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Comparison of Perinatal outcome in growth restricted foetuses with normal and abnormal colour Doppler study

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Abstract

Introduction: Fetal growth restriction (FGR) is defined as inadequate fetal growth with sonographic estimated fetal weight less than 10th percentile for that gestational age. Growth retarded foetuses have eight to ten-fold increase in perinatal mortality and morbidity as compared to Appropriate for gestational age (AGA) foetuses.

Material and Methods: Pregnant women with period of gestation >28weeks attending antenatal clinic were screened. Those fulfilling the inclusion and exclusion criteria were enrolled after proper counselling and written consent.

Results: Pregnant mothers with FGR with normal colour doppler indices, named as GROUP A and pregnant mothers with FGR with abnormal doppler index findings, named as GROUP B. Mean age was found to be 23.2 ± 9.011, 24.9 ± 6.35 in each group respectively. There were 6(12%) and 43(86%) in Group A and B respectively who had Hypertensive disorder of pregnancy as an complicating factor. 2(4%) and 3(6%) subjects in Group A and Group B had anaemia. None of the subjects in group A and 1(2%) in group B had other risk factors like Type 2 DM.

The gestational age at delivery in pregnant mothers complicated with FGR for Group A (normal Doppler control group) compared with Group B (abnormal Doppler study group)

Conclusion: We concluded that Fetal growth restriction has considerable perinatal and long-term effects. The abnormal Doppler waveform is associated with higher caesarean section delivery, neonatal intensive care unit admission, Low APGAR score at 1 min and 5 min, respiratory distress syndrome, neonatal sepsis, neonatal

hyperbilirubinemia, early neonatal death and stillbirths as compared to normal Doppler flow.

Keywords: Fetal Growth, Pregnancy, Doppler

Introduction

Fetal growth restriction (FGR) is defined as inadequate fetal growth with sonographic estimated fetal weight less than 10th percentile for that gestational age.[1] FGR is considered to be one of the most common and complex problems in modern obstetrics according to the American College of Obstetricians and Gynaecologist (ACOG).[2] Growth retarded foetuses have eight to ten-fold increase in perinatal mortality and morbidity as compared to Appropriate for gestational age (AGA) foetuses.[3] There is a considerable difference in the incidence of FGR across different populations. In babies born with a birth weight less than 2500 grams, its prevalence is almost 33%. The incidence of FGR is 9.65% (National Neonatal Perinatal Database of India).[4] In nearly 35-40% of the cases, FGR is the consequence of an abnormal environment sur rounding the foetus. Factors like placental in sufficiency, maternal hyper tension, cardiovascular disease, diabetes, infections, low socio-economic status, previous history of preeclampsia are some of the known risk factors for FGR.[5] Poor pregnancy outcome has shown a strong link with FGR; more than half of the stillbirths are associated with FGR and nearly 10% of perinatal mortality is consequent to undetected FGR.

Higher perinatal mortality has been reported in association with absent and reversed end-diastolic flow velocities in the umbilical arteries.[6]

The maintenance of good utero-placental circulation is of utmost importance to continue a normal pregnancy. The progression of pregnancy is marked by a number of changes and adaptations in the maternal, placental and fetal vasculatures.[7] Early identification and prediction of FGR, to a great extent, relies on the ability to identify these maternal, placental and fetal vascular patterns effectively and efficiently.

Accurate antenatal diagnosis of FGR is one of the most important factor for improving perinatal consequences.[8] However, clinical management of FGR, which includes appropriate identification of the truly growth restricted foetuses, selection of correct fetal surveillance and optimization of the delivery time faces some major challenges at present.[9,10] A metanalysis of randomized controlled studies showed that UA Doppler in combination with standard antepartum testing, was associated with a significant reduction of up to 38% in perinatal mortality rate.[11]

Doppler ultrasonography, a vital obstetric diagnostic tool for 30 years [B8] is believed to be an effectual method of FGR monitoring.[12] It is used to assess utero-placental, foe to-placental and fetal blood circulations.[13] Doppler ultrasound of the utero-placental circulation provides information of the placental resistance and that of the foe to-placental circulation detects fetal response towards hypoxia. UA Doppler velocimetry is the most meticulously studied non-invasive test for accurate measurement of volume and velocity of foe to-placental blood flow.[14] In fact, abnormality in UA waveform indicates a fetal compromise[15] and is subsequently considered to be a marker for utero-placental in sufficiency. UA absent end diastolic flow (AEDF) indicates high risk of fetal hypoxia due to altered blood velocity and reversed end diastolic flow (REDF) represents acidotic foetus.[15]

In fact, a series of Doppler ultrasound in FGR foetuses showed a progressive reduction of MCA PI.[16] Uterine artery (Ut A) Doppler waveform analysis aids to

differentiate between the placental causes of growth restriction from other causes.[17] Hence, PI of MCA and UA are considered to be valuable Doppler indices for predicting pregnancy complications associated with FGR.[17]

Identification of FGR plays a pivotal role in mitigating the global burden of perinatal mortality. Knowledge gaps in women about antenatal care and follow-up constraints in identifying and appropriately managing women with FGR foetuses. Colour Doppler sonography is one such tool which aids in diagnosing FGR with minimal loss to follow up and thus helps to intervene timely. This study aimed to assess the perinatal outcome in clinically significant FGR cases in normal colour doppler study findings as compared to abnormal colour doppler findings.

Material and method

A prospective hospital-based study was conducted in Department of Obstetrics and Gynaecology, PBM and Associated Group of Hospitals, attached to Sardar Patel Medical College, Bikaner. Duration of study was 12 months from 1st September 2020 to 31st August 2021. Pregnant women with period of gestation >28weeks attending antenatal clinic were screened. Those fulfilling the inclusion and exclusion criteria were enrolled after proper counselling and written consent. Total 100 cases were enrolled in the study. The inclusion criteria that women with clinically significant FGR, with reliable dating of pregnancy by either confirmed LMP or early trimester sonography and singleton pregnancy with more than 28 weeks gestation

The exclusion criteria were women in active labour, or with history of rupture of membrane, lethal congenital anomalies, Twin/triplet pregnancies, clinically normal SFH and Antepartum haemorrhage.

General physical examination, Obstetrical examination was done and samples for blood investigations like CBC, BT/CT, Viral markers, RFT/LFT were taken. Urine albumin, USG imaging and other relevant investigations were done. Subjects were divided into two groups based on the colour Doppler findings, Group A: Normal colour Doppler indices and Group B: Abnormal Colour Doppler indices.

Results

The cases were organized in two study groups, pregnant mothers with FGR with normal colour doppler indices, named as GROUP A and pregnant mothers with FGR with abnormal doppler index findings, named as GROUP B. The fetal outcome was defined as APGAR score of <7 at 1min & 5min, admission to NICU, Birth weight < 10th percentile.

Mean age was found to be 23.2 ± 9.011, 24.9 ± 6.35 in each group respectively. The mean age owes to higher conception rate and early marriages in India. Minimum participants in the research study were from the age group of below <20 years in group A and group B patients were found to be 1 (02%), 2 (04%), respectively. 12 (24%) subjects of group A and 12 (26%) subjects of Group B were of 26-20year age group. Graduation/ Post-Graduation educational status had 11 (22%), 12 (24%) in Group A and Group B respectively. Subjects among primary education group were 5 (10%) and 7 (14%) in Group A and Group B respectively. The majority of Normal Doppler and abnormal Doppler patients were found to be in urban area 35 (70%), 40 (80%) which was clinically insignificant (p=0.035).

Maximum number of subjects in both Groups A and B were primiparous 24 (48%), 25 (50%) respectively but the difference was statistically insignificant (p-value = 0. 069).

There were 6(12%) and 43(86%) in Group A and B respectively who had Hypertensive disorder of pregnancy as an complicating factor. 2(4%) and 3(6%) subjects in Group A and Group B had anaemia. None of the subjects in group A and 1(2%) in group B had other risk factors like Type 2 DM.

The gestational age at delivery in pregnant mothers complicated with FGR for Group A (normal Doppler control group) compared with Group B (abnormal Doppler study group). Maximum number of subjects 40(80%) and 26(52%) in Group A and Group B respectively were delivered at Gestational Age of 37weeks and above. Minimum number of subjects 1(2%) and 3(6%) in Group A and B respectively delivered at the gestational age of 28-32weeks. 2(4%) and 8(16%) subjects of Group A and B delivered at the GA of 32-34 weeks. 7(14%) and 13(26%) subjects of Group A and B respectively had delivered at GA of 34-37 weeks.

Various indications of Caesarean section delivery for pregnant mothers complicated with FGR for Group A (normal Doppler control group) compared with Group B (abnormal Doppler study group). Maximum number of subjects 6(12%) and 13(26%) were delivered by Caesarean section in Group A and Group B for the indication of Previous LSCS. 3(6%) and 6(12%) subjects in Group A and B underwent Caesarean section for Fetal Distress. 2 (4%) and 5(10%) patients of Group A and B delivered by Caesarean section for Previous 2 LSCS. 1(2%) and 4(8%) subjects of Group A and Group B were taken for Caesarean section for PIH. 1(2%) and 2(4%) subjects of Group A and B were taken for C section for Mal presentation. 1(2%) and 3(6%) subjects of Group A and B were delivered by Caesarean section for Oligohydramnios respectively. (Table 1) 28(56%) cases had EFW between 2000-2500g in Group A, and 21(42%) between 1500-2000g in Group B. This may be due to higher premature interventions due to jeopardised foetus in abnormal Doppler study subjects. 2(4%) and 12(24%) had EFW between 1000-1500g in Group A and B respectively. The results were statistically insignificant. (Graph 1)

The abnormal Umbilical artery indices in small for gestational age (SGA) and constitutionally small (non-SGA) neonates. SGA neonates had a higher frequency of abnormal UA Doppler than non-SGA neonates ($p< 0.001$). 2(28%) has abnormal UA S/D, 3(42%) had abnormal UA PI and 2(28%) had abnormal UA RI in SGA infants while 1(1%), 2(2%), 1(1%) of the total non-SGA infants has abnormal UA S/D, abnormal UA PI, abnormal UA RI respectively. These values are statistically significant. ($p<0.001$) (Table 2)

The abnormal Middle Cerebral Artery indices in small for gestational age (SGA) and constitutionally small (non-SGA) neonates. SGA neonates had a higher frequency of abnormal MCA Doppler than non-SGA neonates ($p< 0.001$). 3(27%) had abnormal MCA S/D, 4(36%) had abnormal MCA PI and 4(36%) had abnormal MCA RI in SGA infants while 1(1.1%), 0(0%), 1(1.1%) of the total non-SGA infants had abnormal MCA S/D, abnormal MCA PI, abnormal MCA RI respectively. These values are statistically significant. ($p<0.001$)

The abnormal Uterine Artery indices in small for gestational age (SGA) and constitutionally small (non-SGA) neonates. SGA rate was 13% (13/100) in our study. SGA neonates had a higher frequency of abnormal Ut A Doppler than non-SGA neonates ($p< 0.001$).

There were 48(96%) and 43(86%) live births in Group A and Group B respectively. There were 0, 1(2%) still births in group A and B. 2(4%), 6(12%) died in early

neonatal period. The results of present study were found to be statistically significant (p<0.021). (Table 3)

Low APGAR score (<7) at 1min and 5min was seen in 3(6%) and 4(8%) in Group A as compared to 8 (16%) and 13 (26%) in Group B. 7(14%) neonates got admitted in NICU in Group A, out of those 4 (8%) stayed in NICU for <24hrs, and 3(6%) stayed for >24hrs. While, 32 (64%) neonates of Group B got admitted in NICU, out of those 12(24%) got discharged in <24hrs and 20(40%) stayed in NICU for >24hrs. These values were statistically significant (p=<0.001) (Table 4)

Discussion

Accurate antenatal diagnosis is needed to differentiate between constitutionally small foetuses and growth restricted foetuses. Doppler velocimetry is a valuable tool for its diagnosis. It can examine the utero-placental, foe to-placental and fetal circulation by Ut A flow, UA flow and MCA flow respectively. 100 women with FGR foetuses based on clinical findings and were referred for colour doppler ultrasound. Subjects with singleton pregnancy of more than 28 weeks and clinically significant FGR were recruited in the study. Colour doppler were performed between 28-40 weeks and the indices were compared. Colour doppler indices which were taken into account were Ut A PI, RI, S/D Ratio; UA PI, RI and S/D ratio and fetal MCA PI, RI AND S/D Ratio.

The cases were organized in two study groups, pregnant mothers with FGR with normal colour doppler indices, named as Group A and pregnant mothers with FGR with abnormal index findings, named as Group B. The fetal outcome was defined as APGAR score of <7 at 1min & 5min, admission to NICU, Birth weight < 10th percentile.

Least number of participants in the research study were <20 years of age in both groups. Rajesh Met al[18] reported that out of their 118 cases, 47% were between 21-25 years of age.

In our study, maximum number of patients were from urban area 35 (70%) and 40 (80%), while 15 (30%) and 10 (20%) subjects belonged to the rural area in Group A and Group B respectively. This is probably because of sedentary lifestyle. (Table 4) Tolu et al[19] found in there that majority of study population belonged to urban area (p=0.762)

14 (28%) and 14 (30%) of study participants were primiparous. Rajesh Met al[18] found that 49% out of the 118 cases were primipara in their study.

Present study showed that there were 6(12%) and 43(86%) subjects in Group A and B respectively who had hypertensive disorder of pregnancy as an antenatal complicating factor.

40(80%) and 26(52%) in our study had period of gestation of 37weeks and above at the time of delivery. Rajesh Met al[18] observed that majority of cases (31%) had 35.1–37 weeks period of gestation at delivery.

In our study, Maximum number of subjects 36 (72%) and 15 (30%) had delivered vaginally in Group A and Group B. 14 (28%) and 35 (70%) subjects of Group A and Group B underwent Caesarean section respectively. The difference was statistically significant. (p=0.003) Tolu et al[19] observed that most common mode of delivery was by vaginal route in 67% subjects (p=0.005)

In our study, 28 (56%) had an Estimated Fetal Weight between 2000-2500g in Group A, 21 (42%) had EFW between 1500-2000grams in Group B. Rajesh Met al[18] found that maximum number of new born (29%) were found to have birth weight between 2000 and 2100grams.

SGA neonates had a higher frequency of abnormal UA Doppler than non-SGA neonates (p< 0.001). 2(28%) had abnormal UA S/D, 3(42%) had abnormal UA PI and 2(28%) had abnormal UA RI in SGA infants while 1(1%), 2(2%), 1(1%) of the total non-SGA infants. These values are statistically significant. (p<0.001) Therefore, antenatal UA doppler sonography proves beneficial and should be done in high risk FGR cases. Hamayel et al[20] found that abnormal UADS in foetuses is statistically significantly associated with SGA and NICU admission.

Our study showed that SGA neonates had a higher frequency of abnormal Ut A Doppler than non-SGA neonates (p< 0.001). Cnossen J Set al[21] found that an increased UT A PI alone or in combination with notching best predicted severe FGR in low-risk patients, and increased resistance index in high-risk patients.

There was a higher incidence of poor perinatal outcome like death in early neonatal period in Group B 6(12%) as compared to Group A 2(4%). There was 1(2%) case of stillbirth amongst subjects in Group B as compared to 0 SB in Group A. The results of present study were found to be statistically significant (p<0.021).

The incidence of perinatal complications in our study was found to be higher in Group B as compared to Group A. 8(16%), 34(68%) had a need for resuscitation in Group A and B respectively (p=0.001). 6(12%), 26(52%) had RDS in Group A and B (p=0.005). Meconium Aspiration Syndrome (MAS) was seen in 2 (4%) and 3 (6%) of subjects (p=.564) in both groups respectively. Neonatal sepsis was a complication in 4 (8%) and 12 (24%) (p=0.001). Neonatal Hyperbilirubinemia was seen in 1 (2%) and 3 (6%) in Group A and B respectively. (p=0.001) It was found that there is definitely a higher risk of perinatal complications in subjects with abnormal colour doppler indices. Tolu et al[19] found that new born with abnormal Doppler studies were 2.3 times more likely to develop RDS and required resuscitations. Also, they were 2.5 and 2 times more likely to develop neonatal sepsis, and neonatal hyperbilirubinemia respectively compared to those with normal Doppler studies.

Low APGAR score (<7) at 1 and 5min was seen in 3(6%) and 4(8%) in Group A as compared to 8 (16%) and 13 (26%) in Group B. 7(14%) neonates got admitted in NICU in Group A, out of those 4 (8%) stayed in NICU for <24hrs, and 3(6%) stayed for >24hrs. While, 32 (64%) neonates of Group B got admitted in NICU, out of those 12(24%) got discharged in <24hrs and 20(40%) stayed in NICU for >24hrs. These values were statistically significant (p=<0.001). Tolu et al[19] found that new born with abnormal doppler findings had two times higher NICU admission rate. Also, they were 2 times more likely to have low 5th minute APGAR score as compared to those with normal doppler findings.

Conclusion

In our study, we concluded that Fetal growth restriction has considerable perinatal and long-term effects. Once it is suspected on clinical examination, careful Colour Doppler evaluation can improvise in identification of foetuses at risk, thereby allowing antenatal risk estimation and prognostication. In-utero transfer to tertiary care centres can be considered based on the Doppler findings, thus allowing better antenatal management and perinatal outcome. The abnormal Doppler waveform is associated with higher caesarean section delivery, neonatal intensive care unit admission, Low APGAR score at 1 min and 5 min, respiratory distress syndrome, neonatal sepsis, neonatal hyperbilirubinemia, early neonatal death and stillbirths as compared to normal Doppler flow.

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Legend Tables and Figures

Table 1: shows the various Indications of Caesarean section delivery for pregnant mothers complicated with FGR for

		Group A		Group B		
Variable	Category	Number	Percentage	Number	Percentage	P-value
Indications for cesarean delivery.	Previous 1 LSCS	6	12%	13	26%	(0.013)
	Fetal Distress	3	6%	6	12%	
	Previous 2 LSCS	2	4%	5	10%	
	PIH	1	2%	4	8%	
	Mal-presentation	1	2%	2	4%	
	Oligohydramnios	1	2%	3	6%	
	FGR	0	0	2	4%	

Group A (normal Doppler control group) compared with Group B (abnormal Doppler study group).

Table 2: Abnormal Umbilical Artery (UA) Doppler indices in small for gestational age (SGA) and constitutionally small (non-SGA) neonate2

	SGA (N=7)		Non-SGA (N=93)		
Variable	Number	Percentage	Number	Percentage	P value
Abnormal UA S/D	2	28.57	1	1.08	< 0.001
Abnormal UA PI	3	42.86	2	2.15	< 0.001
Abnormal UA RI	2	28.57	1	1.08	< 0.001

Table 3: Perinatal Outcome of Neonates for pregnant mothers complicated with FGR for Group A (normal Doppler control group) compared with Group B (abnormal Doppler study group).

Variable	Group A		Group B		(P-value)
	Number	Percentage	Number	Percentage	
Live	48	96	43	86	9.465 (0.451)
Stillbirth	0	0	1	2	3.651 (0.251)
Early neonatal death	2	4	6	12	19.645 (0.021)

Table 4: Comparison of APGAR score at 1min, 5min, NICU admission and NICU stay in neonates for pregnant mothers complicated with FGR for Group A (normal Doppler control group) compared with Group B (abnormal Doppler study group)

Variable	Group A		Group B		
	Number	Percentage	Number	Percentage	(P-value)
Low 1-min APGAR score (<7)	3	6	8	16	(0.001) *
Low 5-minute APGAR score (<7)	4	8	13	26	(0.001) *
NICU admission	7	14	32	64	(0.001) *
NICU Stay (<24hrs)	4	8	12	24	(0.001) *
NICU stay >24hrs	3	6	20	40	(0.001) *

Graph – 1: