Assessment of Fetal Wellbeing in Diabetic Pregnant Women by Using Biophysical Profile and Fetal Doppler Studies of Middle Cerebral And Umbilical Arteries

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Abstract: Back ground: Infants born to mothers with glucose intolerance are at an increased risk of morbidity and mortality related to the following: Respiratory distress, growth abnormalities (large for gestational age [LGA], small for gestational age [SGA]), hyperviscosity secondary to polycythemia, hypoglycemia, congenital malformations, hypocalcemia, hypomagnesemia, and iron abnormalities. **Objective:** To asses fetal wellbeing in diabetic pregnant women by using biophysical profile and fetal doppler studies of middle cerebral and umbilical arteries. **Material and method:** This study was conducted on 100 diabetic pregnant females to evaluate the role of biophysical profile and doppler of umbilical and middle cerebral arteries in assessment of fetal wellbeing. Fetal outcome was assessed regarding neonatal acidosis, gestational age at delivery, hypoglycemia, ICU admission and neonatal deaths. **Results:** It was found that there was statistically significant relation between abnormal MCA Doppler and abnormal neonatal outcome, Regarding umbilical artery Doppler, there was no significant difference in pH and Apgar 5-min between the 2 groups (p>0.05) however there was significance regarding gestational age of delivery and Apgar 1-min.

Introduction

International Diabetic Federation (IDF) estimates that 20.9 million or 16.2% of live births to women in 2015 had some form of hyperglycaemia in pregnancy. An estimated 85.1% were due to gestational diabetes, 7.4% due to other types of diabetes first detected in pregnancy and 7.5$ due to diabetes detected prior to pregnancy. 1

Infants born to mothers with glucose intolerance are at an increased risk of morbidity and mortality related to the following: Respiratory distress, growth abnormalities (large for gestational age [LGA], small for gestational age [SGA]), hyperviscosity secondary to polycythemia, hypoglycemia, congenital malformations, hypocalcemia, hypomagnesemia, and iron abnormalities. These infants are likely to be born by cesarean delivery for many reasons, among which are such complications as shoulder dystocia with potential brachial plexus injury related to the infant's large size.**2**

Assessment of fetal wellbeing is primarily directed at the detection and prevention of hypoxic stress, which may cause fetal or neonatal death, or permanent neurological damage. The challenge for prenatal surveillance is to identify those fetuses whose physiological defense mechanisms are compromised, in order to act before decompensation has occurred.**3**

Umbilical artery (UA) Doppler reflects downstream placental vascular resistance, strongly correlated with the fetal surveillance. Abnormalities are progressive, with reduction, loss, and finally a reversal of diastolic flow. When umbilical arteries become abnormal, the differentiation of fetal status requires Doppler information from systemic vessels.**4**

Representing downstream resistance in cerebral micro-circulation, the middle cerebral artery (MCA) provides an important insight into systemic circulatory responses. MCA changes begin when the redistribution of cardiac output reflects rising placental resistance, with a reduction in the cerebro-placental ratio. Later, overt MCA change appears as increased diastolic velocity; 'brain-sparing'.**5**

Studies suggest that the cerebroplacental ratio may be a highly sensitive doppler index for assessment of wellbeing and prediction of outcome in fetuses in high risk pregnancies.

2. Patients and Methods

This prospective study will be conducted at the Department of Obstetrics and Gynecolog at el zaitoun

specialized Hospital and Imbaba General Hospital. The study population consists of 100 singleton diabetics. pregnant females in the 3**rd** trimester. All study cases will be precisely dated based on reliable menstrual dates that is consistent with early examination or early ultrasonography (≤ 20 weeks).

Inclusion criteria:
    1. Diabetic pregnant females.
    2. Singleton pregnancy.
    3. With no history of rupture of membranes.

Exclusion criteria
    1. Multiple pregnancy.
    2. Fetuses with anatomical defects.
    3. Pregnant females with other medical disorders.

All cases will be subjected to detailed history taking, complete general with special attention to the history of diabetic condition, diabetic complications and treatment and obstetric examination, laboratory investigations (including complete blood picture, fasting and 2 hours postprandial blood sugar, liver function tests, kidney function tests, and complete urine analysis), and interval ultrasonographic biometry. Doppler velocimetry of the UA and MCA will be performed when delivery is indicated.

Adverse (or abnormal) perinatal outcome is defined as any perinatal complications such as: perinatal death, cesarean section for fetal distress, meconium staining of the amniotic fluid, 5-minute Apgar score <7, IUGR (fetal weight <10**th** percentile for gestational age), hypoglycemia (glucose level <45 mg/dL), or stay in the neonatal intensive care unit for >24 hours.

Ultrasound equipment capable of high resolution gray-scale, pulsed wave and color Doppler modes was used, (accuvix XQ, Medison, Suol, Korea) using 3.5 MHZ probe.

All recordings were obtained in the absence of fetal breathing and fetal movements. For each vessel, an average of three consecutive Doppler velocity waveforms was used for statistical analysis.

The Apgar score is used in the evaluation of fetal condition after birth. The score includes the heart rate, respiratory effort, muscle tone, reflexes and color. In general the higher the score (up to 10), the better the condition of the infant. The 1 minute Apgar score determines if immediate resuscitation is needed**.**

A score of 7 or higher indicates good infant condition and no need for aid more than nasopharyngeal suction. Mild to moderate depressed infants scores 4 to 7 at 1 minute. Severely depressed infant scores 0 to 4. Resuscitation should be started immediately. The 5 minute Apgar score correlates best with neonatal morbidity and mortality.

3. Results

Table (1) shows indications of delivery where 44% was spontaneous labour, 20% was elective delivery, 14% abnormal Doppler and 18 % non reactive CTG.

Table 2 shows mode of delivery where 68% was Cesarean section and 32% normal vaginal delivery.

Table 3 shows distribution of data of both umbilical artery and middle cerebral artery Doppler, 72% of cases has normal umbilical artery Doppler and 28% has abnormal Doppler while 86% has normal MCA Doppler and 14% has abnormal MCA Doppler.

Table 4 shows neonatal outcome where 90% of neonates have normal 1 minute Apgar score and 16% has Apgar score <4 at 1 min. it also shows the Apgar at 5 min, where 94% was normal and 6% was <7. Acidosis was found in only 8% of neonates. Neonatal death was another parameter occurred in only 6%. 26% need ICU admission while 74% did not need, 30% show RDS, 2% seizures, 4% sepsis and 24% hypoglycemia.

Table 5 shows the outcome parameters related to UA Doppler. In cases with normal UA Doppler the mean of the gestational age at delivery was 39.1 compared to 36.8 in cases with abnormal UA Doppler. Neonatal acidosis (pH <7.2) was found in only 2.7% if UA Doppler was normal and increased to 21% with abnormal Doppler. As regard's the Apgar score <4 after 1 min., it was 2.7% only with normal Doppler increased to become 28.5% in cases with abnormal Doppler. As for the Apgar after 5 min, it was <7 in 2.7% of cases if normal UA Doppler changed to 14.3% in cases with abnormal Doppler, the third parameter which is the neonatal death occurred in 2.7% only with normal UA Doppler increased to 14.3% in cases with abnormal Doppler. There was no significant difference in pH and Apgar 5-min between the 2 groups (p>0.05) however there was significant difference in gestational age of delivery and Apgar 1-min.

Table 6 demonstrates the outcome related to MCA Doppler showing that the mean for gestational age with normal Doppler was 39.3 weeks decreased to 36.9 weeks in cases with abnormal Doppler. Neonatal acidosis pH <7.2 was seen in only 0% in normal Doppler & 57.4% in abnormal Doppler. As regards the Apgar score after 1 min. it was <4 in 9.3% only if normal MAC Doppler increased to become 42.8% if they have abnormal Doppler. The Apgar score after 5 min was <7 in 2.3% of cases if they have normal Doppler increased to 28.5% if the Doppler was abnormal. The fourth parameter which is neonatal death demonstrated no deaths if the Doppler was normal compared to 42.8% deaths if the Doppler was abnormal. Comparing the *p*-value of. the four parameters we find it significant.

Table (1): Indications of delivery

	Number	*Percent*
Spontanous Labour	44	44
Elective Delivery	24	24
Abnormal Doppler	14	14
Non Reactive CTG	18	18
Total	100	100

Table (2): Mode of delivery

	Number	*%*
CS	68	68
VD	32	32
Operative VD	0	0
Total	100	100

Table (3): Distribution of Doppler

		Number	*%*
UA	High PI	24	24
	AED V	2	2
	RED V	2	2
	Normal	72	72
MCA	Abnormal	14	14
	Normal	86	86

Table (4): Neonatal outcome

		Number	*%*
1 min	Normal >4	90	90
	Abnormal <4	10	10
5 min	Normal >7	94	94
	Abnormal <7	6	6
Acidosis	Yes	8	8
	No	92	92
Neonatal death	Yes	6	6
	No	94	94
ICU admission	Yes	26	26
	No	74	74
RDS		30	30
Sepsis		4	4
Seizures		2	2
Hypoglycemia		24	24

Table (5): Outcome parameters related to UA Doppler

	UA abnormal N = 28	*UA normal N =72*	p-*value*
GA at delivery	36.8± 3.1	39.1± 2.7	0.0125
Neonatal acidosis	21% 6 cases	2.7% 2 cases	0.0612
Apgar 1 min <4	28.5% 8 cases	2.7% 2 cases	0.0180
Apgar 5 min <7	14.3% 4 cases	2.7% 2 cases	0.1857
Neonatal death	14.3% 4 cases	2.7% 2 cases	0.1857

Table (6): Outcome parameters related to MCA Doppler

	MCA abnormal N = 14	MCA normal N = 86	p-value
GA at delivery	36.9 ± 2.1	39.3± 2.8	0.0355
pH<7.2	57.4% 8 cases	0% 0 case	0.0002
Apgar 1 min <4	42.8% 6 cases	9.3% 4 cases	0.0156
Apgar 5 min <7	28.5% 4 cases	2.3% 2 case	0.0479
Neonatal deaths	42.8% 6 cases	0 % 0 case	0.0018

4. Discussion

Early detection of fetal risk is one of the main issues in today obstetrics. Ultrasound diagnosis plays a significant role, as the introduction of Doppler imaging method in the evaluation of blood flow has enabled non-invasive assessment of uteroplacental circulation.

Graves also reported that Pregnancies complicated by diabetes mellitus are associated with an increased risk of fetal and neonatal risks compared with pregnancies in the healthy gravida. Data suggest that stillbirth and perinatal mortality may be increased as much as 5 times for patients with insulin-dependent diabetes than in the general population. Pregnancies complicated by preexisting diabetes should undergo twice weekly surveillance with nonstress test or biophysical profile or a combination of both. Doppler studies should be reserved for those patients with vascular disease, intrauterine growth restriction, or hypertensive disorders[7].

Sieroszewski revealed that evaluation of blood flow in the middle cerebral artery, and in particular pulsatility index PI, reflects the risk to fetus. Flow in the middle cerebral arteries represented the central circulation, and flow in the umbilical artery the uteroplacental circulation. However, they added that, evaluation of the blood flow in fetal vessels is a significant element of prenatal diagnostics, but due to its low sensitivity, it should be compared with the results of other biophysical tests, to achieve complex evaluation of the condition of the fetus[9]. *On the other hand Yalti* stated that Umbilical velocimetry, is a test of placental function that does not always directly reflect foetal status. In their study, sensitivity, positive predictive values of umbilical artery Doppler indices alone were 30 and 50 per cent respectively.[10]

In this study; We found that when performing UA Doppler that the majority of the cases (72%) was normal while in 24% there was an increased pulsitiliy index and there was an equal proportion of those with absent or reversed end diastolic volume (2%), all the outcome parameters including pH<7.2, apgar at 5 min <7, and neonatal death were insignificant (p- value >0.005). When comparing cases with normal UA Doppler against those with abnormal UA, Cases with abnormal. UA Doppler the apgar score at 1 min {<4} showed a statistically significant difference between cases with normal and abnormal UA Doppler.

Also in this study when we performed the MCA Doppler which was found preserved in majority of cases (86%) diminished only in 14%. We found it to have significant difference between cases with normal and abnormal MCA Doppler regarding outcome parameters including neonatal PH {< 7}, apgar score at 1 min {<4} and neonatal death with abnormal MCA Doppler. The only parameter that was insignificant with abnormal MCA Doppler was the apgar score at 5 min.

In a study to investigate the correlation between Doppler parameters in the umbilical and fetal middle cerebral arteries and pregnancy outcome in women with GDM, 169 women with singleton GDM pregnancies, UA PI, MCA PT and peak systolic velocity (V max) was measured every 4 weeks until delivery from time of diagnosis of GDM. They concluded that Doppler study of the UA-PI, MCA-PI and MCA-V max was not useful in the prediction of abnormal pregnancy outcome in GDM.[11]

To and MOK compared Doppler measurements of UA and UV in diabetic and non diabetic pregnancies near term patients with gestational diabetes mellitus (GDM) were prospectively recruited from a regional obstetric service over an 8-month period. Doppler assessment of the UA and LIV done within 10 days from delivery were used for analysis.

Similar measurements were performed in a control group of non-diabetic non-hypertensive patients near term. They found that umbilical arterial and venous Doppler measurements near term were unable to distinguish between diabetic and non diabetic pregnancies, Umbilical venous flow was apparently more sensitive to the size of the fetus than to the maternal diabetic state[11].

Conclusion

From this study we can conclude that managing patients with diabetes mellitus requires close observation and team management between obstetrician and diabetologist. the best means of evaluating the fetus is MCA Doppler as there is no significance of UA Doppler measurement regarding fetal outcome parameters as neonatal PH, Apgar score at 5 min. and neonatal death, the outcome parameters that were affected by an abnormal UA Doppler were the apgar score at 1 min and gestational age at delivery but there was significance of MCA Doppler regarding all the outcome parameters except apgar score at 5 min. But still, there is considerable debate on the frequency of monitoring the fetus.

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