

ORIGINAL ARTICLE

Association of Adverse Outcomes with Abnormal Umbilical Artery Waveform in Intrauterine Growth Restricted Pregnancies

ANDLEEB SARWAR¹, HUMA AFRIDI², BEENISH RIAZ³, ITAAT ULLAH KHAN AFRIDI⁴

¹Senior Registrar Obs & Gynae

²Assistant Professor of Obs & Gynae Sialkot Medical College, Sialkot

³Assistant Professor of Obs & Gynae Islamic International Medical College, Rawalpindi

⁴Prof of Paediatrics, Nawaz Sharif Medical College, Gujrat

Correspondence to Dr. Itaat Ullah Khan Afridi, Email: itaatafridi@yahoo.com, Cell: 0331-9624483

ABSTRACT

Background: Intrauterine growth restriction refers to a fetus with a fetal weight in the 10th percentile on ultrasonography who has not reached its biologically set growth potential due to a pathologic condition.

Aim: To determine the association of adverse outcome with abnormal umbilical artery waveform groups in intrauterine growth restricted pregnancies.

Methods: This Cohort Study was conducted from February 2019 to 12 February 2020 at Gynae & Obs Department, Imran Idrees Teaching Hospital Sialkot, Sialkot Medical College, Sialkot 120 pregnant females, attending Department of Gynae & Obs were recruited into the study after 28 weeks of gestation. The women were divided into two groups depending on their Doppler findings. One group (exposed) comprised of women with intrauterine growth restriction, with absent or reversed diastolic flow in the umbilical artery. The control (unexposed) group included women with small-for-date fetuses, with normal umbilical artery Doppler flow.

Results: The mean age of females was 27.40 ± 4.77 years. The mean gestational age was 30.69 ± 2.19 weeks. The mean birth weight of neonates was 2.37 ± 0.90 kg. The mean AGPAR score of neonates was 6.60 ± 1.70 . It was observed that there was significant association between groups and low birth weight with p-value = 0.002. Admissions to NICU were significantly lower in normal Doppler wave form group having p-value = 0.001.

Conclusion: The percentage of NICU admission was 46.7% and the percentage of low birth weight was 46.7% in intrauterine growth restriction. The mean birth weight was significantly lower in exposed group and the mean APGAR score was also significantly lower in exposed group.

Keywords: Apgar score, neonatal intensive care unit, Intrauterine Growth Restriction, Doppler ultrasound,

INTRODUCTION

Intrauterine growth limitation (IUGR) is a disorder in which a developing fetus is unable to reach its genetically set maximum size. This functional definition aims to identify a group of fetuses who are at risk of poor outcomes that are changeable.¹ This criteria eliminates fetuses that are small for gestational age (SGA) but not pathologically tiny from consideration². Growth at the tenth percentile for fetal weight at that gestational age is defined as SGA. Not all SGA fetuses are pathologically stunted; in fact, some may be constitutionally tiny. Similarly, not all fetuses that have not reached their genetic development potential are in the specific percentile for projected fetal growth^{3,4}.

Only around 40% of all fetuses at or below the 10th percentile for growth are at high risk of possibly avoidable perinatal mortality. Another 40% of these fetuses have a tiny constitution. Because this diagnosis can only be confirmed with confidence in neonates, a large proportion of healthy babies with SGA will be exposed to high-risk procedures, perhaps resulting in iatrogenic preterm^{5,6}.

The remaining 20% of SGA fetuses are inherently undersized as a result of genetic or environmental factors. Trisomy 18, CMV infection, and fetal alcohol syndrome are all examples. Prenatal intervention is less likely to assist these fetuses, and their prognosis is most strongly linked to the underlying etiology^{7,8}. The challenges to the clinicians are to detect the IUGR fetuses whose health is jeopardized in utero due to a hostile intrauterine environment, monitor them, and

act as needed. Identifying tiny but healthy fetuses and preventing iatrogenic damage to them or their moms is also a difficulty⁹⁻¹².

So we planned to conduct this study to get association of adverse neonatal outcome in pregnant females with IUGR females showing abnormal Doppler findings. This would help to attain local magnitude and enable the obstetricians and pediatricians to collaborate and improve the outcome of such pregnancies.

The objective of the study was to determine the association of adverse outcome with abnormal umbilical artery waveform groups in intrauterine growth restricted pregnancies.

MATERIALS & METHODS

This cohort study was conducted in the Department of Gynecology & Obstetrics in collaboration with Department of Pediatrics, Imran Idrees Teaching Hospital Sialkot, Sialkot from February 2019 to February 2020 after permission from IRB.

Sample size: Using WHO sample size calculator, keeping Confidence level = 95%, anticipated population proportion = 25% with absolute precision required at 8%, the total sample size was 120. Sampling technique used was non-probability consecutive sampling.

Inclusion Criteria: Females of age 20-35 years, presented with singleton fetus having intrauterine growth restriction at gestational age >28 weeks with first trimester antenatal booking scan. IUGR was defined as when fundal height is 3cm less than gestational age and/or ultrasonography shows *asymmetrical IUGR* (i.e. ratio of head circumference to abdominal circumference is elevated by greater than 2 standard deviations above the mean for gestational age).

Received on 02-04-2021

Accepted on 12-08-2021

Exclusion criteria: females with twin or multiple fetus pregnancy on ultrasound, congenitally abnormal fetuses, pre-labor rupture of membranes or malnourished mother (BMI<18 kg/m²) were not included in the study.

Data collection: Informed written consent was taken from females before inclusion in the research project. The women were divided into two groups depending on Doppler findings. One group (exposed group) comprised of females having IUGR fetus, with absent or reversed diastolic flow in the umbilical artery. The other group (unexposed group) included females having IUGR fetus, with normal umbilical artery Doppler flow. Then females were counseled and followed-up till delivery of fetus. On delivery, mode of delivery will be noted as well as gestational age at the time of delivery was also noted. Then major outcome (study variables) were also observed at the time of delivery. Pediatrician was called for assessment of neonates. Birth weight was assessed. Apgar score after 5 minutes of birth was noted. If Apgar score was <7 after 5 minutes, then neonates were referred to neonatal intensive care unit (NICU) and NICU admission was noted. All the findings were noted on Performa and were later on, analyzed in SPSS (V. 22). Relative risk (risk ratio) was estimated to measure whether the significant association exist between adverse fetal outcome with abnormal Doppler findings in pregnant females with IUGR fetuses.

RESULTS

In this study, the mean age of females in exposed group was 27.40±4.77 years while in unexposed group was 28.51± 5.23 years. The mean gestational age at the time of recruitment of females in the study was 30.69±2.19 weeks in exposed group while 31.52±1.92 weeks in unexposed group. The difference in gestational age at recruitment was insignificant (p-value > 0.05). The mean gestational age at the time of delivery was 36.12 ± 5.63 weeks in exposed group while 37.91 ± 3.69 weeks in unexposed group. The difference in gestational age at recruitment was significant (p-value < 0.05). Out of 60 females in exposed group, 39 (65.0%) underwent delivery through cesarean section while 21 (35.0%) females had vaginal delivery. Among 39 females with cesarean section in this group, 20 (51.3%) had emergency cesarean section, while out of 21 females who had vaginal delivery 12 (57.1%) had spontaneous delivery. Out of 60 females in unexposed group, 28 (46.7%) underwent delivery through cesarean section while 32 (53.3%) females had vaginal delivery. Among 28 females with cesarean section in this group, 11 (39.3%) had

emergency cesarean section, while out of 32 females who had vaginal delivery 24 (75.0%) had spontaneous delivery. The difference in both groups for mode of delivery was significant (p<0.05). The mean birth weight of neonates at delivery was 2.07 ± 0.90 kg in exposed group while in unexposed group, mean birth weight of neonates at delivery was 2.48 ± 1.12 kg. The difference was significant (p-value < 0.05). The mean Apgar score neonates after 5 minutes of delivery was 6.60 ± 1.70 in exposed group while in unexposed group, mean Apgar score neonates after 5 minutes of delivery was 7.95 ± 2.47. The difference was significant (p-value < 0.05). Table 1

By using the 2 x 2 contingency table, it was observed that low birth weight was noticed in 37 (61.7%) patients in exposed group while in 19 (31.7%) patients in unexposed group. There was significant association of low birth weight was observed with abnormal Doppler waveform i.e. risk ratio was 1.839 (95% Confidence interval = 1.261, 2.681, p-value < 0.001). By using the 2 x 2 contingency table, it was observed that need for NICU admission was noticed in 43 (71.7%) patients in exposed group while in 13 (21.7%) patients in unexposed group. There was significant association of low birth weight was observed with abnormal Doppler waveform i.e. risk ratio was 2.891 (95% Confidence interval = 1.877, 4.453, p-value < 0.001) (Table 2).

Table 1: basic characteristics of females in both groups (n = 120)

Feature	Doppler Wave Form		p-value
	Abnormal	Normal	
Age	27.40 ± 4.77	28.51± 5.23	0.227
Gravidity	2.97 ± 1.28	2.44± 1.15	0.019
Parity	1.64 ± 0.79	1.87 ± 0.91	0.142
Gestational age at recruitment	30.69 ± 2.19	31.11± 1.92	0.266
Gestational Age at delivery	36.12 ± 5.63	37.91± 3.69	0.042
Mode of delivery			
Cesarean section	39 (65.0%)	28 (46.7%)	0.043 ¹
Elective	19 (48.7%)	17 (60.7%)	
Emergency	20 (51.3%)	11 (39.3%)	
Vaginal	21 (35.0%)	32 (53.3%)	
Spontaneous	12 (57.1%)	24 (75.0%)	
Assisted	9 (42.9%)	8 (25.0%)	
Birth Weight	2.07 ± 0.90	2.48 ± 1.12	0.029
Apgar Score at 5 minutes	6.60 ± 1.70	7.95 ± 2.47	0.001

¹ difference between cesarean and vaginal delivery

Table.2 Association of adverse neonatal outcome with abnormal Doppler findings

Neonatal outcome		Doppler Wave Form		Total	RR 95% CI
		Abnormal	Normal		
Low Birth Weight	Yes	37 (61.7%)	19 (31.7%)	56 (46.7%)	1.839 1.261, 2.681
	No	23 (38.3%)	41 (68.3%)	64 (53.3%)	
Need for NICU admission	Yes	43 (71.7%)	13 (21.7%)	56 (46.7%)	2.891 1.877, 4.453
	No	17 (28.3%)	47 (78.3%)	64 (53.3%)	

P - value < 0.001 (Significant association observed)

DISCUSSION

In our study, we observed that the low birth weight was significantly associated with abnormal Doppler waveform findings i.e. 37 (61.7%) patients in exposed group while in 19(31.7%) patients in unexposed group and risk ratio was 1.839 (95% Confidence interval =1.261, 2.681, p-value <0.001). It was also observed that need for NICU admission was also significantly associated with abnormal Doppler waveform findings i.e. 43(71.7%) patients in exposed group

while in 13(21.7%) patients in unexposed group and risk ratio was 2.891 (95% Confidence interval = 1.877, 4.453, p-value < 0.001).

In a previous research, total of 39 IUGR detected newborns who fulfilled the selection criteria, including 41 gestational age infants and 33 birth weight infants. The IUGR group, gestational age group, and birth weight group had mean birth weights and gestational ages of 744 g and 29.6 weeks, 1370 g and 29.7 weeks, and 781 g and 25.5 weeks, respectively. IUGR newborns had a higher mortality rate than

gestational age infants (20.5% vs. 0%), although it was lower than birth weight infants (30%). Total ventilator days, total oxygen days, days to full feeds, and patent ductus arteriosus were greater in IUGR newborns than gestational age infants in surviving infants, but lower in birth weight infants¹³.

In another study, 18 individuals (39.63%) were diagnosed with IUGR, whereas 28 patients (60.48%) were identified as non-IUGR. Asymmetrical IUGR was found in 66.24% of IUGR infants, whereas symmetrical IUGR was found in 33.76%. On SFH, 39.53% of infants were suspected of having IUGR, while 28% of IUGR babies were suspected on ultrasound. As an outcome measure, 25% of babies were born with birth weights below the 10th percentile¹⁴.

According to previous study, 43(52.4%) of 82 growth-restricted patients had normal Doppler results, whereas 27(32.9%) had impaired arterial parameters and 12 (14.6%) had impaired venous parameters. The mean first-minute Apgar scores for the group with normal Doppler flows were 7.57 ± 1.53 , 6.8 ± 2.00 for the group with a compromised arterial system, and 4.00 ± 1.94 for the group with a compromised venous system. Two patients in the normal Doppler flow group (n=42), four instances in the impaired arterial flow group (n=27), and eleven cases in the impaired venous flow group (n=11) had fifth minute Apgar scores of less than six¹⁵.

The incidence of IUGR in preterm infants and neonates was 13.1% over five years. Premature infants with IUGR made up 18.6% of the total. The total mortality rate was 4.1%, 3.6% for perinatal deaths, and 2.7% for neonatal deaths. Intrauterine foetal mortality was found in 1.4% of cases, all of which were linked to birth weights below the third percentile. The typical pregnancy lasted 34 weeks and 4 days. There was a high pr%. Deformities were found in 11.4% of preterm newborns with IUGR, and chromosomal abnormalities were found in around 2%. About 46.4% of children have been admitted to the NICU¹⁶.

Perinatal morbidity and death were shown to be considerably higher in the group with a compromised umbilical artery blood type in previous studies. Group I had a birth weight of 742 ± 126 grams, whereas group II had a birth weight of 1680 ± 259 grams. This was a statistically significant change ($P=0.0001$). Reverse end-diastolic flow fetuses experienced higher morbidities than absent end-diastolic flow fetuses¹⁷.

The frequency of oligohydramnios and abnormal non-stress test was greater in fetuses with aberrant umbilical flow velocimetry than in fetuses with normal umbilical flow, according to current research. In fetuses with aberrant umbilical Doppler velocimetry, the average birth weight, diagnosis to delivery interval, and gestational age at delivery were all lower, with a greater likelihood of admission to the neonatal critical care unit. In that study, there was no perinatal death.¹⁸ As well as in our study, we did not observed any neonatal or perinatal death.

CONCLUSION

The percentage of NICU admission was 46.7% and the percentage of low birth weight was 46.7% in intrauterine growth restriction. The mean birth weight was significantly lower in group I and the mean APGAR score was also significantly lower in group I. Effect modifiers like age, gestational age, gravidity and parity have significant effect on APGAR score and admission to NICU.

Conflict of interest: Nil

REFERENCES

1. Kesavan K, Devaskar SU. Intrauterine Growth Restriction: Postnatal Monitoring and Outcomes. *Pediatric Clinics* 2019;66(2):403-23.
2. Hartkopf J, Schleger F, Keune J, Wiechers C, Pauluschke-Froehlich J, Weiss M, et al. Impact of Intrauterine Growth Restriction on Cognitive and Motor Development at 2 Years of Age. *Frontiers in Physiology [Original Research]* 2018 2018-September-19;9(1278).
3. Wang J, Feng C, Liu T, Shi M, Wu G, Bazer FW. Physiological alterations associated with intrauterine growth restriction in fetal pigs: Causes and insights for nutritional optimization. *Molecular Reproduction and Development* 2017;84(9):897-904.
4. Bahado-Singh RO, Yilmaz A, Bisgin H, Turkoglu O, Kumar P, Sherman E, et al. Artificial intelligence and the analysis of multi-platform metabolomics data for the detection of intrauterine growth restriction. *PLOS ONE* 2019;14(4):e0214121.
5. Hu J, Benny P, Wang M, Ma Y, Lambertini L, Peter I, et al. Intrauterine Growth Restriction Is Associated with Unique Features of the Reproductive Microbiome. *Reproductive Sciences* 2021 2021/03/01;28(3):828-37.
6. Sacchi C, Marino C, Nosarti C, Vieno A, Visentin S, Simonelli A. Association of Intrauterine Growth Restriction and Small for Gestational Age Status With Childhood Cognitive Outcomes: A Systematic Review and Meta-analysis. *JAMA Pediatrics* 2020;174(8):772-81.
7. Guy C, Maxwell MD, Waurin JL, Buller-Burckle A, Rabin DS, Strom C. Confined Placental Trisomy 18 Mosaicism Detected by Maternal Serum and Prenatal cfDNA Screening [21M]. *Obstetrics & Gynecology* 2017;129(5):S138.
8. Zhen L, Li Y-J, Yang Y-D, Li D-Z. The role of ultrasound in women with a positive NIPT result for trisomy 18 and 13. *Taiwanese Journal of Obstetrics and Gynecology* 2019 2019/11/01;58(6):798-800.
9. Amdi C, Lynegaard JC, Thymann T, Williams AR. Intrauterine growth restriction in piglets alters blood cell counts and impairs cytokine responses in peripheral mononuclear cells 24 days post-partum. *Scientific Reports* 2020 2020/03/13;10(1):4683.
10. Chen C-P, Chen M, Wang L-K, Chern S-R, Wu P-S, Ma G-C, et al. Low-level mosaicism for trisomy 16 at amniocentesis in a pregnancy associated with intrauterine growth restriction and a favorable outcome. *Taiwanese Journal of Obstetrics and Gynecology* 2021 2021/03/01;60(2):345-9.
11. Chen C-P, Tsai C, Lin M-H, Chern S-R, Chen S-W, Lai S-T, et al. Application of non-invasive prenatal testing in late gestation in a pregnancy associated with intrauterine growth restriction and trisomy 22 confined placental mosaicism. *Taiwanese Journal of Obstetrics and Gynecology* 2017 2017/10/01;56(5):691-3.
12. Chen C-P, Ko T-M, Chern S-R, Wu P-S, Chen S-W, Wu F-T, et al. Prenatal diagnosis of maternal uniparental disomy 16 associated with mosaic trisomy 16 at amniocentesis, and pericardial effusion and intrauterine growth restriction in the fetus. *Taiwanese Journal of Obstetrics and Gynecology* 2021 2021/05/01;60(3):534-9.
13. Aucott SW, Donohue PK, Northington FJ. Increased morbidity in severe early intrauterine growth restriction. *Journal of perinatology : official journal of the California Perinatal Association* 2004 Jul;24(7):435-40.
14. Amin L, Asif S. Intrauterine growth restriction: antenatal diagnosis and fetal outcome. *Ann King Edward Med Uni* 2005;11:529-32.
15. Kazandi M, Guven C, Akercan F, Zeybek B, Cirpan T, Ergenoglu M, et al. Relation between Doppler findings and perinatal outcomes in fetuses with intrauterine growth restriction. *Clinical and experimental obstetrics & gynecology* 2010;37(4):269-72.
16. Meyberg R, Boos R, Babajan A, Ertan AK, Schmidt W. [Intrauterine growth retardation--perinatal mortality and postnatal morbidity in a perinatal center]. *Zeitschrift fur Geburtshilfe und Neonatologie* 2000 Nov-Dec;204(6):218-23.
17. Malhotra N, Chanana C, Kumar S, Roy K, Sharma JB. Comparison of perinatal outcome of growth-restricted fetuses with normal and abnormal umbilical artery Doppler waveforms. *Indian journal of medical sciences* 2006 Aug;60(8):311-7.
18. Baschat AA, Weiner CP. Umbilical artery doppler screening for detection of the small fetus in need of antepartum surveillance. *American journal of obstetrics and gynecology* 2000 Jan;182(1 Pt 1):154-8.