hypertension, renal disease, cardiac and pulmonary disease, etc.) and Patients with a diagnosis such as oligohydramnios, preeclampsia and intrauterine growth retardation.

Ultrasound examination was performed at 36–37 weeks of gestation with Voluson E6 equipped with a 3.5 Hz transabdominal probe.

Ultrasound examination included fetal biometry (biparietal diameter, abdominal circumference, femur length) and estimated fetal weight were calculated automatically according to hadlock’s formula additionally.

The sonographic cross sectional area of umbilical cord, the umbilical arteries and the umbilical vein were measured in a free loop of the umbilical cord using the software of the ultrasound device.

The cross–sectional area of Wharton’s jelly was computed by subtracting the cross–sectional area of the vessels from that of the umbilical cord.

The interventricular septum thickness was measured. HbA1c levels was measured for diabetic patients.

These patients were followed up till delivery.

The neonates were weighed and fetal macrosomia was diagnosed if fetal weight is 4 kg or more.

**Sample size justification**

A sample size of 40 diabetic and 40 non–diabetic pregnant women is enough to predict if there is a correlation between umbilical cord thicknesses, inter ventricular septum thickness, the HbA1c level and fetal macrosomia.

**Statistical analysis**

Statistical analysis will be performed using Microsoft Excel 2007 and Statistical Package for Social Science (SPSS®) version 17.0. Data will be prescribed as range mean and standard deviation (for parametric variables), range, median and quartile range (for non–parametric variables) and number and percentage (for categorical variables). Differences between variables of two groups will be analyzed by using student’s T–Test (for quantitative parametric measures). Mann–Whitney’s test V–test (for quantitative non–parametric measures). Person’s correlation coefficient (for parametric values) and Spearmann’s correlation coefficient (for rank variables). A receiver–operating characteristic (ROC) curve “cutoff” between two variables will be estimated in terms of sensitivity, specificity, positive and negative predictive values and accuracy as well as likelihood ratios.

**Statistical methods**

Data were analyzed using IBM® SPSS® Statistics version 23 (IBM® Corp., Armonk, NY, USA). Normality of numerical data distribution was examined with the Shapiro–Wilk. Continuous numerical variables were presented as mean ± SD and inter–group differences were compared using the unpaired Student t test. Discrete numerical variables were presented as median and interquartile range and between–group differences were compared using the Mann–Whitney U test. Categorical variables were presented as number (%) and inter–group differences were compared using Fisher’s exact test. Receiver–operating characteristic (ROC) curve analysis was used to examine the value of umbilical cord dimensions, IVS thickness, or HbA1c level for discrimination between cases with gestational DM and normal controls, and for discrimination between women with or without macrosomic babies. The DeLong method was used to compare the area under different ROC curves. A two–sided p–value <0.05 was considered statistically significant.

**Results**

This study was conducted on 88 pregnant women with their mean age was (31±8) years, mean parity (1–3), mean previous abortions from (0–2) gestational age by LMP ranges from (27 to 39 wks). 17 among the 40 diabetic patients had macrosomic neonates (higher or equal to 4 kg) (42.5%) while there was no macrosomic neonates for the non–diabetic pregnant women (0%) (Figures 1–3). Large umbilical cord diameter was measured, among the diabetic group with mean (2.77±1.19) cm, among the control group (2.06±0.77) cm with specificity, positive and negative predictive values of sonographic large umbilical cord in the prediction of birth weight > 4000 g were...
82.5%, 50%, 89.7% respectively. Umbilical artery measures were (0.67±0.47) cm among diabetic group and (0.51 ± 0.16) cm among non-diabetic group, with specificity, positive and negative predictive values of sonographic. Large umbilical artery diameter in prediction of fetal macrosomia were 33.3%, 25%, 87.5% respectively. Umbilical vein diameter varied from (0.83 ± 0.41) cm among diabetic women and (0.53 ± 0.2) cm among non-diabetic women, with specificity, positive and negative predictive values in the prediction of fetal macrosomia (52.4, 34.8%, 97.1%) respectively. Large Wharton’s Jelly area was measured in diabetic group (65.03±17.56) mm² and (44.6±8.99) mm² in non-diabetic group with specificity, positive and negative predictive values of fetal macrosomia (95.2%, 80%, 92.3% respectively). Mean IVS (0.86±0.33) among macrosomic fetuses and (0.65±0.24) among non macrosomic fetuses. IVS has sensitivity, specificity, positive predictive value and negative predictive value 64.7%, 73%, 39.3%, 88.5% respectively. HbA1c is more sensitive (82.4%) than umbilical cord diameter (64.7%) (Tables 1,2).

**Discussion**

Fetal macrosomia affects 20–30% of gestational diabetes pregnancies 4. Delivery of a macrosomic fetus is correlated to unfavorable clinical outcomes at maternal and fetal levels. Brachial plexus injuries and shoulder dystocia issues could be experienced in gestations affected by fetal macrosomia particularly when causative gestational DM exists. Macrosomic fetuses have higher incidence of morbidity and mortality.
in comparison to normal weight fetuses. Operative vaginal delivery interventions required in some case scenarios could result in postpartum hemorrhage, third and fourth degree vaginal lacerations [15]. In the current research study conducted, the recruited 80 gestations have been assessed and evaluated by abdominal sonography and expected fetal weight calculated by obtained fetal parameters was tabulated in addition to neonatal weight. Forty gestations were in diabetic research group and 40 subjects were in research control group (i.e non diabetic). 17 Within the 40 diabetic gestations 42.5% of them had macrosomic neonates (neonatal weight greater or equal to 4 kg) whereas there was no macrosomic neonates in the control research group (0%). Sonographically measured umbilical cord diameter, within the gestational DM research group had mean +/- SD value of 2.77±1.19 cm, within the research control group had a mean +/- SD value of 2.06±0.77 cm with statistically obtained specificity, positive and negative predictive values of sonographically measured large umbilical cord in predictability of birth weight > 4000 g have been 82.5%, 50%, 89.7% consecutively. Sonographically measured large umbilical artery diameter, umbilical vein diameter and Wharton’s Jelly area have been obtained and assessed in addition within the research diabetic group. Umbilical artery diameter indices had a mean +/- SD value of 0.67±0.47 cm within diabetic research group and 0.51 ± 0.16 cm within non diabetic research group with statistically calculated specificity, positive and negative predictive values of large umbilical artery diameter in predictability of macrosomic fetus 33.3%, 25%, 87.5% consecutively. Umbilical vein diameter indices have shown variability ranging from 0.83 ± 0.41 cm within diabetic gestations and 0.53 ± 0.2 cm within non–diabetic gestations, with calculated specificity, positive and negative predictive values in the predictability of macrosomic fetus (52.4, 34.8%, 97.1%) consecutively. Large Wharton’s Jelly area have been assessed and obtained in diabetic research group having a mean +/- SD value of 65.03±17.56 mm² and 44.6±8.99 mm² in non diabetic research group with obtained specificity, positive and negative predictive values for macrosomic fetus 95.2%, 80%, 92.3% consecutively. A prior research study conducted in a prospective manner investigated the correlation between umbilical cord thickness (diameter or area) and HbA1c in the predictability of macrosomic fetus pathological development with cut off value > 0.71. This is in harmony with Gracia-Flores et al. research study [16], as they mentioned and concluded that IVS thickness > 0.71 is the most sonographically important parameter to reveal the impact of glycemic control on the fetal cardiac interventricular septum. In that research study mean +/- SD IVS value = 0.86±0.33 within fetuses with macrosomia and 0.65±0.24 within non macrosomic fetuses. IVS had a calculated sensitivity, specificity, positive predictive value and negative predictive value 64.7%, 73%, 39.3%, 88.5% consecutively. That research study displayed that prenat al interventricular septal thickness is considered a reliable parameter in predictability of macrosomic fetus pathological development with cut off value > 0.71. This is in harmony with Gracia–Flores et al. research group [17], as they mentioned and concluded that IVS thickness is the most sonographically important parameter to reveal the impact of glycemic control on the fetal heart development, the observation of a hypertrophic IVS requires evaluation and assessment of systemic, systolic and diastolic functional flow and parameters. Nonexistence of functional abnormalities in fetuses with hypertrophic IVS could not exclude fetal risk, since it could be correlated with greater perinatal mortality due to pathological development of diabetic fetopathy, and could denote a hidden and unknown poor maternal glycemic control.

References


