

Prediction of Neonatal Outcome by Umbilical Artery Velocimetry in Intrauterine Growth Restriction: A Study in Western Nepal

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Abstract The introduction of Doppler velocimetry to obstetrics offered a noninvasive and safe imaging modality of indirectly assessing the fetal and uteroplacental circulation. Obstetric Doppler ultrasound plays an important role in detecting Intra Uterine Growth Restriction (IUGR). The early diagnosis of IUGR with the help of abnormal flow patterns in umbilical, uterine and middle cerebral arteries using Doppler ultrasound may help in reducing perinatal and neonatal mortality and morbidity as well as reducing perinatal complications. This provides for timely interventions to prevent progression from IUGR to Intrauterine death (IUD). The study was carried out in 140 patients in Manipal Teaching Hospital, Pokhara for a period of twenty months from October 2013 to June 2015. All the cases presented to Radiology department for obstetric Doppler with clinical suspicion of IUGR were taken up for the study and obstetric doppler of umbilical artery was performed. Seventy two out of 140 (51.50%) had abnormal umbilical artery Doppler velocimetry. Fifty seven out of these 72 subjects (positive predictive value – 79.2%) with abnormal umbilical artery Doppler were later born with small for gestational age (SGA). The S/D ratio of umbilical artery of 3 or greater was considered abnormal in predicting IUGR and it showed sensitivity, specificity, positive predictive value, and negative predictive value of 76%, 76.9%, 79.2% and 73.5% respectively. Admission to the Neonatal Intensive Care Unit (NICU) and incidence of perinatal and neonatal mortality increased with the worsening of Doppler velocimetry. Twenty seven out of one hundred and forty neonates developed perinatal asphyxia, out of which 26 (96.3%) had abnormal umbilical artery velocimetry. NICU admissions comprised of a total of 30 neonates, out of which 27(90%) had abnormal umbilical artery Doppler velocimetry prenatally. Fifteen out of thirty didn't survive, all of whom had abnormal umbilical artery Doppler velocimetry prenatally. There were 3 still born and all of them had abnormal umbilical artery velocimetry prenatally. The study could underline that abnormal Doppler velocimetry has a fairly good sensitivity and specificity for predicting IUGR and it is related with poor neonatal outcomes.

Keywords: *obstetric doppler, doppler velocimetry, waveform analysis, IUGR, Nepal*

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1. Introduction

The introduction of Doppler velocimetry to obstetrics offered a noninvasive method of indirectly assessing the fetal and uteroplacental circulation [1]. Doppler ultrasound is non-invasive method for the study of fetal hemodynamics and monitoring fetoplacental and uteroplacental circulation during pregnancy. It is safe in pregnancy and hence can be repeated as and when indicated. It can predict adverse perinatal outcome and is considered sensitive tool in early detection of fetal compromise and thereby for timely intervention [2]. Maternal uterine artery and fetal middle cerebral artery doppler gives information on uteroplacental perfusion and fetal brain oxygenation status. Doppler evaluation of peripheral arteries of fetus in organs like brain and kidneys give information on hemodynamic rearrangements that occur in fetus in response to fetal

hypoxemia. The Doppler patterns follow a longitudinal trend with early changes in the middle cerebral artery and umbilical artery followed by other peripheral arteries which indicates redistribution of blood flow in growth restricted fetuses and therefore caution us to closely monitor the fetus and intervene before the situation becomes unsalvageable. If adequate measures are not taken at this point, venous changes appear in the severely compromised fetus. These are strong predictors of poor perinatal outcome and indicate impending irreversible damage [3].

Umbilical artery Doppler waveform is one of the most rigorously evaluated and frequently used noninvasive tests of fetal well-being. The value of Doppler velocimetry in the assessment of low-risk populations has not been proven. Several Doppler-derived indices of umbilical, uterine and middle cerebral arteries have been used in clinical practice to identify fetuses that are at risk of increased perinatal death and morbidity that may benefit

from closer surveillance or elective delivery. Among them umbilical artery systolic/ diastolic (S/D) ratio, resistance index (RI) and pulsatility index (PI) are used most commonly [4,5]. Umbilical artery is useful in the late second and third trimesters of pregnancy in cases suspected to have uteroplacental and fetoplacental insufficiencies as in IUGR, maternal hypertension, pregnancy induced hypertension and others. Doppler studies are also beneficial in initial evaluation and follow up of high risk pregnancy cases [6]. Small for gestational age (SGA) fetuses are either constitutionally small fetuses or fetuses that have failed to achieve their growth potential (IUGR) [7]. The erroneous diagnosis of IUGR only from clinical suspicion leads to unnecessary aggressive interventions in constitutionally small, not IUGR fetus. Also timely recognition of IUGR and necessary interventions helps to prevent perinatal mortality and morbidity.

Intrauterine growth restriction (IUGR) is a condition in which a fetus fails to achieve its growth potential and is consequently at a risk of increased perinatal morbidity and mortality [8].

The timely diagnosis of IUGR may help in reducing perinatal and neonatal mortality and morbidity as well as reducing perinatal complications. The literature regarding role of Ultrasonography (USG) and obstetric Doppler in IUGR are scanty in this part of the world. The proposed study will try to describe the role of Obstetric Doppler in clinically suspected IUGR.

2. Aim and Objectives

1. To evaluate the role of umbilical artery velocimetry in predicting fetal outcome in suspected IUGR cases.
2. To determine Sensitivity, Specificity, Positive predictive value and Negative predictive value of S/D ratio of umbilical artery in IUGR cases.

3. Materials and Methods

The study was a nonrandomized, hospital based prospective study carried out at the department of Radiodiagnosis and Imaging in Manipal Teaching Hospital, Pokhara in western region of Nepal for a period of twenty months from October 2013 to June 2015.

3.1. Inclusion Criteria

1. Singleton pregnancy
2. Fetal gestational age of 32 weeks or more as confirmed with prior US examination at or before 20 weeks or as calculated from last menstrual period
3. Clinically suspected IUGR of more than and equal to 2 weeks
4. Informed consent.

3.2. Exclusion Criteria

1. Uncertain gestational age
2. Multiple pregnancy
3. Maternal or fetal conditions requiring immediate hospitalization and intervention
4. Any pregnancy with a documented major congenital or chromosomal abnormality or both.

All the cases (as per inclusion criteria) sent to Radiology department for obstetric Doppler with clinical suspicion of IUGR who attended to outpatient department (OPD) or admitted in ward of Obstetrics department were taken up for the study and properly followed up. Data and investigations of antenatal check up were collected from patients including previous USG reports if done any (dating scan done at /before 20 weeks). Doppler was done using either ACUSON X 300 by SIEMENS or/and LOGIQ P3 by Wipro GE USG machines using 3-7 MHz curvilinear transducer. The umbilical artery Doppler measurements were made from free loop of umbilical cord located between the placental and abdominal wall insertion.

The flow velocity waveforms, S/D, RI of umbilical artery were computed automatically. The average values of three such recordings were obtained. S/D > 3 and RI >0.7 in umbilical artery velocimetry were considered abnormal. The patients were sent for repeat Doppler study if clinically indicated. Data were collected within 24 hours of delivery which includes birth weight, mode of delivery, maturity score of the neonate (using New Ballard Scoring System) and plotted in standard weight for gestational age chart. The neonates were then categorized as SGA or AGA after plotting their birth weight against their weeks of maturity age.

3.3. Data Collection and Analysis

The data collected was compiled and entered in the Microsoft excel sheet. Statistical analysis was done using Microsoft Excel.

3.4. Ethical Clearance

Ethical clearance was obtained from the institutional ethical clearance committee.

3.5. Sample Size Calculation

In a pilot study done prior to the original study taking umbilical artery S/D ratio more or equal to 3 and followed up for small for gestational age ;it showed 74% sensitivity. With precision 10% and 95% confidence interval, number of diseased subjects needed were 74 [9].

4. Results

A total of 150 patients were enrolled in the study. Ten lost to follow up. Finally, the study was conducted in 140 singleton pregnancies with clinical suspicion of IUGR who presented to the hospital either in Out Patient Department (O.P.D.) or admitted in Obstetrics ward.

One hundred and twenty patients were aged between 18 and 38 years (average 25 years). Ten were aged below 20 years and 10 were aged above 30 years. Fifteen out of 140 (10.7%) subjects gave past obstetric history either in the form of fetal or neonatal loss. Twenty five percent subjects (35 out of 140) had history of pregnancy induced hypertension (PIH). Eighteen out of 140 (12.9%) subjects had history of delivery via lower segment caesarean section (LSCS) in the previous pregnancies. Five percent subjects (7 out of 140) were previously diagnosed with hypertension under dietary management only and none were taking any anti hypertensive drugs. Five out of 140

(3.6% subjects) were diagnosed diabetes mellitus with controlled blood sugar by diabetic dietary management. Fifteen out of 140 (10.7% subjects) had anemia with hemoglobin of less than 10 gm/dl.

The subjects under study had 37 weeks 4 days of average gestation age (range of 33 weeks 6 days to 40 weeks 6 days) as per their history of last menstrual period. Average gestation age of fetus by ultrasound was calculated as 34weeks 1 days (range of 31 weeks 1 day to 38 weeks 6 days). Sixty five were born with appropriate for gestation age. Seventy five neonates were born with small for gestation age and hence IUGR.

USG was used to calculate the gestation age of fetus, expected birth weight including Amniotic Fluid Index (AFI). Doppler velocimetry included calculation of S/D ratio, RI of the umbilical artery. AFI ranged from 1.6 cm to 25.84 cm with average of 9.6 cm. AFI was more than 10 cm in 61 subjects. Seventy nine patients had AFI less than 10 cm, out of which 24 subjects had AFI less than 5 cm and 55 subjects had between 5-10 cm. The average expected fetal weight calculated by USG was 2345 grams. The minimum weight measured was 1690 grams whereas maximum weight measured was 3420 grams. The various Doppler velocimetry findings of the umbilical artery is depicted in Table 1.

Table 1. Various Doppler Velocimetry Quantitative Analysis

Doppler Indices	S/D Ratio Average	S/D Ratio Range	RI Average	RI Range
Umbilical Artery	3.32	2.45 – 9.2	0.74	0.42 - 2.9

The average S/D ratio measured in umbilical artery was 3.32 (Range of 2.45 – 9.2). Umbilical artery S/D > 3 was calculated in 51.4% (72 out of 140 subjects). Four subjects among these 72 showed absent end diastolic flow (AEDF) whereas no subjects had reverse end diastolic flow (REDF). The average RI measured in umbilical artery was 0.74 with a range of 0.42 to 2.9.

Post Delivery/ Perinatal Outcome

The average birth weight was 2.1 kg with a range of 1.45kg to 3.75 kg. A total of 75 neonates (53.5%) were born with small for gestation age (SGA) after plotting their birth weight against weeks of maturity in the standard Ballards scoring chart. Similarly 46.5% (65 out of 140) neonates were born with appropriate for gestational age (AGA). However there was no neonate born large for gestation age. Forty nine out of 75 (65.3%) SGA neonates were delivered by LSCS whereas 34.7% (26 out of 75) neonates were delivered by normal vaginal delivery. Twenty seven neonates (19.3%) developed perinatal asphyxia. NICU admissions comprised of a total of 30 neonates. There were 15 neonatal deaths. Three SGA neonates were stillborn.

Table 2. Findings of Umbilical Arteries S/D in SGA Neonates

	SGA	AGA	Total
Umbilical Artery S/D > 3	57	15	72
S/D <3	18	50	68
Total	75	65	140

Findings of Doppler Velocimetry in SGA Neonates

Among 75 SGA neonates, 57 had abnormal umbilical artery Doppler velocimetry (abnormal S/D ratio>3) as

depicted in bar diagram 1. The S/D ratio of 3 or greater for predicting of IUGR in the study gave the sensitivity, specificity, positive predictive value, and negative predictive value of 76%, 76.9%, 79.2% and 73.5% respectively.

Table 3. Results of S/D Ratio of Umbilical Artery of 3 or More in Fetuses with IUGR

	Umbilical Artery of S/D Ratio of 3 or More
Sensitivity	76%
Specificity	76.9%
Positive Predictive Value	79.2%
Negative Predictive Value	73.5%

Perinatal Outcome in Abnormal Umbilical Artery Doppler Studies

Seventy two out of 140 subjects with suspected IUGR showed abnormal umbilical artery doppler velocimetry. Fifty seven out of these seventy two (79.2%) subjects with abnormal umbilical artery doppler were later born SGA. Twenty seven neonates developed perinatal asphyxia, out of which 26 (96.3%) had abnormal umbilical artery doppler velocimetry. NICU admissions comprised of a total of 30 neonates, out of which 27 (90%) had abnormal umbilical artery Doppler velocimetry prenatally. Fifteen out of these thirty neonates did not survive and all of them had abnormal umbilical artery doppler velocimetry prenatally. There were 3 still born and all these had abnormal umbilical artery velocimetry prenatally as depicted in bar Figure 1.

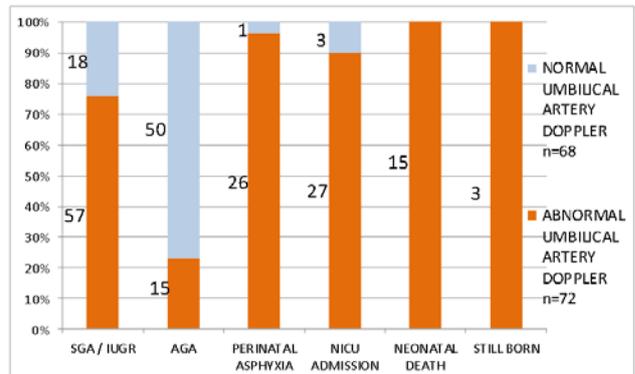


Figure 1. Neonatal Outcome in Cases with IUGR

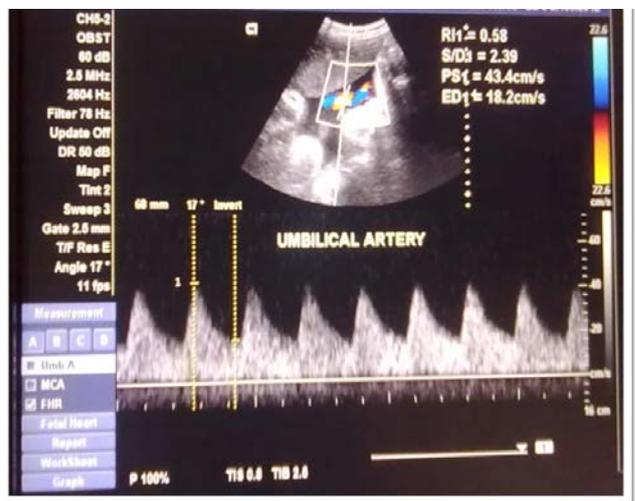


Figure 2. Normal Umbilical Artery Flow with Waveform

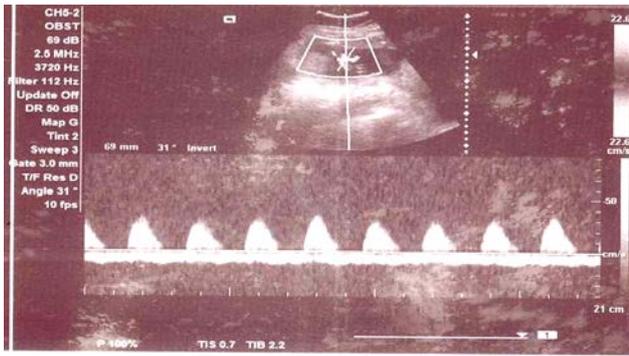


Figure 3. Absent End Diastolic Flow in Umbilical Artery

5. Discussions

Out of these 140 singleton pregnancies with clinical suspicion of IUGR, 84 were primigravida and 56 were multigravida. The average expected fetal weight calculated by USG was 2345 grams. The average birth weight at delivery was 2.1 kg with a range of 1.45 kg to 3.75 kg. Seventy five (53.6%) were born with SGA in this study. The average S/D ratio measured in umbilical artery was 3.32 (range of 2.45 – 9.2). Seventy two out of 140 (51.4%) had abnormal umbilical artery Doppler velocimetry in the current study. Fifty seven out of these 72 subjects with abnormal umbilical artery Doppler later were born with IUGR.

In a study conducted in 118 cases of high risk singleton pregnant women in China, [10] the prevalence of IUGR in the study population was 16.9%. In another study conducted in Thailand by Chanprapaph et al. [11] there were 212 singleton pregnancies, clinically suspected IUGR with gestational age between 30-42 weeks. They were followed up for 30 months. The prevalence of IUGR was 50.9% which is slightly lower than our study which showed prevalence in our study of 53.6%. However no inference can be made because of our smaller sample size. Patients were not followed up for longer duration as in above study. In a prospective study by Ghosh GS et al [12] in Sweden that included 353 singleton pregnancies, abnormal flow pattern in umbilical artery was seen in 102 (28.4%). In a study conducted by Borowski D et al. [13] in fetuses with signs of the intrauterine growth restriction after 28th weeks of gestation., there were 77.8% of abnormal flow pattern in umbilical artery. Similar finding was detected in our study with abnormal umbilical arterial flow in 79.2%

The sensitivity, specificity, positive predictive value and negative predictive value of S/D of 3 or more in our study was 76%, 76.9%, 79.2% and 73.5% which is comparable to study done by Chanprapaph [11] et al which showed 66.7%, 78.85%, 74.42% and 65.08% respectively. Fleischer A et al reported S/D ratio greater than 3 had a sensitivity of 78 percent in predicting IUGR [14] which is comparable to our study. In a study conducted in 118 cases of high risk singleton pregnant women in China [10] the sensitivity, specificity and positive predictive value of umbilical arterial S/D ratio to predict IUGR were 80.0%, 83.7% and 50.0%. The prevalence of IUGR in the study population was 16.9%.

The subjects under study had 37 weeks 4 days of average gestation age as per their history of last menstrual period. The average birth weight at delivery was 2.1 kg.

Twenty seven neonates (19.3%) developed perinatal asphyxia, 26 out of these 27 (96.3%) neonates with asphyxia had abnormal umbilical artery doppler velocimetry. NICU admissions comprised of a total of 30 neonates, out of which 27 (90%) had abnormal umbilical artery doppler velocimetry prenatally. Fifteen out of these thirty had neonatal death. In a study conducted in 578 singleton pregnancies with diagnosis of IUGR referred for Doppler velocimetry in Italy [15], the mean age at delivery was 35 weeks 5 days with mean birth weight of 1.85 kg. 547 fetus were born alive and there were 28 (4.8%) intrauterine deaths, 3 elective terminations of pregnancy and 26 neonatal deaths. In a prospective study by Ghosh GS et al [12] in Sweden that included 353 singleton pregnancies, abnormal flow pattern in umbilical artery was seen in 102 (28.4%) with adverse perinatal outcome related to abnormal umbilical artery velocimetry.

Forty-four of the 134 (32.8%) pregnancies with low birth weight had abnormal doppler waveforms in the umbilical arteries in an Indian study by Arora et al. [16]. 85% of NICU admissions had abnormal umbilical artery doppler velocimetry prenatally.

6. Conclusion

The abnormal umbilical artery S/D ratio of 3 or greater for predicting of IUGR in the study gave the sensitivity, specificity, positive predictive value, and negative predictive value of 76%, 76.9%, 79.2% and 73.5% respectively. Admission to the NICU and incidence of perinatal complications including mortality increased with the worsening of Doppler velocimetry. The study shows that abnormal obstetric umbilical artery Doppler velocimetry is a good predictor of IUGR and this is followed with poor neonatal outcome in terms of increased NICU admission, perinatal complications and even neonatal death.

Doppler Ultrasound is a non invasive, non traumatic, cost effective and easily available diagnostic tool. The early diagnosis of IUGR with the help of abnormal flow patterns in umbilical artery using Doppler ultrasound may help in reducing perinatal and neonatal mortality and morbidity as well as reducing perinatal complications. This provides for timely interventions to prevent progression from IUGR to Intrauterine death(IUD).

Declaration of Conflicting Interests

The authors declare that there is no potential conflicts of interest with respect to the research, authorship and /or publication of this article.

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