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COMPARATIVE STUDY OF DUCTUS VENOSUS DOPPLER VERSUS UMBILICAL ARTERY DOPPLER IN MANAGEMENT OF INTRA UTERINE GROWTH RESTRICTION AND PERINATAL OUTCOME

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ABSTRACT

Current challenges in the clinical management of IUGR include accurate diagnosis of the truly growth restricted fetus, selection of appropriate fetal surveillance and optimizing the timing of delivery. This study was conducted to evaluate the role of umbilical artery Doppler and ductusvenosus Doppler in management of IUGR pregnancy and perinatal outcome. Total 80 patients who were presented to the in-patient and out-patient department of obstetrics and gynecology of SSKM and IPGME&R Hospital between 28-36 weeks POG with IUGR pregnancy were included in the present study. They were evaluated with umbilical artery Doppler and ductusvenosus Doppler indices such as S/D ratio, PI and RI value. IUGR were detected by EFW <10th centile for the gestational age, and 7 patients, 68 patients and 55 patients were included in 28weeks, 32 weeks and 36 weeks respectively. Only 7 patients with IUGR were included at 28weeks after exclusion of congenital anomalies. Consequently they were followed up and new patients also added in 32 weeks, and patients number was 68 and at 36 weeks the patients had delivered earlier were excluded and number were 55. The mean gestational age at termination was 35.2554 weeks. The mean SFH was 30.4325. In this study 51.3% were PIH, 12.5% were heart disease and 5% was with typeII DM or GDM with vasculopathy. Cut off level of S/D ratio, PI value and RI values were taken as >95th percentile of normal range for the gestation. The study shows comparative predictive values of umbilical artery Doppler indices such as S/D ratio and PI values at 28 weeks and 36 weeks were more significant than ductusvenosus Doppler indices such as S/D ratio and PI values. As there is progressive deceleration in growth velocity and abnormal feto-placental Doppler patterns in IUGR associated with placental insufficiency, ductusvenosus Doppler and umbilical artery Doppler were used to evaluate IUGR pregnancy outcome, mode of delivery and perinatal outcome.

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INTRODUCTION

Intra uterine growth restriction (IUGR) is an important disease affecting 15% of pregnancy and it is associated with significant short term and long term morbidity& mortality (Sharma, 2016).

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According to ACOG intrauterine growth restriction is "one of the most common and complex problems in modern obstetrics". Current challenges in the clinical management of IUGR include accurate diagnosis of the truly growth restricted fetus, selection of appropriate fetal surveillance and optimizing the timing of delivery (Sankaran, 2009). Despite the potential for a complicated course, antenatal detection of IUGR and its ante partum surveillance can improve outcomes. The cornerstone investigation of IUGR is serial foetal biometric measurement, amniotic fluid index and the velocimetry analysis of umbilical artery middle cerebral artery and

ductusvenosus. Doppler USG (ultrasonography) waveform helps a better understanding of hemodynamic changes and so it becomes an essential clinical tool for foeto maternal surveillance in high risk pregnancies. So it can be credited to cause significant decreasein foetal mortality and morbidity (Kiserud *et al*., 2006). When the ductusvenosus and umbilical venous Doppler studies become abnormal, the risk for stillbirth increases dramatically, compared to when only the umbilical and middle cerebral artery Doppler studies are abnormal although this is not a sufficient reason to recommend routine usage of such testing, it might be utilized by centers with experience in venous Doppler. Using the combination of arterial and venous Doppler testing can result in identification of the majority of fetuses with acidemia (sensitivity 70-90% and specificity 70-80%). The sequence of arterial and venous Doppler findings is mostly limited to the preterm idiopathic IUGR fetus and has not been well documented in gestations at >34 weeks (Maiz *et al*., 2008). There is growing evidence that the fetal heart contributes to the hemodynamic redistribution by shifting the main cardiac output to the left ventricle maximizing the oxygen supply to brain. In IUGR, there is decreased oxygen supply and secondary to this anaerobic metabolism, metabolic acidosis, myocardial cell necrosis and fibrosis occur and all of these affect myocardial compliance. Ductusvenosus would allow the diversion of highly oxygenated blood to left heart and brain. In Ductusvenosuspulsatility index (PI) >95th percentile is an earlier sign of reverse velocities and 50% case of abnormal ductusvenosus precedes the loss of short term variability in the fetal heart rate and 48-72 hours before the biophysical profile changes. In this study serial ultrasonography Doppler of umbilical artery and ductusvenosus to be done at 28 weeks, 32 weeks 36 weeks.

From these Doppler finding Systolic/Diastolic pressure(S/D) ratio, pulsatility index and resistibility index will be compared and conclusion to be made about pregnancy outcome and foetal outcome (Baschat *et al*., 2004). If this theory is correct, one would expect that women with severe preeclampsia and those with CHTN with superimposed preeclampsia would have the highest risk of IUGR with the latter having the highest risk due to a 'cumulative effect (Kiserud *et al*., 2006)'. On the basis of this proposed pathogenesis, we would expect that women with mild preeclampsia compared with severe disease might be less likely to have fetuses affected by IUGR. Umbilical artery S/D ratio is the most sensitive index (66.6%) in predicting any adverse perinatal outcome. The sensitivity of the Doppler studies can be significantly increased by studying multiple vessels (91.6%).

Hence we conclude that Doppler studies of multiple vessels in the fetoplacental circulation can help in the monitoring of compromised fetus and can help us predicting neonatal morbidity. This may be helpful in determining the optimal time of delivery in complicated pregnancies. Uteroplacental blood flow decreases in pregnancies that are complicated by hypertension and IUGRs. This decrease is associated with a pathologic condition of spiral arteries, thought to arise during placentation in the first trimester of pregnancy; thus, it might be possible to predict the development of these conditions by assessing uteroplacental blood flow early in pregnancy with color Doppler (Lausman *et al*., 2009). Doppler assessment of uterine and umbilical arteries velocity waveforms are as a method of screening for these antenatal complications. An abnormal test result is represented by an abnormal flow velocity ratio (systolic/diastolic (S/D) ratio), resistant index, or the presence of an early diastolic notch (Engy Mahmoud Abdelhalim *et al*., 2014). Despite the absence of any treatment that reverses the disease process once started, screening for preeclampsia and IUGR has been a major clinical and research issue since the disease was first reported. So we have planned to study the role of Doppler imaging in prediction of high-risk pregnancies and their outcomes. Sequential studies of IUGR Doppler waveforms from different vascular areas can be used to assess the overall wellbeing of the fetus at risk for acidosis, death, or cardiac failure. Nonetheless, uncertainties concerning the relationship between Doppler changes and their metabolic equivalent remain with the exception being the triumph of middle cerebral artery (MCA) in cases of fetal anemia (Gudmundsson, 1988).

Gestational age, Doppler waveforms, antenatal testing, and maternal status should all be taken into consideration to guide optimal timing of delivery to minimize extreme prematurity but also to prevent intrauterine injury in the case of the IUGR fetus. Studies are ongoing to determine the optimal timing of the severely growth restricted fetus remote from term (Tyrrell *et al*., 1990). As part of ascertainment of a temporal sequence of events preceding fetal hypoxia, acidemia, or death in the IUGR fetus, many investigators have turned to the ductusvenosus study. The ductusvenosus carries the most rapidly moving blood in the venous system, and thus is easily identifiable by the aliasing seen on Doppler ultrasound. Abnormal ductusvenosus flow is currently thought to herald the last stage of fetal deterioration and an absent or reversed atrial waveform is always concerning. Several authors have reported that reversal of atrial systole in the ductusvenosus is an indication for delivery, especially after 32 weeks' gestation or administration of antenatal corticosteroids. The aims of our study were

- To determine and compare accuracy of umbilical artery Doppler and ductusvenosus Doppler in management of IUGR.
- To assess the perinatal outcome from ductusvenosus and umbilical artery Doppler velocimetry.
- Optimization of delivery time for better neonatal outcome.

MATERIALS AND METHODS

Study Design, Study Area and Period of Study: An observational and prospective study was conducted at the Department of Obstetrics & Gynaecology, I.P.G.M.E. &R. & S.S.K. M Hospital from June 2016 – May 2017.

Definition of Population: Antenatal mother attending the Obstetrics and Gynecology department of I.P.G.M.E &R. and S.S.K.M. Hospital: Both indoor and outdoor.

Inclusion Criteria

- Antenatal women of 18 years to 35years age.
- Gestational age between 28-36 weeks (as determined by LMP or Dating scan) having intra uterine growth restricted foetus (EFW< 10th centile for gestational age).
- High risk pregnancy including pregnancy induced hypertension, gestational diabetes, heart disease, chronic kidney disease, anti-phospholipid antibody syndrome.

Exclusion Criteria

- Multifetal gestation.
- Antenatal women aged more than 35 years.
- Present baby with congenital anomaly detected at 20 weeks.
- Any IUGR detected before 20 weeks.
- Maternal condition like jaundice or any infectious condition of the mother

Study Tools

- First Ultrasonography (USG) Doppler was done at 28 weeks.
- Second USG Doppler was done at 32 weeks.
- Third USG Doppler was done at 36 weeks.\
- All three USG Doppler of umbilical artery and ductusvenosus were done by same person to eliminate bias.
- Neonatal examination was carried out immediately after delivery by a neonatologist to clinically corroborate intra uterine growth restriction (IUGR), still birth and neonatal intensive care unit (NICU) admission.
- Baby morbidity and mortality status in neonatal intensive care unit (NICU).

Definition of Outcome: To determine the sensitivity and efficacy of the third trimester USG Doppler study of umbilical artery and ductusvenosus in early diagnosis and effective management IUGR) still birth and neonatal intensive care unit admission in high risk antenatal mothers.

Statistical Analysis: For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 20.0.1 and GraphPad Prismversion 5. Data had been summarized as meanand standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. p-value ≤ 0.05 was considered for statistically significant.

RESULT AND ANALYSIS

The present study evaluates the role of Doppler study in IUGR management and perinatal outcome. The study was conducted in 80 antenatal women between 28 to 36 weeks of gestational age, after excluding those who met the exclusion criteria mentioned previously. An informed consent was taken and these women were subjected to an ultrasound Doppler and these women are followed up. Among the above 7 women are diagnosed with IUGR fetus at 28 weeks and did ductusvenosus Doppler and umbilical artery Doppler and followed up, 68 women are diagnosed with IUGR fetus at 32 weeks, did the both Doppler and followed up and at 36 weeks there is 55 (25 patients terminated the pregnancy earlier than 36 weeks because of Doppler abnormality detected previously, in 32 weeks) patients are diagnosed with IUGR fetus and did the both Doppler and termination of pregnancy was done accordingly. So at 7 patients are analyzed at 28 weeks, 68 patients are analyzed at 32 weeks and 55 patients are analyzed at 36 weeks. The mean age (mean± s.d.) of patients was 27.6750 ± 4.5194 years with range 18.00-35.00 years and the median age was 28.00 years. The mean BMI (mean± s.d.) of patients was 21.6748 ± 3.2359 $Kg/m^2$with range 17.0478 - 27.3000$Kg/m^2$and the median BMI was 21.6016Kg/m^2. 76(95%) patienys had no Gestational Diabetes Mellitus(GDM) and 4(5%) patients had GDM.70(87.5%) patients had no heart disease and 10(12.5%) patients had heart disease.39(48.8%) patients had no Pregnancy Induced Hypertension(PIH) and 41(51.3%) patients had PIH.4(5%) patients were forceps delivery, 62(77.5%) patients were LSCS(Caesarian Section) and 14(17.5%0 patients had normal delivery.79(98.8%) patients were still born and 1(1.2%) patients were alive.24(30%) patients had no need of NICU admission and 55(68.8%) patients had need of NICU admission.21(26.3%) patients had acidosis, 7(8.8%) patients had hypoglycemia, 2(2.5%) patients had hypothermia, 31(38.8%) patients were Low Birth Weight (LBW), 12(15%) patients had RDS.76(77.5%) patients had no neonatal mortality and 3(15%) patients had neonatal mortality.

Difference of mean S/D 28 weeks in two groups was statistically significant (p=0.0001).Difference of mean S/D 32 weeks in two groups was not statistically significant (p=0.0582). Difference of mean S/D 36 weeks in two groups was statistically significant (p<0.0001).Difference of mean Pulsatility Index (PI) 28 weeks in two groups was statistically significant (p<0.0001).Difference of mean PI 32 weeks in two groups was not statistically significant (p=0.9758). Difference of mean PI 36 weeks in two groups was statistically significant (p<0.0001).Difference of mean Resistibility Index (RI) 28 weeks in two groups was not statistically significant (p=0.1026). Difference of mean RI 32 weeks in two groups was not statistically significant (p=0.2756).

DISCUSSION

The use of Doppler ultrasound in IUGR pregnancies appears to improve a number of obstetric care outcomes and promising in reducing perinatal deaths. Fetuses with abnormal velocimetryhad a significantly higher incidence of oligohydramnios, LBW, IUFD, still birth, acidosis and admission in NICU. Umbilical velocimetry however is a test of placental function that does not always directly reflect foetal status. In IUGR, first there is decreased diastolic flow in the umbilical artery due to increase in the resistance that occurs in small arteries of the tertiary villi. This raises the S/D ratio; PI and RI of umbilical artery as later reverses. Some fetuses have decreased diastolic velocity that remains constant with advancing gestation and never become absent or reversed which may be due to a milder form of placental insufficiency. In this study 80 patients in third trimester were analyzed to determine IUGR pregnancy outcome and fetal outcome. The mean age of the study population was 27.6750 years. Mean BMI was 21.6748 Kg/m^2.In this study the mean BMI is within the normal range and average gestational age for termination is 35.2554 weeks. Engy Mahmoud Abdelhalim *et al*[8] found that mean age of the studied patients was 26.9 ± 5.07 years.

Table 1. Distribution of mean Age, BMI, Gestational age, AFI, EFW, Birth weight, APGAR SCORE, NICU stay

	Number	Mean	SD	Minimum	Maximum	Median
Age (Years)	80	27.6750	4.5194	18.0000	35.0000	28.0000
BMI (Kg/m^2)	80	21.6748	3.2359	17.0478	27.3000	21.6016
Gestational age (in weeks) of pregnancy termination	80	35.2554	1.7875	32.0000	37.1400	36.0000
AFI	80	7.9666	1.0490	5.0000	9.4743	8.3299
EFW(in Kg)	80	1.6951	.3445	1.1240	2.3580	1.6620
Birth weight (in Kg)	80	1.5059	.3531	0.9680	2.2120	1.5020
APGAR SCORE	74	6.4324	1.6967	2.0000	9.0000	7.0000
NICU stay (in Days)	79	5.3151	3.3035	2.0000	15.0000	5.0000

Table 2. Distribution of GDM, heart disease, PIH, mode of delivery, still born, NICU admission, neonatal morbidity and mortality

		Frequency	Percent
GDM	NO	76	95.0%
	YES	4	5.0%
	NO	70	87.5%
	YES	10	12.5%
PIH	NO	39	48.8%
	YES	41	51.3%
MODE OF DELIVERY	FORCEPS	4	5.0%
	LSCS	62	77.5%
	ND	14	17.5%
STILL BORN	NO	79	98.8%
	YES	1	1.2%
NICU ADMISSION	NA	1	1.2%
	NO	24	30.0%
	YES	55	68.8%
NEONATAL MORBIDITY	ACIDOSIS	21	26.3%
	HYPOGLYCEMIA	7	8.8%
	HYPOTHERMIA	2	2.5%
	LBW	31	38.8%
	NA	7	8.8%
	RDS	12	15.0%
NEONATAL MORTALITY	NA	1	7.5%
	NO	76	77.5%
	YES	3	15.0%

Table 3. Distribution of mean S/D and PI at 28, 32 and 36 weeks according to DuctusVenosus Doppler and Umbilical Artery Doppler

		Number	Mean	SD	Minimum	Maximum	Median	p-value
S/D 28 WEEKS	DuctusVenosus Doppler	7	2.0139	.0709	1.9148	2.1000	2.0160	0.0001
	Umbilical Artery Doppler	7	2.6818	.3036	2.0400	2.9700	2.7645	
S/D 32 WEEKS	Ductus Venosus Doppler	68	3.2256	1.8930	1.7428	7.4766	2.1060	0.0582
	Umbilical Artery Doppler	68	2.7494	.8006	2.0470	4.7600	2.4908	
S/D 36 WEEKS	Ductus Venosus Doppler	55	1.7992	.5014	0.5580	2.2623	1.9811	<0.0001
	Umbilical Artery Doppler	55	3.6615	1.6612	1.7533	7.3300	2.6000	
PI 28 WEEKS	Ductus Venosus Doppler	7	.6138	.0216	0.5836	0.6400	0.6144	<0.0001
	Umbilica Artery Doppler	7	1.3630	.0652	1.2694	1.4500	1.3637	
PI 32 WEEKS	Ductus Venosus Doppler	68	1.1077	.8390	0.5311	3.1620	0.6418	0.9758
	Umbilical Artery Doppler	68	1.1109	.2366	0.7120	1.5300	1.1326	
PI 36 WEEKS	Ductus Venosus Doppler	55	.6141	.0496	0.4735	0.7245	0.6136	<0.0001
	Umbilical Artery Doppler	55	1.1682	.4506	0.6675	2.9100	1.2225	

Table 4. Distribution of mean RI according to 28 and 32weeks

		Number	Mean	SD	Minimum	Maximum	Median	p-value
RI 28 WEEKS	Ductus Venosus Doppler	7	0.4987	0.0176	0.4741	0.5200	0.4992	0.1026
	Umbilical Artery Doppler	7	0.4794	0.0229	0.4465	0.5100	0.4797	
RI 32 WEEKS	Ductus Venosus Doppler	68	0.6319	0.1942	0.4316	1.1016	0.5215	0.2756
	Umbilical Artery Doppler	68	0.6030	0.0981	0.4361	0.7900	0.5785	

Gestational age at presentation ranged from 28 weeks and 6 days to 34 weeks and 2 days. 4.1% have DM, 27.7% have gestational hypertension, 5.5% have chronic hypertensionand 13.8% have pre-eclampsia. History of anemia was present in 70.8% of the patients. 4.2% of patients were found to have HELLP syndrome. Mahmoud Abdelhalim *et al*. (2014) found that Most of patients have living fetus (81.9%) while three patients have stillbirth and ten patients have postnatal death. CS was the common mode of delivery (68.2%). Apgar score was found to be less than 5 in 12.5% and ≥8 in 62.5%. Mahmoud Abdelhalim *et al* shows that at the time of presentation 72.2% of patients have normal UA Doppler (<0.72), 15 have increase RI, four patients have absent EDF and one patient has reversed EDF. At the time of delivery UA Doppler showed that 48.6% of patients have normal UA Doppler, 27.7% have increase RI, 13.8% of have absent EDF and 9.7% have reversed EDF. Umbilical vein Doppler was normal in 90.3% of patients and abnormal in 9.7%.In my study 5% patients were diabetics, 12.5% patients were having heart disease and 51.3% were having PIH. So, most of the patients were having PIH (Engy Mahmoud Abdelhalim *et al*., 2014).

Gudmundsson *et al*concluded that in normal pregnancies the three indices; S/D. PI and RI decrease with advancing gestation in umbilical artery. But in IUGR first there is decreased diastolic flow in the umbilical artery due to increase in the resistance that occurs in small arteries and arterioles of the tertiary villi. This raises the S/D ratio, PI and RI of the umbilical artery. As the placental insufficiency worsens, first there is decrease in diastolic flow, then it becomes absent, and in advances stages it reverses. Some foetuses have decreaseddiastolic velocity that remains constant with advancing gestation and never becomes absent or reversed which may be due to a milder form of placental insufficiency.[9]Various studies have confirmed the clinical benefits of umbilical artery dopplervelocimetry in high risk pregnancies, where this method has been compared with conventional NST, BPP and ultrasound foetometry.

Doppler studies also allow more precise targeted prenatal monitoring and obstetric interventions, as pathological Doppler findings maybe detected several hours to days before any abnormality, in cardiotocographic tracings (Tyrrell *et al*., 1990; Almstrom *et al*., 1992; Chauhan *et al*., 2005). Cut off level of S/D ratio, PI value and RI values were taken as >95th percentile of normal range for the gestation. The study shows comparative predictive values of umbilical artery Doppler indices such as S/D ratio and PI values at 28 weeks and 36 weeks were more significant than ductusvenosus Doppler indices such as S/D ratio and PI values. However RI values and S/D ratio and PI values in 32 weeks were not significant statistically but there is trend towards umbilical artery to be more significant than ductusvenosus Doppler. Eliza Berkley *et al.* (2012) concluded that, among high-risk pregnancies with suspected IUGR, the use of umbilical arterial Doppler assessment significantly decreases the likelihood of labor induction, cesarean delivery, and perinatal deaths (1.2% vs 1.7%; relative risk, 0.71; 95% confidence interval, 0.52–0.98). Antepartum surveillance with Doppler of the umbilical artery should be started when the fetus is viable and IUGR is suspected. We found that mean AFI value was 7.9666 and mean EFW was 1.6951.Chauhan *et al.* (2007) found that among fetuses with IUGR, the LR of oligohydramnios to predict cesarean delivery for non reassuring fetal heart tracing was 2.0 (range, 0.8 to 5.0); for newborns small for gestational age, 1.9 (range, 1.2 to 3.1), and for neonatal intensive care unit admission, 1.4 (range, 0.6 to 2.3) More than 90% of patients with IUGR or SGA have AFI > 5.0 cm, and oligohydramnios with IUGR is a poor predictor of peripartum complications. The pregnancy was terminated by LSCS (77.5%), ND (17.5%) and by forceps is 5%.NehaMuniyar *et al.* (2017) found in their study that 80% cases of IUGR underwent caesarean section and 12% cases had normal vaginal delivery. It is comparable with my study. We found that mean birth weight was 1.5059 kg and there is only one IUFD due to severe preeclampsia and with abruptio placentae. The mean APGAR score was 6.4 and 55% baby required NICU admission and 3 neonatal deaths were occurred. Sehested LT, Pederson P showed in IUGR pregnancy that, total of 73 neonates and their mothers were included, Caesarean delivery was given in 78% of the cases. Maternal risk factors included gestational hypertension (33%), smoking (24%) and placental infarction (17%). Hypoglycaemic episodes developed in 31% of the neonates. At 12 months, 90% had caught up growth and 7% had a neurologically poor outcome. No infants died.

Conclusion

We can conclude from the present study that Doppler study of umbilical artery & ductusvenosus in third trimester can be used as a valuable tool to manage IUGR pregnancy outcome and perinatal outcome. As there is progressive deceleration in growth velocity and abnormal feto-placental Doppler patterns in IUGR associated with placental insufficiency, ductusvenosus Doppler and umbilical artery Doppler were used to evaluate IUGR pregnancy outcome, mode of delivery and perinatal outcome. This in turn helps in counseling the couples regarding the risk of SGA, stillbirth, low APGAR and acidosis of newborn and further management. So it is very much helpful for active management. Based on the results of this study and data available from literature it is certain that abnormal umbilical artery Doppler indices such as S/D ratio

and PI values are more significant for IUGR pregnancy and management and fetal outcome than ductusvenosus Doppler. But there is uncertainity regarding the RI value for poor outcome in IUGR pregnancy.

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