Ratio of Middle Cerebral Artery / Umbilical Artery Doppler Velocimetry and Status of Newborn in Postterm Pregnancy

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Abstract: Objective: Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being providing an opportunity to improve fetal outcome. The present study was undertaken to evaluate the role of middle cerebral to umbilical artery blood velocity waveform's systolic/diastolic ratio (MCA/UA) as a predictor of perinatal outcome in posttrem pregnant women. Patients and Methods: This prospective case control study included one hundred pregnant women who were stratified into two groups. Fifty pregnant women during the third trimester (control group = group A) and fifty pregnant women with gestational age > 41 weeks (case group = group B). The results of the MCA/UA ratio were evaluated with respect to the outcome of the infants and adverse perinatal outcome, defined as perinatal death, cesarean delivery for fetal distress, admission to the neonatal intensive care unit, days in the neonatal intensive care unit (NICU) or low Apgar score. Results: The MCA RI/UA RI ratio with cutoff value = 0.85 was found to be the most sensitive parameter in the prediction of adverse prenatal outcome. Among 22 cases admitted in NICU, 15 of them had a ratio below 0.85 (73.7%) and only 7 cases above 0.85 (26.3%). The Cereboplacental ratio screening efficiency for prediction of prenatal outcome (Birth weight <10th percentile) was 47% Sensitivity, 90% Specificity, 95% positive predictive value, 43% Negative predictive value, and for prediction of admission to NICU was 43.5% Sensitivity, 90% Specificity, 91% Positive predictive value, 45% Negative predictive value compared with the results of the present study (MCA/UA) PI ratio showed a 73.7% sensitivity and 68.3% specificity and a 52% PPV and 85% NPV in prediction of prenatal outcome (Birth weight <10th percentile) and 71% sensitivity and 72% specificity and a 79% PPV and 63% NPV in prediction of admission to NICU. Conclusion: Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being, yielding an opportunity to improve fetal outcome. Although the sample size of our study was small, our results suggested that the MCA/UA Doppler ratio of less than 1 was a good predictive tool for neonatal outcome in postterm pregnant women and could be used to identify fetuses at risk of morbidity.

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Key Words: Doppler – middle cerebral artery to umbilical artery ratio - postterm pregnancy.

1. Introduction:

Postdate pregnancy is a common obstetric problem. Its incidence has been estimated to be between 4-14% with an average of 10.5%[1]. A safe limit for continuation of pregnancy beyond expected date of delivery cannot be established as there is little agreement as to when exactly the fetal jeopardy begins. There is also controversy on whether risk of fetal hypoxia can be accurately predicted in these pregnancies. Rayburn and Chang[2] suggested that risk of postmaturity starts at 40 weeks. Postdate pregnancies have been associated with increased perinatal morbidity and mortality which increase after 42 weeks[3]. Increased incidence of induction of labor, instrumental delivery, cesarean section, shoulder dystocia, lower Apgar score, congenital malformations, meconium aspiration, and fetal asphyxia have been associated with these pregnancies [3,4]. These problems can be decreased by routine antepartum fetal surveillance prior to onset of spontaneous labor[5,6]. The current methods of fetal surveillance like nonstress test (NST), amniotic fluid index (AFI), biophysical score (BPS), umbilical artery (UA) S/D ratio and middle cerebral artery (MCA) pulsatility index (PI) cannot accurately predict fetus at risk of adverse perinatal outcome [3,6].Various studies [7,8] have investigated MCA and UA (CU) ratio in post-term pregnancies with high risk complicating factors like chronic hypertension, pregnancy induced hypertension (PIH) and diabetes, and found it to accurately predict fetal compromise. These conditions however, are known to affect the vascular bed and placental circulation, and hence the blood flows to the fetus. Very few studies have been done on the value of CU ratio in determining the perinatal outcome in low risk postdate pregnancies. Hence this study was designed to study the Doppler waveforms in UA and MCA, and CU ratio in uncomplicated postdate pregnancies, and to correlate these findings with the perinatal outcome. It also

aimed to determine the cutoff value of CU ratio for predicting adverse perinatal outcome in these pregnancies.

2. Patients and Methods:

This prospective case control study include 100 pregnant patients admitted at Ain Shams university maternity hospital, fifty of them have normal pregnancy and fifty of them have post term pregnancy.

A. Patients:

Group 1(Control Group) consisted of 5O pregnant females with the following criteria:

1. Singleton, viable pregnancy.
2. Gestational age: during third trimester (31-41 weeks)
3. Medically free

Group 2 (Post Term Group) consisted of 50 pregnant females with the following criteria:

I. Singleton, viable pregnancy.
2. Gestational age: during third trimester (after 4l weeks)
3. Medically free

The exclusion criteria included the following:

I. Medical disorder with pregnancy as (hypertension, diabetes mellitus (DM), Antiphospholipid syndrome and RH, isoimmunization … etc.).
2. Any maternal complication other than post term pregnancy.

The inclusion criteria included the following:

1. No obstetric or medical complications of pregnancy apart from post term pregnancy.
2. Single & viable pregnancy.
4. Gestational age: during third trimester (after 41 weeks)

B. Methods:

Both groups were subjected to:

1. A detailed history taking.
2. Physical examination.
3. Ultrasound study: Gestational age determination & Fetal weight estimation.
4. Doppler study*:* Umbilical artery S/D, UA PI**,** UA RI, middle cerebral artery S/D, MCA PI, MCA RI and ratio of MCA RI to UA RI were calculated.
5. Apgar score estimation of the neonate**.**

Technique of ultrasound & Doppler Examination:

1. Transabdominal ultrasound was performed to all patients while woman was in a slightly tilted position with the head of the bed raised 30 degrees and with a small pillow under the right loin
2. The instrument is sonoace 8800 (Medison Digital GAIA) ultrasound machine with Doppler unit and a convex linear transducer (3-5 MHz).
3. Biometric measurement to assess gestational age and fetal growth through the determination of fetal biparietal diameter, abdominal circumference and femur length.
4. Measurement of the biparietal diameter (BPD) was obtained at the level of the thalamus and cavum septum pellucidum. The abdominal circumference was obtained from the junction of the umbilical vein and the lateral left portal vein.
5. Estimated fetal weight was detected using the head, abdominal and femur measurements (Hadlock *et al.,* 1984).
6. Intrauterine growth restriction (IUGR) is defined as estimated fetal weight less than the 10th percentile for the gestational age (Sand *et al.,* 2002)
7. Doppler study: The angle between the ultrasonographic beam and direction of blood flow was always <30 degrees. The Doppler signals were recorded with a *3.5* MHz curved array duplex transducer. The Doppler evaluations were performed by one doctor to avoid the Interobserver variation. The attending obstetricians had access to the MCA RI/UA RI ratio value, MCA/UA>1 was considered abnormal (Wog *et al.,* 2002).

Doppler indices were calculated by the dedicated software supplied within the Doppler equipment. The average value of at least four consecutive waveforms was calculated.

Umbilical Artery Doppler:

The patients were placed in a semi-recumbent position with a left lateral tilt, and then the uterine contents are quickly scanned to select an area of amniotic cavity with several loops of umbilical cord. Ideally these cord loops should not be close to the cord insertion (Arias 1994). Using a Pulsed Wave Doppler, the characteristic sound and shape of the umbilical artery wave form were demonstrated and

identified. When the screen showed at least four consecutive waveforms of similar height, the image was frozen and the Doppler indices were estimated. A minimum of three separate readings were averaged before the final values were obtained. Because of the potential effect of fetal breathing movements on waveform variability, recording was performed during periods of fetal apnea.

The Middle cerebral Artery:

The standard plan for measuring the biparietal diameter is visualized. This plane includes the thalamus and the cavum septum pellucidum, the color and flow mapping function was then superimposed and the middle cerebral artery can be seen pulsating at the level of the insula. The middle cerebral artery can be seen running from the internal carotid artery in a lateral direction into the Sylvian fissure (Vermillion *et al.,* 2000). When the screen showed at least four consecutive waveforms of similar height, the image was frozen and the Doppler indices were estimated. A minimum of three separate readings were averaged before the final values were obtained. Care was taken to apply minimal pressure by the transducer on the maternal abdomen, as fetal head compression can alter fetal intra-cranial pressure and hence the arterial flow velocity waveforms (Vyas *et al.,* 2006).

Then MCA (RI) /UA (RI) ratio was calculated

Neonatal Evaluation:

1. The neonates were subjected to APGAR scoring at 1 & 5 minutes.

2. Adverse Neonatal outcome is considered by the following criteria:

I. APGAR score is less than 6 at 5 minutes.

II. Neonatal admission to neonatal intensive care unit.

III. Neonatal death either intrauterine or early after birth.

3. Results

Statistical Analysis:

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

- Description of quantitative variables as mean and SD and range.
- Description of qualitative variables as number and %.
- Unpaired t-test was used to compare two groups as regard a quantitative variable.
- Chi-Square test was used to compare qualitative variables between groups.
- Correlation co-efficient test was used to rank variables against each others positively or inversely.
- ROC (Receiver Operator Characteristic curve) was used to find out the overall productivity the best cut off value.
- P value > 0.05 insignificant, P<0.05 significant (*) & P<0.01 highly significant (**)
- Abbreviations: UA (umbilical artery), MCA (middle cerebral artery), SD (systolic diastolic ratio), RI (resistance index), PI (pulsatility index)

Table (1) shows the clinical characters of the patients in the studied groups

Variables	Cases N=50	Controls N=50	X2	P
Age				
>25yrs	27(54%)	24(48%)	0.3	>0.05
<25yrs	23(46%)	26(52%)		
Mean + SD	26. 2 ± 2.1	25.4 ± 3.78		
Number of labors				
>2	8(16%)	23(46%)	10	<0.01
<2	42(84%)	27(54%)		
Number of abortions				
>2	8(16%)	14(28%)	2	>0.05
<2	42(84%)	36(72%)		
Gestational age (wks)	41+0.14	35.5+1.5	26	<0.01**
Gestional age (U/S)	38.8+1.6	35+1.1	12	<0.01**
Fetal weight (kg)	3130+624	3241+86	1.3	>0.05
Estimated fetal weight (EFW)	3214.6+516	2410+520	0.3	>0.05

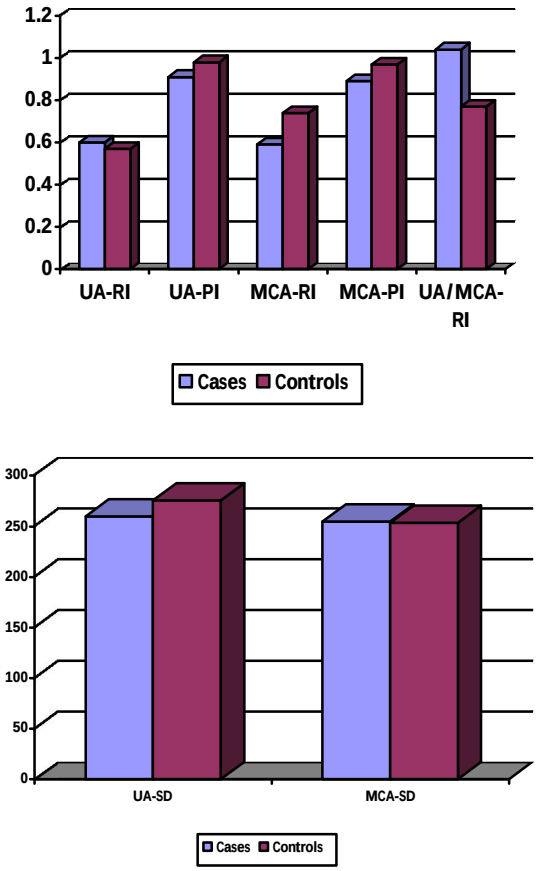

Figure (1): Comparison between cases and controls as regard Doppler indices parameters.

Table (2): Correlation between different Doppler indices parameters, age, number of deliveries and number of abortions among cases.

Doppler indices parameters	Age		No of deliveries		No of abortions	
	r	p	r	p	r	p
UA-SD	0.23	>0.05	0.20	>0.05	0.10	>0.05
UA-RI	0.03	>0.05	0.17	0.05	0.37	<0.01**
UA-PI	0.18	>0.05	-0.12	>0.05	0.19	>0.05
MCA-SD	0.20	>0.05	0.21	>0.05	-0.28	<0.05*
MCA-RI	-0.10	>0.05	0.19	>0.05	-0.29	<0.05*
MCA-PI	0.11	>0.05	0.16	>0.05	0.15	>0.05
UA/MCA-RI	-0.15	>0.05	-0.14	>0.05	0.36	<0.01**

Table (3): Correlation between different Doppler indices parameters, age, number of deliveries and number of abortions among cases.

Doppler indices parameters	Age		No of deliveries		No of abortions	
	r	p	r		r	p
UA-SD	0.10	>0.05	-0.16	>0.05	-0.12	>0.05
UA-RI	0.21	>0.05	-0.04	>0.05	-0.17	>0.05
UA-PI	-0.01	>0.05	-0.11	>0.05	-0.20	>0.05
MCA-SD	0.20	>0.05	0.04	>0.05	0.14	>0.05
MCA-RI	-0.11	>0.05	0.13	>0.05	0.15	>0.05
MCA-PI	0.17	>0.05	0.12	>0.05	0.21	>0.05
UA/MCA-RI	-0.10	>0.05	-0.22	>0.05	-0.03	>0.05

Table (4): Comparison of different Doppler indices parameters between neonates admitted to NICU and neonates not admitted to NICU in the studied cases.

Doppler indices parameters	NICU		t	p
	Not admitted	Admitted		
UA-SD	2477+48	273+49	2.1	<0.05*
UA-RI	0.57+0.07	0.64+0.05	4	<0.01**
UA-PI	0.87+0.18	0.96+0.17	2.2	<0.05*
MCA-SD	266+53	212+33	4.5	<0.01**
MCA-RI	0.65+0.07	0.52+0.06	6.9	<0.01**
MCA-PI	1.02+0.1	0.73+0.1	7.2	<0.01**
UA/MCA-RI	0.86+0.25	1.2+0.17	6.3	<0.01**

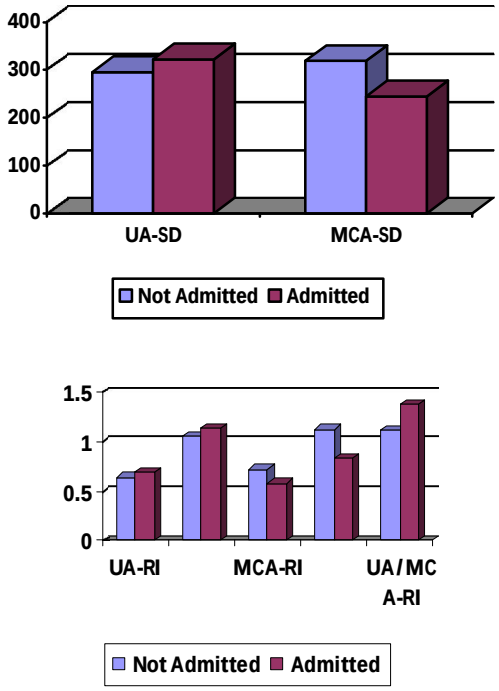

Figure (2): Relation between different Doppler indices parameters versus NICU admission among the studied cases.

Table (5): Validity of Doppler parameters in prediction of fetal outcome among post date cases.

Doppler indices parameters	Cut off	Sensitivity	Specificity	PPV	NPV
UA-SD	257	56%	45%	14%	50%
UA-RA	0.62	50%	92%	85%	63%
UA-PI	0.93	40%	60%	48%	50%
MCA-SD	245	48%	60%	52%	57%
MCA-RI	0.67	40%	39%	40%	42%
MCA-PI	0.94	50%	40%	45%	50%
MCA/UA-RI	0.85	80%	72%	62.5%	77%
All parameters	-	85%	89%	90%	95%

4. Discussion:

The use of Doppler ultrasound in high risk pregnancies appears to improve a number of obstetric care outcomes and promising in reducing prenatal deaths (Neilson and Pretorius, 2000). Fetuses with abnormal Doppler Velocimetry had a significantly higher incidence of oligohydramnios, low birth

weight and admission to NICU. Umbilical Velocimetry, however is a test of placental function that does not always directly reflect fetal status (Arduini *et al*., 2006). Advances in Doppler Ultrasonography have improved access to the fetal circulation. There has been a great deal of interest in the fetal intracranial vessels (Neilson and Pretorius, 2000).

The present study included 100 pregnant women admitted to Ain Shams University maternity hospital. 50 of them have normal pregnancy (31-40 week) and 50 of them have post term pregnancy (above 41 week). They were examined using transabdominal ultrasound and Doppler study for assessment of pregnancy status. The aim was to evaluate the role of transabdominal ultrasound and Doppler study during this period of gestation and detection of the best index from Doppler indices in prediction of adverse prenatal outcome. Data collected from the patients were the age, residency, occupation and special habits as well as full details of the past obstetric history for detection of any previous bad obstetric outcome. Also past surgical or medical history was taken. The current pregnancy status was fully analyzed then physical examination and ultrasound assessment were done.

In the present study, age in postterm group ranged form 23 to 27 year in comparison with control group which ranged from 24 to 26, the mean age was in cases and control 26. 2 ± 2.1 and 25.4 ± 3.78 years respectively, which denotes that there was no significant differences between women with post term and their controls in age (P>0.05). we used (RI, PI, SYS/DIAS ratio) to analyze the middle cerebral and umbilical arteries wave forms, also we used MCA (RI) / UA (RI) ratio to predict a subgroup of patients at high risk for severe neonatal morbidity, and this in accordance with that of (Arduini *et al*., 2006). The UA RI diagnostic accuracy, sensitivity and specificity were 50% and 92% respectively compared with RI (MCA) which was 40% and 39% respectively.

In a similar study done by Ozerena *et al*. 1999, it was found that RI UA diagnostic accuracy and sensitivity was 85% and 69% which was also better than that of PI (MCA) which was 58% and 42% respectively.

In a study done by Dickey *et al*., 1997 found that the increase in the UA RI value shows the hypoxia which is caused by placental insufficiency, but would not directly demonstrate placental vascular resistance. Thus its efficacy in predicting fetal distress is found to be lower than that of the umbilical artery Doppler indices.

In the present study the UA RI/ MCA RI ratio show a higher sensitivity and diagnostic accuracy (80% and 72%) in predicting adverse perinatal outcome when compared with UA PI (40% and 60%), UA S/D ratio (56% and 45%), MCA RI (40% and 39%), MCA PI (50% and 40%) and MCA S/D ratio (48% and 60%).

Ozerena *et al*., *1999* who compared changes in Doppler ultrasound studies of fetal circulation in 125 normal pregnancies with 62 postterm patients both with and without intrauterine growth retardation and demonstrated the best index for predicting adverse prenatal outcome or IUGR. A cross-sectional study was performed on 125 normal pregnancies and 62 postterm patients at 31-40 weeks of gestation in the study the UA S/D ratio showed a higher sensitivity and diagnostic accuracy (88% and 94%) in predicting adverse prenatal outcome when compared with the cerebral umbilical ratio (81% and 85%), the UA PI (69% and 85%) and the MCA PI (42% and 58%). For the prediction of adverse prenatal outcome, the diagnostic inaccuracy of the MCA RI/UA RI ratio and UA Doppler indices was found to be high in patients with post term; the diagnostic accuracy was lower than the SYS/DIAST ratio of the UA.

Seyam *et al*., 2002 examined One hundred pregnant women with growth-restricted fetuses between 28 weeks and 41 weeks by Doppler Velocimetry of the umbilical artery and evaluated fetal outcome among growth restricted fetuses and have shown that those with an abnormal S/D ratio, PI were at increased risk for early delivery, 68% of them reduced birth weight, decreased amniotic fluid at birth, and 22% of them admitted to NICU and 11% of them need positive pressure ventilation.

The sensitivity of the cerebral vessels can be used to predict IUGR of various degrees between 11% and 48% as found in the study by Gramellini *et al*. (1992). In the present study, the MCA RI/UA RI ratio with cutoff value = 0.85 was found to be the most sensitive parameter in the prediction of adverse prenatal outcome. Among 22 cases admitted in NICU, 15 of them had a ratio below 0.85 (73.7%) and only 7 cases above 0.85 (26.3%). The Cereboplacental ratio screening efficiency for prediction of prenatal outcome (Birth weight <10th percentile) was 47% Sensitivity, 90% Specificity, 95% positive predictive value, 43% Negative predictive value, and for prediction of admission to NICU was 43.5% Sensitivity, 90% Specificity, 91% Positive predictive value, 45% Negative predictive value compared with the results of the present study (MCA/UA) PI ratio showed a 73.7% sensitivity and 68.3% specificity and a 52% PPV and 85%NPV in prediction of prenatal outcome (Birth weight <10^{th} percentile) and 71% sensitivity and 72% specificity and a 79% PPV and 63% NPV in prediction of admission to NICU.

De Vore *et al.*, 1987 expressed the values as multiples of the normal median. Receiver-operator characteristic curves (sensitivity vs false-positive rates) were plotted for the prediction of each category of prenatal outcome and the areas under the curves were determined. Stepwise logistic regression analysis were used to determine whether the Cerebroplacental ratio improved outcome prediction over umbilical artery Doppler imaging alone. Differences in the results may originate from study group differences or different criteria in defining adverse prenatal outcome.

Gramellini *et al.* 1992 have used a single cut-off value (1.08) at a gestational age of over 30 weeks and have demonstrated that the cerebral-umbilical ratio has a higher sensitivity and diagnostic accuracy (68% and 90%) when compared with the UA PI (64% and 83%) and the MCA PI (24% and 79%), respectively, Our results seem to be similar, except that in the present study the cutoff value was (1) and also higher diagnostic accuracy in the UA S/D, a parameter which Gramellini did not consider. Differences in the literature may originate from study group differences or different criteria in defining adverse prenatal outcome.

Increased placental resistance is associated with impaired fetal growth, and the severity of growth restriction is associated with the degree and duration of placental insufficiency. Thus the sensitivity of the umbilical artery Doppler indices increases in asymmetrical growth retardation. Since placental insufficiency and the cerebral adaptation mechanism are considered together, the use of the cerebral umbilical ratio shows a high diagnostic accuracy in predicting IUGR as reported in previous studies (Arias, 1994)

In fetuses with abnormal 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 (Yalti *et al.*, 2004).

In the current study, sensitivity, positive predictive values of umbilical artery Doppler indices (RI, SYS/DIAS ratio) alone were 50, 92, 56 and 45 per cent respectively in comparison with (Yalti *et al.*, 2004) 30 and 50 percent respectively, who his study had small number of cases.

Yalti *et al.*, 2004 evaluated the role of middle cerebral artery and umbilical artery Doppler wave forms, and biophysical profile in prediction of fetal outcome. Although their study had a smaller number of cases their findings similar to that of the present study.

Advances in Doppler ultrasonography have improved access to the fetal circulation. There has been a great deal of interest in the fetal intracranial vessels Knowledge of Doppler flow Velocimetry of the fetal MCA may assist in prenatal diagnosis and management of complicated pregnancies (Kurjok and Kupesik, 2004). Doppler Velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being, yielding an opportunity to improve fetal outcome. (Kurjok and Kupesik, 2004).

In the current study, sensitivity and positive predictive values of MCA PI alone were 50 and 45 percent respectively. So the MCA PI alone is not reliable indicator.

Ozerena *et al.* 1999 found the MCA PI values were lower 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. Compared with the current study in which the MCA PI values were higher in the preeclamptic groups it may be due to smaller number of control group (30) in comparison with (125) in the other study.

The umbilical artery Doppler indices are related to placental vascular resistance, the increase in the UA RI value shows the hypoxia which is caused by placental insufficiency, but would not directly demonstrate placental vascular resistance. Thus its efficacy in predicting fetal distress is found to be lower than that of the umbilical artery Doppler indices. There is no significant relationship between fetal brain sparing and the prenatal outcome in pregnancies with increased resistance to blood in the feto-placental circulation (Arias, 1994).

In the present study the umbilical - cerebral ratio shows a higher sensitivity (80%) in predicting adverse prenatal outcome when compared with the UA S/D ratio (56%) the UA PI (40%) and the MCA PI (50%). As regard the sensitivity of all parameters together shows higher percent (85%) in prediction adverse prenatal outcome when compared with the cerebral – umbilical ratio (80%) the UA RI (50%) and MCA RI (40%). A similar correlation between the umbilical artery and middle cerebral artery Doppler indices and predictions of adverse prenatal outcome was found in previous study (Elebrashy and Edris 2006).

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