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Role of color doppler sonography in the intrauterine growth restriction and perinatal outcome

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Abstract
Background: Intra uterine growth restriction (IUGR) is defined as a fetal growth less than 10th percentile for the gestational age. IUGR can be classified as intrinsic (symmetrical) and extrinsic (asymmetrical), intrinsic IUGR is caused by fetal conditions such as infections or chromosomal abnormalities. Accurate antenatal diagnosis offers the best opportunity to reduce complications associated with IUGR.
Methods: This prospective observational study was conducted in the department of Obstetrics and Gynaecology at SMGS HOSPITAL, Government Medical College. The patients were taken from out-patient department with clinical suspicion of IUGR and also who were admitted for IUGR. Doppler Ultrasonography evaluation was performed after the grey scale USG assessment. All the relevant parameters were evaluated that are associated with perinatal outcome.
Results: We observed that the mean age of patients was (27.8) years ranging from 20 to 34 years with majority patients being primigravidae (40%) falling in the age interval of (25-29) years old. Pregnancy induced hypertension and chronic hypertension constituted major risk factor (19%). CPR had highest sensitivity of 93.1% for predicting adverse perinatal outcome with diagnostic accuracy of 90% in comparison to UA PI and MCA PI.
Conclusions: The study concluded that CPR is best predictor for assessing adverse perinatal outcome with highest sensitivity, specificity, NPV, PPV and diagnostic accuracy.

Keywords: intra uterine growth restriction, perinatal outcome, colour doppler

Introduction
Intra uterine growth restriction (IUGR) is defined as a fetal growth less than 10th percentile for the gestational age (Battaglia FC *et al.*, 1967) [1]. IUGR can be classified as intrinsic (symmetrical) and extrinsic (asymmetrical), intrinsic IUGR is caused by fetal conditions such as infections or chromosomal abnormalities. These fetuses have slow growth because their growth potential has been permanently affected usually by a severe insult in the first trimester and they show low percentile growth on growth chart. Medical interventions to improve fetal growth usually have little effect. On the other hand extrinsic IUGR occur when the growth failure is due to an event outside of the fetus such as uteroplacental insufficiency, restriction in nutrients supply. Accurate antenatal diagnosis offers the best opportunity to reduce complications associated with IUGR. Approximately 70% of fetuses with a birth weight below the 10th percentile for gestational age are constitutionally small and in the remaining 30%, the cause is pathological (Cunningham FG *et al.*, 2010) [2]. IUGR fetuses have a 30-50% likelihood of intrapartum hypoxic distress and a 50% risk of neonatal complications caused by feto-maternal and placental conditions. Neonatal complications include hypoglycaemia, meconium aspiration syndrome and long- term growth impairment like neurodevelopment disability, cardiovascular disorders etc can be seen (Raghupathy R *et al.*, 2012) [3]. Some factors leading to FGR include maternal causes (hypertension, diabetes, cardiopulmonary disease, anaemia, malnutrition, smoking, drug use), fetal causes (genetic disease including aneuploidy, congenital malformations, fetal infection, multiple pregnancies), and placental causes (placental insufficiency, placental infarction, placental mosaicism) (Fardiazar Z *et al.*, 2013) [4]. Pregnancies having above mentioned associated risk factors usually have high likelihood of developing complicated features of IUGR and most of these patients exhibit in their 3rd trimester for the first time on their antenatal examination. These patients invite a specific and precise diagnostic tool which can preferably be noninvasive in nature and can be exploited for optimal patient and perinatal outcomes.

The color Doppler tool is a better tool to detect the IUGR (Benson Carl B *et al*., 2005) [5]. The normal value of Umbilical Artery Pulsatility Index (UAPI) is 2.0 in the early trimester and around 1.0 near term (Kok JH *et al*., 1998) [6]. The absent or reversed end -diastolic flow in umbilical artery signifies increased impedance to umbilical artery blood flow. It is due to poorly vascularised placental villi and is seen in extreme cases of fetal growth restriction. The hypoxic growth restricted fetus attempts brain sparing by reducing cerebro-vascular impedance and thus increasing blood flow to brain (Meybery R *et al*., 2000) [7]. Doppler Ultrasound studies of the human fetal circulation have shown that in fetuses with IUGR there is a significant reduction of Middle Cerebral Artery Pulsatility Index (MCAPI) when compared with those in normal fetuses (Fawaz A *et al*., 2005) [8]. Results of several studies suggest that the MCA PI/UA PI (CPR) ratio is more accurate in the prediction of adverse perinatal outcome than UA Doppler USG alone (Neilson JP *et al*., 1998) [9]. The purpose of this study is determine the accuracy of USG color Doppler in clinically suspected IUGR fetuses and to predict perinatal outcome based on color Doppler changes.

Materials and Methods

This prospective observational study was conducted in the department of Obstetrics and Gynaecology at SMGS HOSPITAL, Government Medical College, Jammu over a period of one year w.e.f November 2019 to October 2020 after obtaining clearance from ethical committee. The collaboration of the Department of Radiology was availed for the purpose of radiological assistance. Apart from admitted IUGR patients, the patients were also taken from outpatient department with clinical suspicion of IUGR. However, the following criterion was adopted for the random selection of 100 patients.

Inclusion criteria

- Singleton pregnancies
- Clinically suspected IUGR
- Gestational age 32-36 weeks

Exclusion criteria

- Multifetal gestation
- Gestational age <32 weeks and >36 weeks
- Fetuses with congenital anomalies.

Determination of gestational age was based on a best estimate from menstrual history, clinical gestational age or fetal biometry preferably in the first trimester or early trimester. Doppler ultrasonography evaluation was performed after the grey scale USG assessment and after fulfilling all the prerequisite formalities mandatory for precise radiological evaluations. Follow up Doppler studies were performed if clinically indicated to determine a favorable or a worsening trend in the Doppler studies.

Results and observations

In the present study, we observed that average age was 27.8 ranging from 20-34 years. Most of them (49%) were falling in the age group of (25-29) years followed by (34%) in the age group of (30-34) years. Out of 100 patients, (38%) had first gravidity, (29%) had gravida 2, (27%) had 3rd gravidity and only (6%) patients had 4th gravidity. The risk factors were analyzed among studied patients and it was found that most common risk factors are: gestational hypertension (16%) followed by GDM (5%) and RH –ve pregnancy (5%), Anaemia and cholestatis of pregnancy (4%) each, Consanguineous marriage (3%), chronic hypertension (3%) and T2DM in (3%), Elderly Primi (2%) and PCOS (2%) patients and only one (1%) had APH as risk factor. However, we found that (52%) did not have any associated risk factor. In the present study we observed that majority of patients accounting for (80%) had (35-36) weeks gestational age, followed by (12%) patients with gestational age in (34-35) weeks in, (6%) patients had their gestational age in (33-34) weeks and only (2%) had their gestational age (32-33) weeks.

Table 1: Amniotic fluid index (AFI) of study patients.

AFI	Number	Percentage
Normal	84	84%
Abnormal	16	16%
Total	**100**	**100%**

We observed that (84%) patients had normal AFI whereas (16%) had abnormal AFI.

Table 2: Color Doppler findings in Umbilical artery (UA) in study patients.

Umbilical artery		Number	Percentage
Pulsatility Index (PI)	Normal	53	53%
	Abnormal	47	47%
End Diastolic Flow	Normal	70	70%
	Reversed	8	8%
	Reduced	4	4%
	Absent	18	18%

We observed that (53%) had normal UA PI whereas 47 (47%) reflected abnormal UA PI. The end –diastolic flow was normal in (70%) patients, reversed in (8%) and reduced in (4%) patients.

Table 2: Color Doppler findings in middle cerebral artery (MCA) in study patients.

Middle cerebral artery		Number	Percentage
Pulsatility Index (PI)	Normal	39	39%
	Abnormal	61	61%
Cerebroplacental Ratio(CPR)	< 1	48	48%
	> 1	52	52%

The colour doppler findings in MCA revealed normal PI in (39%) patients and abnormal in (61%) patients. CPR was observed abnormal in 48(48%) patients and normal in 52(52%) patients.

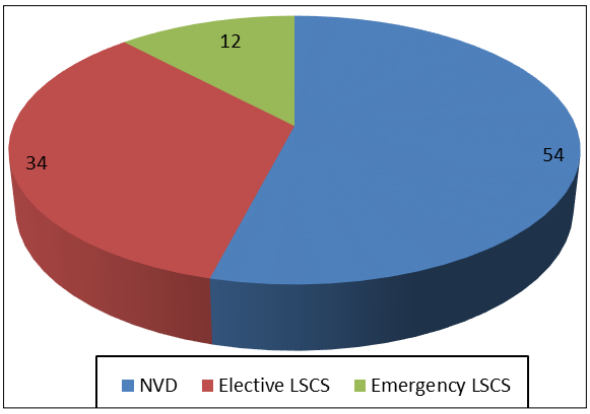

Fig 1: Mode of delivery in study patients

We observed that (54%) patients were delivered vaginally whereas (46%) underwent LSCS. Of patients undergoing LSCS, (34%) were elective and (12%) were of emergency nature.

Table 3: Perinatal outcome in study patients.

		Number	Percentage
Apgar score at 5 Min	< 7	20	20%
	≥ 7	80	80%
NICU admission	Yes	40	40%
	No	60	60%
Perinatal death	Yes	14	14%
	No	86	86%
Birth weight(kg)	< 2.5	54	54%
	≥ 2.5	46	46%

We analyzed the perinatal outcome in patients and observed that (20%) fetuses had 5 min APGAR <7 whereas (80%) had >7 score. Around (40%) neonates were admitted to NICU and (14%) neonates died perinatally. The percentage of patients having birth weight <2.5kg were (54%) whereas (46%) had birth weight ≥2.5kg.

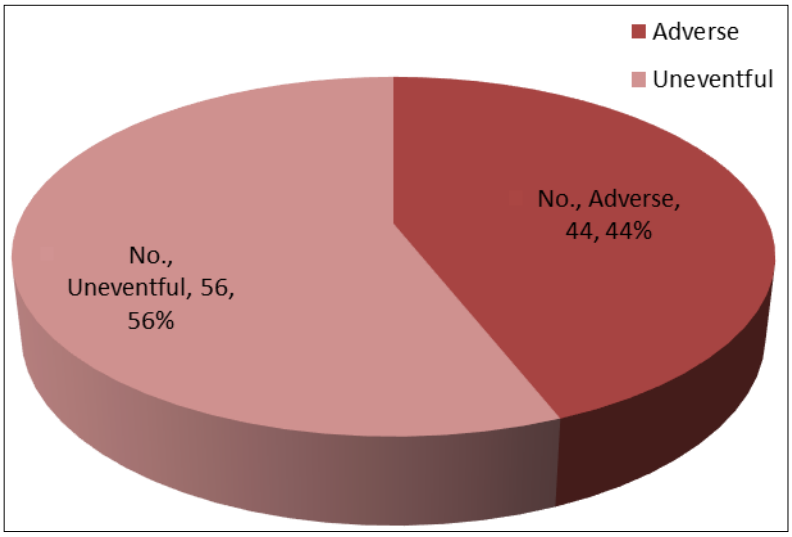

Fig 2: Distribution of patients showing pregnancy outcome

Table 4: Comparison of Diagnostic accuracy of CP ratio, UA PI and MCA PI in diagnosis of pregnancy outcome.

Variable	CP ratio		UA PI		MCA PI	
	Value	95% CI	Value	95% CI	Value	95% CI
Sensitivity	93.1	81.7-97.7	88.6	76.1-95.0	79.6	65.5-88.9
Specificity	87.5	76.4-93.8	85.7	74.3-92.6	53.6	40.7-65.9
PPV	85.4	72.8-92.7	82.9	69.9-91.1	57.4	44.9-68.9
NPV	94.2	84.3-98.0	90.6	79.8-95.9	76.9	61.6-87.4
Accuracy	90.0	82.6-94.5	87.0	79.0-92.3	65.0	55.3-73.6

We analyzed and compared the accuracy of CPR, umbilical artery PI and middle cerebral artery PI in diagnosing the pregnancy outcome of studied patients nd observed that CPR has the highest sensitivity of (93.1%), highest specificity of (87.5%), highest PPV (85.4%), highest NPV (94.2%) and highes acuuracy of (90%) in diagnosing pregnancy outcome.

Table 5: Pregnancy outcome as per Doppler findings.

Pregnancy outcome	Normal Doppler Findings		Abnormal Doppler Findings		P-value
	No.	%age	No.	%age	
Normal	24	88.9	32	43.8	<0.001*
Abnormal	3	11.1	41	56.2	
Total	**27**	**100**	**73**	**100**	

We observed that those patients who had normal Doppler findings, only (11.1%) patients of them resulted in adverse pregnancy outcome whereas those patients who reflected abnormal Doppler findings, (56.2%) of them had adverse pregnancy outcome. The difference in pregnancy outcome as per Doppler investigation was found statistically highly significant with a p-value < 0.001.

Discussion

In the present study, we observed that average age of patients was 27.8 years, ranging from 20-34 years. Most of them (49%) were falling in the age group of (25-29) years followed by (34%)

in the age group of (30-34) years. Almost similar observations were made by numerous authors; Anjum S *et al*., (2019) reported that (69.7%) patients were in age group (21 to 35) years [10]. Likewise Sharbaf *et al.,* (2018), reported the mean maternal age as (27.83±5.85) years [11]. In a study conducted by Geeta M *et al.,* (2016), 83% patients were in age group (21 -30) years [12]. In our study, out of 100 patients, (38%) had first gravidity, (29%) had gravida 2, (27%) had 3rd gravidity and only (6%) patients had 4th gravidity. In consonance to our study Anjum S *et al*., (2019) also reported maximum percentage of primigravidae [10]. Another study by Geeta M *et al.,* (2016) showed 40% primigravidae patients [12]. Even though other studies did not mention much about gravidity of patients but majority of studies reported primigravidae as maximum patients which is similar to our observation. The risk factors were analyzed among studied patients and it was found that most common risk factors were: gestational hypertension (16%) followed by GDM (5%) and RH –ve pregnancy (5%), Anaemia and cholestatis of pregnancy (4%) each, Consanguineous marriage (3%), chronic hypertension (3%) and T2DM in (3%), Elderly Primi (2%) and PCOS (2%) patients and only one (1%) had APH as risk factor. However, we found that (52%) did not have any associated risk factor. In similar kind of study by Anjum S *et al*., (2019), pregnancy induced hypertension was present in (38%) patients making it most important risk factor, diabetes in 2% cases, anaemia in (30%) cases [10]. So, this study was similar to our study in proving pregnancy induced hypertension as most important risk factor. Likewise Geeta M *et al.,* (2016), reported maternal hypertension in (42%) cases and anaemia in (2%) cases [12]. In another study by Shah D *et al.,* (2017), 48% cases had pregnancy induced hypertension [13]. These findings are much similar to our observations. In the present study, we observed that majority of patients accounting for (80%) had (35-36) weeks gestational age, followed by (12%) patients with gestational age in (34-35) weeks in, (6%) patients had their gestational age in (33-34) weeks and only (2%) had their gestational age (32-33) weeks. Geeta M *et al.,* (2016), reported in a likewise study that 72% cases were >32 weeks of gestational age [12]. In a similar kind of study by Bhownik P *et al.,* (2017), mean gestational age (35.2±3.46) weeks almost similar to our observation [14]. We observed that (84%) patients had normal AFI whereas (16%) had abnormal AFI. Likewise Geeta M *et al.,* (2016) and Shah D *et al.,* (2017) and reported (27%) and (24%) patients with abnormal AFI respectively which in consonance to our results [12, 13] . We observed that (53%) had normal UA PI whereas (47%) reflected abnormal UA PI. The end –diastolic flow was normal in (70%) patients, reversed in (8%) and reduced in (4%) patients. In a study by Sharbaf FR *et al.,* (2018), 77% had normal UA PI and 23% had abnormal UA PI [11]. Similarly Bano S *et al*., (2010) reported 76.4% patients with normal UA PI and 23.6 with abnormal UA PI [15] . In study by Bhownik P *et al.,* (2017), 18% had absent end-diastolic flow and 8% had reversed flow, Similar to our study. In the present study, color Doppler findings in MCA revealed normal PI in (39%) patients and abnormal in (61%) patients [14]. CPR was observed abnormal in 48(48%) patients and normal in 52(52%) patients. Contrary to the literature, Sharbaf FR *et al.,* (2018) reported 59% had normal MCA PI and 41% abnormal MCA PI [11]. In another study by Bano S *et al.,* (2010), 73% had normal MCA PI and 27% abnormal MCA PI [15]. We analyzed the perinatal outcome in patients and observed that (20%) fetuses had 5 min APGAR <7 whereas (80%) had >7 score. Around (40%) neonates were admitted to NICU and (14%) neonates died perinatally. The percentage of patients having birth weight <2.5kg were (54%) whereas (46%) had birth weight ≥2.5kg. In study by Bhownik P *et al.,* (2017), 14% cases had 5min APGAR less than 7. And in 16% cases, there was NICU admission, (60%) reportedly had birth weight <2.5kg almost similar to our observation [14] . In another study by Geeta M *et al.,* (2016), 30% had 5 min APGAR <7, 38% NICU admission rate, 69% cases have birth weight <2.5kg and perinatal death in 18% cases [12]. Anjum S *et al*., (2019) reported that 10.9% had perinatal deaths, 51.8% neonates were admitted to NICU in consonance to our results [10]. We analyzed and compared the accuracy of CPR, umbilical artery PI and middle cerebral artery PI in diagnosing the pregnancy outcome of studied patients among studied patients and found that CPR has the highest sensitivity of (93.1%), highest specificity of (87.5%), highest PPV (85.4%), highest NPV (94.2%) and highest acuuracy of (90%) in diagnosing pregnancy outcome. Contemporary to the literature Bhownik P *et al.,* (2017), also reported the highest sensitivity, highest specificity, highest PPV and highest NPV of CPR with percentages as 95.8%, 84.6%, 85% and 95% respectively in comparison to MCA PI and UA PI, they reported the diagnostic accuracy of CPR is 90% much similar to our observations [14]. Similarly, Gramellini D *et al*., (1992), also reported that diagnostic accuracy of CPR as 90% [16]. In another study by Bano S *et al.,* (2010), CPR had 100% specificity and PPV, 83.3% sensitivity and 94.3% NPV. In a likewise study by Singh M *et al.,* (2013), CPR ratio had highest sensitivity, specificity, NPV, PPV and accuracy when compared to UA PI and MCA PI [17]. We observed that those patients who had normal Doppler findings, only (11.1%) patients of them resulted in adverse pregnancy outcome whereas those patients who reflected abnormal Doppler findings, (56.2%) of them had adverse pregnancy outcome. The difference in pregnancy outcome as per Doppler investigation was found statistically highly significant with a p-value (< 0.001). In a similar kind of study due to Singh M *et al*., (2013) patients with abnormal Doppler findings had adverse outcome in higher percentage of patients compared to those with normal Doppler findings and their results were statistically significant in consonance to what we observed [17].

Conclusion

The diagnosis of utero -placental insufficiency causing fetal growth restriction identifies a group of fetuses who are prone for perinatal complications. Doppler ultrasound velocimetry is a non-invasive, repeatable and simple method for antepartum fetal surveillance in these patients with IUGR. There is a strong correlation between fetal hypoxemia and Doppler measured flow indices of the fetal arterial circulations. Grading of the Doppler abnormalities can accurately predict the perinatal outcome of the potentially compromised IUGR baby much earlier than NST and thus it can be used as a prognostic tool as proved in our study. Cases with normal Doppler had good perinatal outcome. Thus, Color Doppler can be precisely used in patients with IUGR to identify impending hypoxia in order to optimize the time of delivery and perinatal outcome.

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