DOI: https://doi.org/10.53350/pjmhs02024181586

ORIGINAL ARTICLE

Antenatal Predictors of Adverse Perinatal Outcomes in Preterm Fetuses with Intrauterine Growth Restriction- A Prospective Study

SYED SAHAR ZAHRA[1], SHAGUFTA JABEEN[2], MARIYAM JAVEED[3], SYEDA TAYYBA HUSSAIN[4], MUHAMMAD ASIM IQBAL QURESHI[5], MIAN ADNAN ASLAM JAVAID[6]

[1]*Assistant Professor, Department of Gynecology & Obstetrics, Bahawalpur Medical and Dental College, Bahawalpur*
[2]*Deputy Chief Medical Officer, Department of Gynecology and Obstetrics, Pakistan Atomic Energy Commission Hospital, Chasma Mianwali*
[3]*SR, Department of Gynecology & Obstetrics, Bahawalpur Medical and Dental College, Bahawalpur*
[4]*WMO, National Diagnostic Centre, Multan*
[5]*Associate Professor, Department of Gynecology and Obstetrics, Bakhtawar Amin Trust Hospital, Multan*
[6]*Statistical Analyst, Bahauddin Zakariya University, Multan*
Correspondence to: Syed Sahar Zahra, Email: drsaa0848@gmail.com

ABSTRACT

Background: In developing countries like Pakistan, health care services and facilities are not optimal so it is difficult to determine the appropriate delivery time in intrauterine growth restriction mothers

Objective: This study was conducted to assess predictors of antenatal outcomes in preterm fetuses with intrauterine growth restriction.

Methodology: A prospective, cross-sectional study was conducted in the Gynecology and Obstetrics Department of Bahawalpur Medical and Dental College from May 2022 to May 2023. A total of 200 pregnant women with a single pregnancy, gestation age of 24-33 weeks at birth, and Doppler umbilical arterial pulsatility index > 2SD for gestation age at admission were selected by consecutive sampling. Doppler was performed for the umbilical artery, ductus venosus, and middle cerebral artery. The last Doppler assessment was done 24 hours before delivery and the last ultrasound was performed a week before delivery for weight estimation. Birth weight, gestation age at birth, and 1-minute and 5-minute Apgar score were noted. The presence of at least one of the morbid conditions in the NICU was considered an adverse perinatal outcome. Mortality was defined as postnatal death or stillbirth

Results: Composite poor outcome was associated with fetal weight, gestation age at birth, reversed end-diastolic velocity, and abnormal DVPI. Birth weight, gestation age, ventilator support, and myocardial dysfunction were strong risk factors for poor outcomes ($p<0.001$).Gestation age at birth ($26^{6/7}$ and 29^{07} weeks) and estimated fetal weight (700 and 850 g) were predictors of survival and intact survival respectively. A strong association between birth weight and estimated fetal weight was observed for predicting survival and intact survival. A z score of -3.14 was a good predictor of survival (AUC 0.70, 69.5% specificity, and 71.2% sensitivity) and a score of -3.23 was a good predictor of intact survival (AUC 0.70, 45% specificity, and 80.1% sensitivity).

Conclusion: Fetal weight and gestation age were the strongest predictors of neonatal outcomes in preterm fetuses with intrauterine growth restriction. Intact survival was best predicted by fetal weight and gestation age or a combination of Doppler parameters and fetal weight z-scores.

Keywords: Intrauterine growth restriction, IUGR, Neonates, Placental insufficiency

INTRODUCTION

Uteroplacental insufficiency is a serious condition that occurs due to insufficient transmission of blood to the placenta.[1]It is a frequent cause of intrauterine growth restriction which is related to malnutrition and hemodynamic imbalance that can cause fetal death. IUGR can also lead to preterm birth, low birth weight, NICU admission, and long-term health conditions.[2]Placental insufficiency cannot be treated before birth; hence it is important to monitor the correct timing of neonatal delivery. Normally, the insufficient fetus is delivered when there is a higher risk of irreversible damage or miscarriage than risks associated with premature delivery.[3]

In the last three decades, the radiological findings of placental intrauterine growth restriction have been researched thoroughly.[4, 5]It has been reported that elevated umbilical arterial pulsatility indexes on Doppler are considered early fetal abnormality and anomalies in fetal veins indicate advanced placental insufficiency.[6]However, there is a contradictory opinion regarding the standard protocol of fetal features that mandates birth, especially in the early stages of insufficiency.[7, 8]

In developing countries like Pakistan, health care services and facilities are not optimal so it is difficult to determine the appropriate delivery time. This may vary obstetrics outcomes in such countries as compared to literature reported in developed countries.[9]This study was conducted to assess predictors of antenatal outcomes in preterm fetuses with intrauterine growth restriction.

Received on 11-06-2023
Accepted on 16-12-2023

METHODOLOGY

A prospective, cross-sectional study was conducted in the Gynecology and Obstetrics Department of Bahawalpur Medical and Dental College from May 2022 to May 2023. A total of 200 pregnant women with a single pregnancy, gestation age of 24-33 weeks at birth, and Doppler umbilical arterial pulsatility index > 2SD for gestation age at admission were selected by consecutive sampling. The sample size was calculated by Epi Info keeping a 5% margin of error, 95% CI, 50% population proportion among a population size of 415 patients. Women with twin births and fetal congenital abnormalities or infections were excluded. All women provided their consent to become a part of the study. The ethical committee of the hospital approved the study R/NO.14/21 dated 15-04-2023.

The attending OBGYN recorded the time of delivery based on maternal complications or fetal compromise. Ultrasound and PW Doppler were performed by obstetrics specialists with at least 2 years of experience in obstetrics sonography. Estimated fetal weight was calculated by the Hadlock formula and converted into z-scores. Amniotic fluid volume was estimated by amniotic fluid index. Fetal growth restriction was regarded as birth weight being >2SD below mean BW for gestation age.

Doppler was performed for the umbilical artery, ductus venosus, and middle cerebral artery. Doppler umbilical arterial pulsatility indexes were regarded as normal or abnormal for dichotomous (amniotic fluid index) and continuous parameters. The umbilical artery was also assessed for abnormal flow. A PI <2SD for mean gestation age was also considered an indicator of brain sparing. The last Doppler assessment was done 24 hours before delivery and the last ultrasound was performed a week before delivery for weight estimation.

Birth weight, gestation age at birth, and 1-minute and 5-minute Apgar score were noted. Gross intact neonatal survival was an absence of morbid conditions including intraventricular hemorrhage grade III or IV, retinopathy of prematurity, bronchopulmonary dysplasia, and necrotizing enterocolitis till discharge. The presence of at least one of these conditions in the NICU was considered an adverse perinatal outcome as well as myocardial dysfunction and need for ventilator support. Mortality was defined as postnatal death or stillbirth.

Gestation age, estimated fetal weight, birth weight, 5-minute Apgar score <7, Doppler findings, and amniotic fluid findings were assessed as individual predictors and fetal weight, gestation age at birth, reversed end-diastolic velocity, and abnormal DVPI were evaluated as composite predictors.

All data was analyzed by SPSS version 24. Categorical variables were presented by the chi-squared test. T-test and Wilcoxon rank test was used to present and compare continuous variables, respectively. Estimated neonatal survival, mortality, and morbidity were calculated by forward stepwise regression. Dependent variables were neonatal and perinatal mortality, composite outcome, and neonatal morbidity while independent variables were gestation age, estimated fetal weight, birth weight, 5-minute Apgar score <7, doppler findings, and amniotic fluid findings. ROC curves were made for continuous parameters considered significant predictors. Predictive values were calculated by 95% and area under the curve (AUC of 0.7-0.8 was considered good). A p-value of 0.05 was considered significant.

RESULTS

A total of 200 patients were included in the analysis. The average age of mothers was 30 years. There were 110 intact survivors while 90 were non-intact survivors. Abnormal Doppler umbilical artery findings were observed in 145 patients (72.5%) and the DV index was elevated in 68 patients (34%). 196 (98%) neonates were delivered by performing C-section and 4 stillbirths (2%) were delivered vaginally. 74 (82.3%) patients were administered a complete dosage of corticosteroids before birth. Thirteen neonates had a 5-minute Apgar score <7. The outcomes of survivors are shown in Table I.

Table 1: Perinatal and Doppler Outcomes

	Intact survivors (n=110)	Non-intact survivors (n=90)	P	Values of test statistics
Male sex	55 (50%)	54 (60%)	0 (0.500)	
Abnormal umbilical artery flow				
Absent end-diastolic velocity	48 (43.7%)	50 (55.6%)	(0.100)	-1.2858
Reversedend-diastolic velocity	17 (15.5%)	30 (33.4%)	(0.001)	
Ductus venosus				
Elevated UAPI	25 (22.8%)	43 (47.8%)	(<0.001)	-3.1317
Abnormal arterial systolic velocity	8 (7.3%)	12 (13.4%)	(0.278)	-0.5898
Antenatal steroids	88 (80%)	76 (84.5%)	(0.900)	1.2858
Estimated fetal weight	1099 (418-1890)	719 (319-2028)	(<0.001)	-3.1317
Oligohydramnios	39 (35.5%)	41 (45.6%)	(0.215)	-0.7908
GA at birth	29.7 (24-34)	26.4 (23-34)	(<0.001)	-3.1317
Birth weight	1077 (368-1988)	720 (313-1655)	(<0.001)	-3.1317
5-minute Apgar score <7	5 (4.6%)	8 (8.9%)	(0.158)	-1.0052
Surfactant use	48 (43.7%)	74 (82.3%)	(<0.001)	-3.1317
Myocardial dysfunction	8 (7.3%)	23 (25.6%)	(<0.001)	-3.1317

Table 2: Doppler findings

	Mortality (n=34)			Major morbidity (n=88)			Composite adverse outcome (n=78)		
	Odds ratio (95% confidence interval)	P-value	Test statistic	Odds ratio (95% confidence interval)	P-value	Test statistic	Odds ratio (95% confidence interval)	P-value	Test statistic
Fetal parameters									
Umbilical artery end-diastolic velocity									
Absent	1.20 (0.57-3.17)	(0.698)	0.5237	1.31 (0.80-2.10)	(0.386)	-0.2907	1.54 (0.88-2.37)	(0.094)	-1.3283
Reversed	3.33 (1.54-5.45)	(0.001)	-3.3563	2.88 (1.49-4.63)	(0.001)	-3.1866	2.77 (1.60-4.10)	0.001)	-3.1995
Ductus Venosus									
Normal	0.28 (0.22-0.62)	(<0.001)	-3.3563	0.66 (0.43-1.0)	(0.021)	-2.0640	0.57 (0.51-0.75)	(0.001)	-3.1995
Abnormal	4.09 (2.10-7.44)	(<0.001)	-3.3563	1.93 (1.11-2.25)	(0.021)	-2.0640	2.55 (1.49-3.44)	(0.001)	-3.1995
DV a-wave									
Antegrade	0.41 (0.23-0.59)	(0.002)	-3.0944	0.92 (0.63-1.41)	(0.580)	0.2025	0.81 (0.47-1.08)	(0.300)	-0.5266
Absent/retrograde	4.22 (1.65-9.18)	(0.002)	-3.0944	1.32 (0.46-2.18)	(0.580)	0.2025	1.82 (0.82-3.98)	(0.300)	-0.5266
Estimated fetal weight	1.0 (0.988-1.0)	(<0.001)	-3.3563	1.0 (1.0-1.1)	(0.200)	-0.8258	1.0 (1.0-1.1)	(0.060)	-1.5722
Fetal weight z-score	0.36 (0.15-0.71)	(<0.001)	-3.3563	0.81 (0.62-1.05)	(0.081)	-1.4104	0.66 (0.49-1.0)	(0.030)	-1.9089
Fetal growth restriction	4.24 (1.82-8.77)	(<0.001)	-3.3563	1.23 (0.68-2.02)	(0.467)	-0.0831	1.63 (0.89-1.74)	(0.110)	-1.2365
Oligohydramnios	2.62 (1.26-4.99)	(0.005)	-2.7333	1.38 (0.92-2.45)	(0.223)	-0.7656	1.0 (0.61-1.74)	(1)	
Neonatal parameters									
Gestation age greater than 28 weeks	-	-		-	-		4.44 (2.18-8.15)	(<0.001)	-3.1995
Birth weight									
<600g	17.1 (8.21-38.03)	(<0.001)	-3.3563	-	-		-	-	
<800g	-	-		-	-		4.87 (2.51-9.09)	(<0.001)	-3.1995
5-minute Apgar <7	5.22 (1.73-15.79	(0.005)	-2.7333	2.32 (0.67-6.149)	(0.200)	-0.8258	1.20 (0.41-2.83)	(0.812)	0.8905

Morbidity decreased with an increase in gestation age with the highest complication rate between 24 to 26 weeks with 88 neonates experiencing major morbidity. Bronchopulmonary dysplasia was the most frequent complication in 26% of neonates, retinopathy of prematurity in 23%, intraventricular hemorrhage in 11%, and necrotizing enterocolitis in 5% of neonates. Neonatal and fetal Doppler findings are presented in Table II. Composite poor outcome was associated with fetal weight, gestation age at birth, reversed end-diastolic velocity, and abnormal DVPI. Birth weight, gestation age, ventilator support, and myocardial dysfunction were strong risk factors for poor outcomes (p<0.001).

For mortality, absent/reversed DV a-wave velocity was a predictor when gestation age and estimated fetal weight were considered in step-wise regression. When the estimated fetal weight z-score was substituted for these two variables, elevated DV index was a predictor of mortality and morbidity, and morbimortality was predicted by UA Doppler (Table III).

Table 3: Final Predictors of Adverse Neonatal Outcomes

	Odds ratio (95% confidence interval)	P-value
Mortality		
FW z-score	0.40 (0.18-0.61)	(<0.001)
Elevated diastolic velocity index	2.58 (1.17-5.71)	(0.009)
Morbidity		
Umbilical artery absent diastolic flow	2.27 (1.21-4.47)	(0.009)
The umbilical artery reversed diastolic flow	4.60 (1.99-10.26)	(<0.001)
Morbimortality		
Fetal weight z-score	0.66 (0.49-0.88)	(0.030)
Umbilical artery absent diastolic flow	2.29 (0.98-4.43)	(0.018)
The umbilical artery reversed diastolic flow	3.0 (1.11-6.12)	(0.020)

ROC curve in Figure I shows that the best predictor of survival was GA <$27^{6/7}$ weeks (area under the curve: 0.79, 74.2% specificity and 73% sensitivity) (P<0.001), and the best predictor of intact survival was GA= $29^{0/7}$ weeks (AUC= 0.80, 77.8% specificity, 72.5% sensitivity) (P<0.001). A succeeding day in utero increased the chance of intact survival by 7%. An estimated fetal weight of 702 g increased the chance of survival (79% specificity and 80.4% sensitivity) while an EFW of 850 g best predicted intact survival (AUC 0.80, 70.3% specificity, and 74.7% sensitivity).

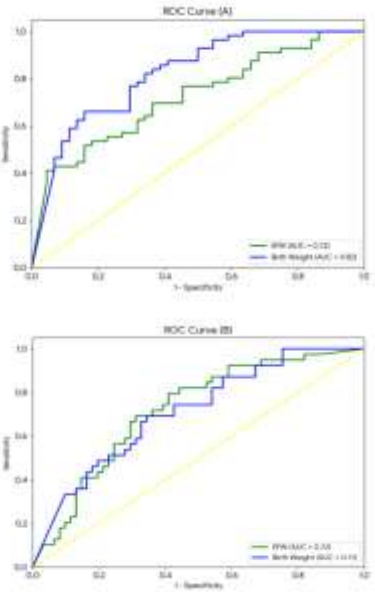

Figure 1: A) ROC curve for survival B) ROC for Intact Survival

A strong association between birth weight and estimated fetal weight was observed for predicting survival and intact survival. A z score of -3.14 was a good predictor of survival (AUC 0.70, 69.5% specificity, and 71.2% sensitivity) and a score of -3.23 was a good predictor of intact survival (AUC 0.70, 45% specificity, and 80.1% sensitivity).

DISCUSSION

This study was conducted to assess predictors of antenatal outcomes in preterm fetuses with intrauterine growth restriction. The findings revealed that gestation age at birth ($26^{6/7}$ and 29^{07} weeks) and estimated fetal weight (700 and 850 g) were predictors of survival and intact survival respectively. These results are consistent with Faquini et al and Dall'Asta with a negligible difference in EFW values.[10, 11]Additionally, a strong association between birth weight and estimated fetal weight was also noted which may serve as the basis for decision-making obstetricians as in previous studies only birth weight was reported as a parameter.[12, 13]

Gestation age and fetal weight were strong predictors of neonatal outcomes including morbidity and death. Ultrasound and Doppler findings were not associated with these variables in predicting poor neonatal outcomes except abnormal DV was a predictor of mortality. These results were also reported by previous studies.[14, 15, 16]

EFW z-score was also strongly associated with poor outcomes but it was a weaker predictor than EFW as its inclusion of the association of the Doppler variable was significant. However, it could be a significant predictor for mortality and morbidity when gestation age and estimated fetal weight are beyond critical thresholds. UA doppler was a stronger predictor of poor outcome and morbidity after considering z scores as compared to DV flow, this fact is also backed up in other studies. A study by Monaghan et al reported that DV a-wave velocity is the strongest risk factor of normal neurological growth in severe intrauterine growth restriction but it must be considered combined with other variables usually in cardiotocography.[17]We did not explore this method due to the unavailability of cardiotocography.

Our study has some limitations. The power of DV abnormalities may not be significant in our study as the delivery timing was decided by the attending OBGYN but every physician may not consider DV deterioration as an indicator of delivery and might want to deliver before. However, our findings can help physicians identify the risk of adverse effects in a timely manner and improve outcomes. Targeted intervention like efforts to optimize fetal growth or improvement placental function may be beneficial in reducing the risk of adverse outcomes.

CONCLUSION

Fetal weight and gestation age were the strongest predictors of neonatal outcomes in preterm fetuses with intrauterine growth restriction. Intact survival was best predicted by fetal weight and gestation age or a combination of Doppler parameters and fetal weight z-scores.

REFERENCES

1. Wardinger JE, Ambati S. Placental insufficiency. 2020.
2. Davenport BN, Wilson RL, Jones HN. Interventions for placental insufficiency and fetal growth restriction. Placenta. 2022;125:4-9.
3. Ahmed B, Abushama M, Konje JC. Prevention of spontaneous preterm delivery–an update on where we are today. The Journal of Maternal-Fetal & Neonatal Medicine. 2023;36(1):2183756.
4. Nisar S. Doppler evaluation of IUGR babies at a tertiary hospital. Hypertension.5(5).
5. Nazir Z, Hussain S, Azam M. Doppler Ultrasound Abnormalities In Intrauterine Growth Restrictions. Pakistan Journal of Medical and Health Sciences. 2021;29(1):6-34.
6. Khadija S, Gilani SA, Butt S, Yousaf M, Bacha R. The Efficacy of Doppler Indices in Third Trimester of IUGR Pregnancies. Obstetrics and Gynecology Research. 2020;3(1):1-9.

7. Nnamani A, Ibewuike C, Okere P, Obikili E. Comparative analysis of umbilical artery doppler indices of normal and suspected IUGR fetuses in the third trimester. Nigerian Journal of Clinical Practice. 2021;24(12):1793-1799.
8. Anjum S, Lakshmi TS. US Doppler indices in umbilical and fetal MCA in diagnosis of IUGR fetuses. Iaim. 2019;6(1):118-127.
9. Dol J, Hughes B, Bonet M, Dorey R, Dorling J, Grant A, et al. Timing of neonatal mortality and severe morbidity during the postnatal period: a systematic review. JBI Evidence Synthesis. 2023;21(1):98-199.
10. Faquini SdLDL, Guerra GVdQL, Galindo MWdS, Gusmão IMBd, Vilela LS, Souza AS. Prognostic factors and perinatal outcomes in early-onset intrauterine growth restriction due to placental insufficiency. The Journal of Maternal-Fetal & Neonatal Medicine. 2022;35(25):7119-7125.
11. Dall'Asta A, Stampalija T, Mecacci F, Minopoli M, Schera GBL, Cagninelli G, et al. Ultrasound prediction of adverse perinatal outcome at diagnosis of late-onset fetal growth restriction. Ultrasound in Obstetrics & Gynecology. 2022;59(3):342-349.
12. Sharp A, Jackson R, Cornforth C, Harrold J, Turner MA, Kenny L, et al. A prediction model for short-term neonatal outcomes in severe early-onset fetal growth restriction. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2019;241:109-118.
13. Inácio QAS, Júnior EA, Nardozza LMM, Petrini CG, Campos VP, Peixoto AB. Perinatal outcomes of fetuses with early growth restriction, late growth restriction, small for gestational age, and adequate for gestational age. Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics. 2019;41(12):688-696.
14. Takahashi M, Makino S, Oguma K, Imai H, Takamizu A, Koizumi A, et al. Fetal growth restriction as the initial finding of preeclampsia is a clinical predictor of maternal and neonatal prognoses: a single-center retrospective study. BMC pregnancy and childbirth. 2021;21:1-8.
15. MacDonald TM, Hui L, Robinson AJ, Dane KM, Middleton AL, Tong S, et al. Cerebral–placental–uterine ratio as novel predictor of late fetal growth restriction: prospective cohort study. Ultrasound in Obstetrics & Gynecology. 2019;54(3):367-375.
16. Stampalija T, Wolf H, Mylrea-Foley B, Marlow N, Stephens KJ, Shaw CJ, et al. Reduced fetal growth velocity and weight loss are associated with adverse perinatal outcome in fetuses at risk of growth restriction. American journal of obstetrics and gynecology. 2023;228(1):71. e71-71. e10.
17. Monaghan C, Kalafat E, Binder J, Thilaganathan B, Khalil A. Prediction of adverse pregnancy outcome in monochorionic diamniotic twin pregnancy complicated by selective fetal growth restriction. Ultrasound in Obstetrics & Gynecology. 2019;53(2):200-207.

This article may be cited as: Zahra SS, Jabeen S, Javeed M, Hussain ST, Qureshi MAI, Javaid MAA: Antenatal Predictors of Adverse Perinatal Outcomes in Preterm Fetuses with Intrauterine Growth Restriction- A Prospective Study. Pak J Med Health Sci, 2023; 18(1): 586-589.