Fetal Middle Cerebral Artery and Renal Artery Doppler Indices in prediction of Fetal Outcome in Cases with Idiopathic Hydramnios

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Abstract:Background: Adverse perinatal outcomes in patients with polyhydramnios have been associated with congenital fetal anomalies in numerous studies. Perinatal morbidity and mortality rates also significantly increase.The etiologic factors of polyhydramnios are varied and may include maternal and fetal conditions such as congenital anomalies, diabetes mellitus, isoimmunization, multiple gestations, and placental abnormalities. But the cause of polyhydramnios remains idiopathic in most cases (60%). Ratios of the fetal Doppler parameters provide the clearest evidence of deterioration in the fetal condition, there is a controversy regarding the value of middle cerebral artery Doppler ultrasound as a single parameter in assessing the fetal wellbeing. However a combination of multiple fetal vessels Doppler study as umbilical, aorta, renal and middle cerebral artery may be more accurate. **Methods:** Group1 (Control): This group consisted of 50 pregnant women with no polyhydramnios. Group 2 (study): This group consisted of 50 pregnant women complicated by idiopathic polyhydramnios (amniotic fluid index ≥ 24cm). We were done Doppler US study of fetal vessels including umbilical, descending thoracic aorta, renal artery (RA) and MCA. Peak systolic volume of the MCA and renal arteryand RA/MCA pulsatile index were done. **Results:** There was significant increase in the mean PI of both umbilical artery and fetal descending aorta (0.76-0.98) and (1.55-2.34) respectively in the cases of polyhydraminos if compared with the controls.The mean PSV of both the UA and fetal descending aorta was reduced below accepted reference values for gestation (40.13--68.47) and (69.03—144.2) respectively in the cases of polyhydramnios denoting brain sparing in case of hypoxia when compared with the controls. **Conclusions:** Middle cerebral artery pulsatility index Doppler velocimetry is considered more valid for prediction of the fetal outcome compared with the renal artery. Middle cerebral artery has the highest negative predictive value (87.9%) than the renal artery (80%). Therefore middle cerebral artery Doppler indices may be useful in identifying those fetuses not likely to have a major perinatal outcome. Our preliminary results suggest that RA/MCA ratio may be a predictor of fetal outcome.

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Key words: Idiopathic Hydramnios; Fetal Doppler Ultrasound; Outcome.

1. Introduction

Polyhydramniosis defined as an excess of amniotic fluid and is diagnosed whenamniotic fluid index (AFI) ≥ 24 cm on real-time obstetric ultrasound, the single deepest pocket (SDP) as being ≥ 8cm, or the examiner's subjective assessment of having an increased amount of amniotic fluid volume**(Magann*et al.*, 2007).**

Adverse perinatal outcomes in patients with polyhydramnios have been associated with congenital fetal anomalies in numerous studies. Perinatal morbidity and mortality rates also significantly increase**(Pauer*et al.*,2003).**

The etiologic factors of polyhydramnios are varied and may include maternal and fetal conditions such as congenital anomalies, diabetes mellitus, isoimmunization, multiple gestations, and placental abnormalities **(Many *et al.*,1996**). But the cause of polyhydramnios remains idiopathic in most cases (60%) **(Ben-Chetrit*et al.*,1990).**

Idiopathic hydramnios is defined as hydramnios that is not associated with any apparent maternal or fetal cause **(Magann*et al.*,2007).** It is an independent risk factor for perinatal morbidity and mortality. Although the precise mechanism is unknown, hydramnios may alter oxygen delivery to the fetus **(Mazor*et al.*,1996).**

Ultrasound technology has evolved from only producing images of the pregnancy to include methods for measurement of both maternal and fetal circulatory functions. The phenomenon of Doppler shift of ultrasonic echoes forms the technical basis for acquisition of information on the maternalfetal hemo-dynamic circulations **(Acharya*et al.*,2005).**

A reduction in fetal growth velocity is preceded by changes observed in the fetal circulation. Ratios of the fetal Doppler parameters provide the clearest evidence of deterioration in the fetal condition **(Harrington *et al.*,1999).**

There is a controversy regarding the value of middle cerebral artery Doppler ultrasound as a single

parameter in assessing the fetal wellbeing. However a combination of multiple fetal vessels Doppler study as umbilical, aorta, renal and middle cerebral artery may be more accurate **(Baschat&Gembrush, 2003).**Non stress test, biophysical profile and contraction stress test , if used in combination with Doppler cerebral artery study, seems to be more predictive according to **(Magnn*et al.*,2007).**

Yalti*et al.*,2004evaluated the role of middle cerebral artery, umbilical artery Doppler waveforms, and biophysical profile in prediction of fetal outcome. They suggested that MCA/UA Doppler ratio of <1 was a good predictive tool for neonatal outcome in preeclamptic and hypertensive pregnant women, could be used to identify fetuses at risk of morbidity.

Özerena*et al.*(1999) found the MCA pulsatility index (PI) values were low in the preeclamptic groups. Incremental changes in cerebral blood flow in cases of hypoxia reflect the degree of the hypoxic stimulus and represent a very fine control mechanism for oxygen delivery to the brain.

Although, the effect of oligohydramnios on fetal Doppler velocimetry is well studied for a long time, there were very few researches on the effect of idiopathic hydramnios on fetal Doppler velocimetry.**Hershkovitz*et al.*,(2001**)reported that a pulsatility index (PI) below the 5th centile for the MCA may be considered abnormal in patients with idiopathic hydramnios and a significant inverse correlation was found between MCA PI and increasing amniotic fluid index (AFI) among patients with hydramnios.

Magnn*et al.*,(2007) found that there was 2 to 5 fold increase in the risk of perinatal mortality and summarized the lack of consensus in monitoring pregnancies affected with idiopathic hydramnios.

Aim of work

The aim of this study is to evaluate the changes in the Doppler velocimetry parameters of middle cerebral artery in combination with the renal artery in cases of idiopathic hydramnios in comparison with low risk pregnancy and correlate these changes to the fetal and neonatal outcome.

2. Patients and Methods

The present study was conducted in Al-Azhar University Hospital in Damietta, from November 2010 till the end of May 2012.

Group1 (The Control Group): This group consisted of 50 pregnant women with no polyhydramnios.

Group 2 (The study group): This group consisted of 50 pregnant women complicated by idiopathic polyhydramnios (amniotic fluid index ≥ 24cm).

Women referred from outpatient clinic were invited to participate in the study if the following inclusion criteria were met: Singleton pregnancy,fetal gestational age of 32-40 weeks as confirmed by menstrual history and US examination, No obstetric or medical complications of pregnancy apart from polyhydramnios in the study group.

Exclusion criteria for the study included: any pregnancy with documented structural congenital abnormality, Evidence of fetal infection, Diabetes mellitus, Rh incompatibility, Placental anomalies and multiple pregnancy.

In this study Doppler US of fetal vessels including umbilical, descending thoracic aorta, renal and MCA. Peak systolic volume of the MCA and renal and RA/MCA pulsatile index were done.

Statistical Analysis

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 12) as follows:

Description of quantitative variables as mean, SD and range, Description of qualitative variables as number and percentage, Unpairedt-test was used for comparison of two groups as regard quantitative variable.

One way ANOVA test (analysis of variance) was used to compare more than two groups as regard quantitative variable.

Correlation coefficient test was used to rank different variables against each other's either positively or inversely. ROC (receiver operator characteristic curve) was used to find out the best cut off value, sensitivity and specificity at this cut off.

Sensitivity = true + ve /true +ve + false –ve

= ability of the test to detect +ve cases

Specificity = true -ve/true-ve+ false +ve

= ability of the test to exclude negativecases

PPV (positive predictive value) = true+/true+ve +false +ve= % of true +ve cases to all positive

NPV = true-/true-ve + false –ve= % of the true – ve to all negative cases

P value >0.05 insignificant,*P*<0.05 significant,*P*<0.01 highly significant

3. Results

Both groups were matched as regards to the maternal age, body mass index, gravidity, parity and gestational age at examination. However, there was a statistically significant difference between the case and the control groups as regards AFI.

There was statistically significant increase in the mean PI of both umbilical artery and fetal descending aorta above the accepted reference values for gestation (0.76-0.98) and (1.55-2.34) respectively in the cases of polyhydraminos if compared with the controls.

In comparison between cases and controls as regards the mean peak systolic velocity (PSV) of UA and fetal descending aorta show that the mean PSV of both the UA and fetal descending aorta was reduced

below accepted reference values for gestation (40.13--68.47) and (69.03—144.2) respectively in the cases of polyhydraminos denoting brain sparing in case of hypoxia when compared with the controls.

The mean PI of RA increased in the cases of polyhydraminos than the controls but still within normal reference values for gestation (1.67—2.96) when compared with the controls. However, the mean MCA PI was reduced below the accepted reference values for gestation (1.13—2.40) in the cases of polyhydramnios.

There was a negative correlation between Middle cerebral artery PI and AFIr=-0.288 $P<0.0001$

Also there was a positive correlation between renal artery PI and AFI. r=-0.366 $P<0.0005$ in the cases.

The mean PSV of the RA decreased in cases of polyhydramnios than in the controls but still within the range of normality of the reference values for gestation (51.6—77.0). However, the mean PSV of the MCA showed significant increase in the cases above the accepted reference values for gestation (38.6—71.2) when compared with the controls.

There was increase in the mean PI of fetal descending aorta, umbilical artery and RA above the accepted reference values for gestation in the cases of polyhydramnios. On the other hand, the mean PI of the MCA is reduced below the accepted reference values for gestation in polyhydramnios cases if compared with the controls due to associated hypoxia.

The mean PSV of the UA, fetal descending aorta and RA was reduced below the reference values for gestation in the cases of polyhydramnios denoting brain sparing in case of hypoxia. On the other hand, the mean PSV of the MCA was increased above the reference values for gestation in the cases of polyhydramnios when compared with the controls.

The best cut off value for MCA PIwas 0.99with a sensitivity 80%, specificity 60%, PPV 40% and NPV 87.9%, andfor the renal artery PI was 1.80 with a sensitivity 15%, specificity 94.5%, PPV 33% and NPV 81%.

Table (1): Comparison between cases and controls as regards results data

Data	Cases (n=50)		Controls (n=50)		*t*	*P*
	Mean	±SD	Mean	±SD		
PIof umbilical	1.00	±0.13	0.88	±0.03	0.26	0.03**
PIof fetal aorta	2.02	±0.35	1.79	±0.11	0.00	0.03**
PI of MCA	0.99	±0.11	1.50	±0.04	0.00	0.00***
PI of RA	1.80	±0.13	1.70	±0.13	0.00	0.053*
PSV offetal aorta	81.46	±16.02	112.93	±9.91	0.00	0.00***
PSV of RA	60.22	±7.33	65.47	±8.16	0.73	0.54*
PSV of MCA	69.79	±9.89	56.44	6.02	0.00	0.03**
PSV ofUA	50.33	±11.34	56.44	±9.16	0.59	0.19*
UA/MCA ratio:	1.01	±0.11	0.59	±0.15	0.01	0.00***
RA/MCA ratio:	1.8	±0.14	1.1	±0.12	0.00	0.03**
Aortic/MCA ratio	2.04	±0.21	1.19	±0.11	0.00	0.00***
Aortic/RA ratio	1.12	±0.13	1.05	±0.14	0.00	0.05*
*non significant, **significant, ***highly significant,SD : Standard deviation						

Table (2): Doppler flowmetry assessment profile of cases according to sensitivity, specificity, positive predictive value and negative predictive value of various fetal vessels.

Data	Cut off value	Sensitivity %	Specificity %	Predictive value	
				+ve	-ve
UA	1.00	50	86.9	60	85.7
MCA	0.99	80	60	40	87.9
RA	1.80	15	94.5	30	80
Aorta	2.02	70	85	33	81
UA/MCA	1.01	59	87.5	53.5	84.6
RA/MCA	1.8	50.5	66.3	33.7	85.6

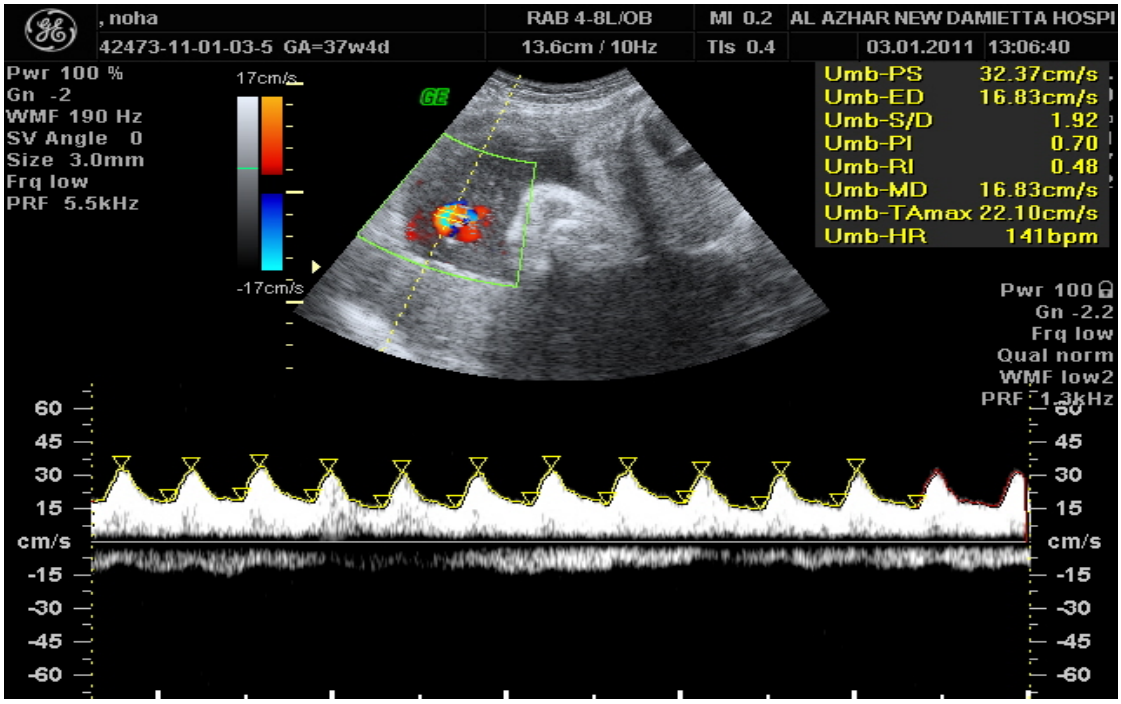

Figure (1): Doppler velocimetry of umbilical artery at 37weeks±4d

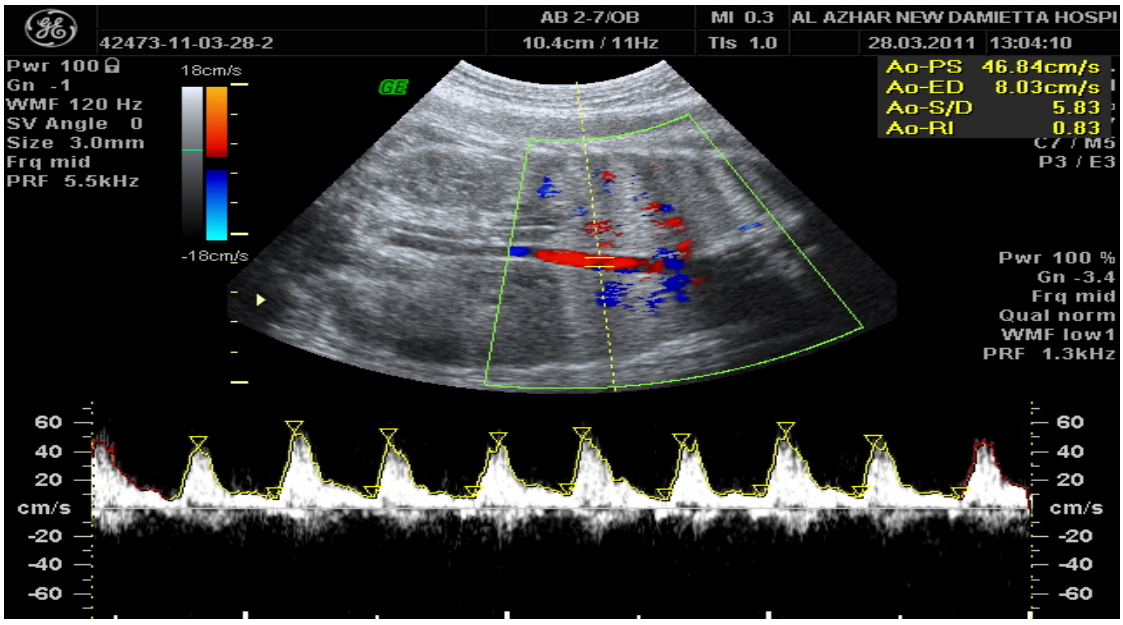

Figure (2): Doppler velocimetry of fetal descending aorta at 36weeks.

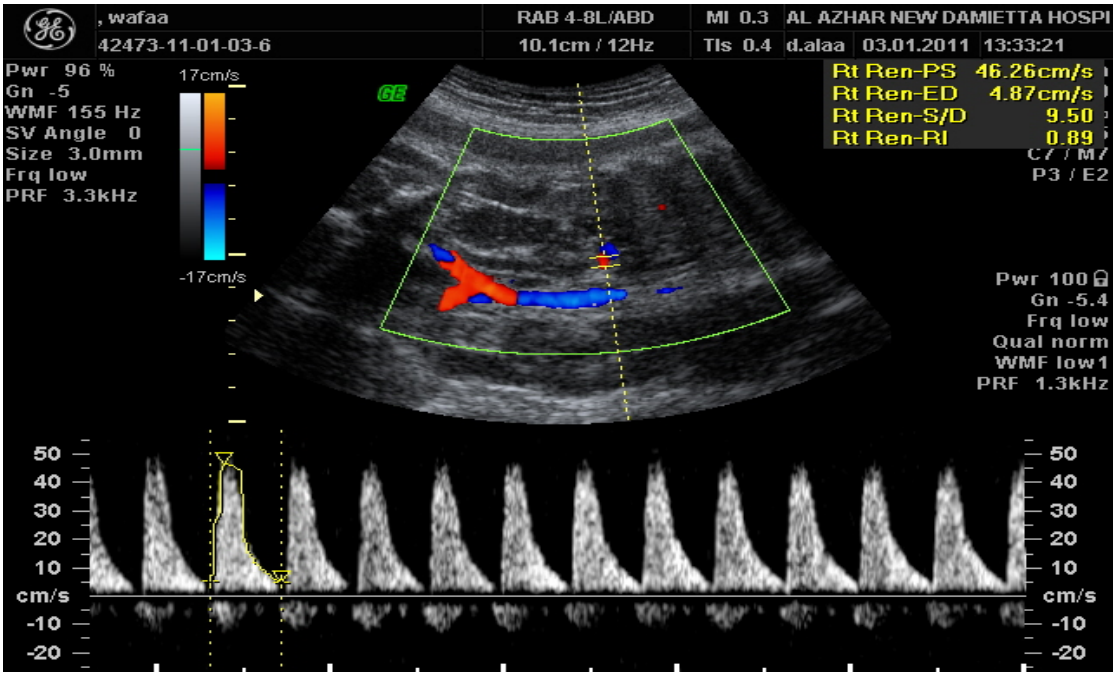

Figure (3): Fetal Renal artery Doppler velocimetry at 35weeks

4. Discussion

This study aimed to evaluate the changes of Doppler velocimetry parameters of the middle cerebral artery and renal artery in case of idiopathic polyhydramnios.

Doppler ultrasound study of idiopathic polyhydramnios:

As regards to umbilical artery **(UA)** blood flow changes in patients with polyhydramnios, it was first described by **Rochelson*et al.* (1990)** who reported thatpolyhydramnios was associated with increased fetal abnormalities such as an abnormal karyotype.

In normal pregnancy, **Khalid *et al.*, 2011,** reported that umbilical artery velocimetry correlates with haemodynamic changes in fetoplacental circulation. With increase in number of tertiary villi and arterial channels, fetoplacental compartment develops and the impedance in the umbilical artery decreases. The mean of all three indices showed a progressive decline with advancing gestational age due to decrease in umbilical artery resistance.

In the present study, the mean value of the pulsatility index **(PI)** of the umbilical artery **(UA)** showed statistically significant increase in the cases than in the controls (1.00±0.13 vs. 0.88±0.03) which were above normal values for gestation (0.76-0.98). On the other hand, the mean peak systolic velocity **(PSV)** of the umbilical artery decreased in the cases of polyhydraminos if compared with the control group (50.33 ±11.34 vs56.44±9.16), which was below the accepted reference values for gestation (40.13-68.47) indicating increased peripheral resistance and consequently decreased diastolic flow which leads to fetal compromise.

This is consistent with the results obtained by **Guzman *et al.*, 1996** who have investigated the UA PI in patients with polyhydramnios, and reported that UA PI was decreased only after therapeutic amniocentesis and not before.

This is in contrast with**Hershkovitz*et al.*, 2002**, who had determined the pulsatility index **(PI)** of both umbilical arteries prospectively between 26 and 41 weeks of gestation in 72 pregnant women with singleton pregnancies and idiopathic polyhydramnios and in 72 pregnant women with normal AFV. They have found that UA velocimetry in patients with idiopathic hydramnios was not significantly different from those with a normal AFV.

As regards to the fetal descending aorta, in hypoxic fetuses, similar to umbilical artery waveform, diastolic velocities in the descending aorta decrease and eventually disappear or even become reversed, a condition called absent or reversed end-diastolic **(ARED)** flow according to **Jouppila and Kirrkinen, 1984.**

In the study by **Adamson and Langille, 1992,** the aortic **PI** reflected not only the vascular resistance but also the pulsatile flow and pressure pulsatility. Thus an increasing fetal aortic **PI** should not be interpreted solely as an expression of increasing placental vascular resistance.

According to **Mandruzzato*et al.*, 2003,** fetal descending aorta is suitable for blood flow velocity measurements because it provides **(1)** a straight course with good visualization from thoracic to abdominal part **(2)** great reliability and reproducibility of sample volume and angle estimation and **(3)** a likelihood that aortic thoracic blood flow velocity waveform reflects the hemodynamic state of a large portion of the fetal circulation (including placental perfusion, peripheral perfusion, and cardiac output).

In the present study, the mean PI of the fetal descending aorta in the cases of polyhydramnios was higher than in the control group (2.02±0.35vs.1.79±0.11) with statistically significant difference.Consequently, there was a statistically high significant decreased PSV of the fetal descending aorta in the cases than in the control group (81.46±16.02 vs. 112.93±9.91).

For the best of our knowledge, this study is the only one that evaluates **PI and PSV** of the fetal descending aorta in cases of idiopathic polyhydramnios but there are many studies on polyhydraminos in cases of IUGR and twin-to-twin transfusion syndrome.

As regards to renal artery Doppler velocimetry, normal Doppler waveform obtained from the renal artery demonstrated a low resistance profile with continuous forward flow throughout the cardiac cycle according to **Radermacher*et al.*, 2001.** Similar findings were obtained by **Mari *et al.*, 2002** who found that the PI of the renal artery in normal fetuses decreased linearly with advancing gestation. The values in the singleton pregnancies complicated by polyhydramnios were in the range of normality for the reference limits for gestation.

The effect of hypoxemia on the fetal renal circulation is complex, as can be deduced from animal experiments**. Peeters*et al.*, 1979** performed experiments in the anaesthetized fetal lamb and studied effects of various levels of oxygenation on organ circulation. They found a gradual increase of renal blood flow in the transition from hyperoxia to hypoxia, followed by an abrupt decrease with more severe hypoxia.

Regarding the mean values of the pulsatility index **(PI)** of the renal artery (RA), it was higher in the polyhydraminos cases than in the control group (1.80±0.13 vs. 1.70±0.13) with statistically insignificant difference between both groups. Also, **PSV of RA** was 60.22±7.33 in the case group that is lower than in the control group (65.47±8.16) with no statistically significant difference between both groups.

In our study, the mean value of **RA** pulsatility index was higher in the cases than in the control group but still virtually all within the normal limits of reference values for gestation (1.67-2.96). Similar findings were obtained for PSV of renal artery (64.3± 12.7).

This is consistent with **Giancarlo *et al.*, 1993,** where they recorded Doppler waveforms in 121 normal fetuses, 10 fetuses with oligohydramnios, ten with polyhydramnios, and 8 sets of diamniotic twins with polyhydraminos in one gestational sac and oligohydramnios in the second sac. They found that normal pregnancies were associated with changes in the renal artery flow velocity waveforms.In fetuses with oligohydramnios, the worst fetal outcome seems to be associated with abnormal renal artery flow velocity waveforms. In fetuses with polyhydramnios, no abnormal RA flow velocity waveforms were found. They concluded that the values of RA pulsatility index in the singleton pregnancies complicated by polyhydramnios were in the range of normality for the reference limits for gestation.

As regards to **MCA** Doppler velocimetry, the pathogenesis of changes in cerebral blood flow in cases with idiopathic polyhydramnios may be attributed to alterations in the amniotic fluid pressure. N**icolini*et al.*, 1989** have shown that amniotic fluid pressure is higher in patients with polyhydramnios in comparison to women with a normal amount of amniotic fluid and those with oligohydramnios. Moreover, **Fisk *et al.*, 1994** have demonstrated impaired blood gases in fetuses with polyhydramnios and increased amniotic fluid pressure. Therefore, determining blood flow velocimetry of the fetal MCA in patients with idiopathic polyhydramnios may be helpful in assessing fetal well-being. Measurement of the MCA blood flow velocity, which is a non-invasive method, may identify fetuses with impaired blood gases that are prone to develop higher rates of morbidity and mortality.

As regards to the mean values of the MCA/UA Doppler ratio, ***Yalti et al., 2004 andShahinaj et al., 2010*** reported thatabnormal **MCA/UA** Doppler ratio is strongly correlated with worse fetal prognosis. In normal pregnancies the diastolic component in the cerebral arteries is lower than in the umbilical arteries at any gestational age. Therefore, the cerebro-vascular resistance remains higher than the placental resistance and the cerebro-placental ratio is greater than 1.

In the present study, **the mean UA/MCA PI** ratiois1.01±0.31 for the case group, vs. 0.59 ±0.15 for the control group**.** This is consistent with the findings of the study of ***Yalti et al. (2004)*** who evaluated the role of middle cerebral artery and umbilical artery Doppler waveforms, and biophysical profile in prediction of fetal outcome. Their explanation for that; the fetoplacental unit is known to be exposed to increased external pressure in cases with polyhydramnios. This leads to pooling of blood in fetal and placental veins, and thereby reduces the effective blood volume of the fetoplacental unit. The result is

increased fetal cerebrovascular perfusion as compensation.

As regards to*RA/MCA PI Doppler ratio*, in the present study **the meanRA/MCA PI ratio** was 1.8 ± 0.11 in the cases and 1.1± 0.12 in the control group with statistically significant difference could be detected between the two groups**.** Our preliminary results suggest that it is a promising prediction of fetal jeopardy when it is ≤ 1.1.

In this study, ***a receiver-operator characteristic (ROC) curve*** was constructed in order to select middle cerebral artery PI and renal artery PI cutoff values that best showed sensitivity and specificity for adverse perinatal outcome.

The best cut-off value for MCA PI will be 0.99, this yields sensitivity of 80%; specificity of 60%. At this cut-off value, the positive predictive value is 40% while the negative predictive value is 87.9%.For renal artery PI the best cut-off value will be 1.80 and this yields a sensitivity of 15%, specificity of 94.5%. At this cut-off value PPV 30% and NPV 80%. Therefore we concluded that MCA PI is considered more valid (good positive and accurate and also better negative test (highest –ve predictive value) for prediction of the fetal outcome compared with RA.

In our study MCA pulsatility index had the highest sensitivity (80%) than UA (50%) and RA (15%). On the other hand RA pulsatility index had the highest specificity (94.5%) than UA (86.9%) and MCA (60%). The UA PI had the highest positive predictive value and the MCA PI had the highest negative predictive value**.**These figures are quite acceptable and mean that we can use these cut-off values in clinical diagnosis and management.

This is in agreement with ***Fong et al., 1999***, where they found thatMCA PI compared with UA PI and RA PI, was more sensitive (72.4% vs. 44.7% and 8.3%) but less specific (58.1% vs.86.6% and 92.6%) in predicting adverse outcome.

In the present study, while an abnormal UA is a better predictor of adverse perinatal outcome (highest +ve predictive value) than an abnormal MCA or RA PI, a normal MCA PI may help to identify fetuses without adverse perinatal outcome. These findings agree with those of ***Chan et al., 1996, and Fong et al., 1999.***

MCA/UA ratio reflects not only the circulatory insufficiency of the umbilical velocimetry of the placenta manifested by alterations in the umbilical S/D ratio but also the adaptive changes resulting in modifications of the middle cerebral S/D ratio according to ***Rath et al.,2000***.

In our study, the best cut-off value for ***UA/MCA PI ratio*** will be 1.01, this yields sensitivity of 59%; specificity of 87.5%. At this cut-off value, the positive predictive value is 53.5% while the negative predictive value is 84.6 %.

We concluded that middle cerebral artery pulsatility index Doppler velocimetry is considered more valid for prediction of the fetal outcome compared with the renal artery. The changes of the renal artery pulsatility index Doppler velocimetry in fetuses with idiopathic polyhydramnios was in the range of normality and this means that renal perfusion was not the primary cause of abnormal increase of amniotic fluid volume.

By reviewing the literature, there is no data regarding the value of RA/MCA ratio before our study. Our preliminary results suggest that it may be a predictor of fetal outcome.

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