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Pregnancy outcome sonographic umbilical artery Doppler assessment in the free loop and Perivesical sites

Amene Abiri[1], **Shafaat Masoumeh**[2]✉, **Salavati Jamileh**[3], **Borna Sedigheh**[4], **Hantoushzadeh Sedigheh**[5], **Khazardoost Soghra**[6]

[1]Fellowship of Perinatology, Perinatology Department, Valiasr Hospital, Imam Khomeini Hospital Complex, TUMS, Iran, Email: abiriamene1397@gmail.com

[2]Resident Ob & Gyn Department, Valiasr Hospital, Imam Khomeini Hospital Complex, TUMS, Iran, Email: masumeshafat@gmail.com

[3]Perinatologist, Kurdistan University of Medical Sciences, Sanandaj, Iran, Email: arsam201012@gmail.com

[4]Professor of Perinatology, Perinatology Department, Valiasr Hospital, Imam Khomeini Hospital Complex, TUMS, Iran, Email: s_borna@hotmail.com

[5]Professor of Perinatology, Perinatology Department, Valiasr Hospital, Imam Khomeini Hospital Complex, TUMS, Iran, Email: hantoushzadeh@tums.ac.ir

[6]Professor of Perinatology, Perinatology Department &Maternal, fetal & neonatal Research center, Valiasr Hospital, Imam Khomeini Hospital Complex, TUMS, Iran, Email: drkhazardoost@yahoo.com

✉**Corresponding author**

Resident Ob & Gyn Department, Valiasr Hospital, Imam Khomeini Hospital Complex, TUMS,
Iran
Email: masumeshafat@gmail.com

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General Note

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ABSTRACT

Aim: The aim of this study was to assess Pregnancy outcome in the intrauterine growth restriction fetuses by the means of free loop and Perivesical umbilical artery Doppler. *Methods:* This is a prospective study performed on 50 singleton pregnancies with IUGR between 26 and 38 weeks of gestation. UA blood flow velocities were measured at the perivesical and free-loop. The pulsatility index (PI), resistance index (RI), S/D (systolic/diastolic) ratio were calculated. At each site of sampling and were compared with each other and with outcomes of pregnancy. *Results:* There were significant differences between gestational age groups and. NICU admission, umbilical artery PH, Apgar score, fetal death. With decreasing gestational age, the results are worse. Birth weight group has different S/D in perivesical umbilical artery. There is significant difference in Perivesical and free loop RI value in the fetal death group. There is 70 percent correlation between S/D in free loop and perivesical umbilical artery. There is 30 percent correlation between PI in free loop and perivesical umbilical artery. There is 90 percent correlation between estimated fetal weight by sonography and neonatal accurate weight. *Conclusion:* UA Doppler parameters are various in the different area. Free loop S/D ratio has 70% correlation to PVUA S/D ratio. PVUA is potentially reproducible in IUGR. Fetuses and sonography follow up to accurate time for delivery. The most important prognostic factors related to the adverse outcome in the management of IUGRs are Gestational age.

Keywords: intrauterine growth restricted; free-loop Doppler; perivesical Doppler, pregnancy outcome

1. INTRODUCTION

Intrauterine growth restriction (IUGR) or fetal growth restriction (FGR) refers to those fetuses which birth weight is under the 10% normal gestational age curve (Bansal et al., 2016). These fetuses could not achieve the genetic growth potential due to placenta-mediated disease which leads to restricted access to nutrient supply (Morris et al., 2011; Sharbaf et al., 2018). In (FGR) infants, the rate of Perinatal morbidity and mortality is ten times more than that of healthy ones (Pankiewicz and Maciejewski, 2017). Also, FGRs are at risk of long-term and neonatal complications, such as pulmonary hemorrhage, chronic adult diseases, asphyxia, RDS (Respiratory Distress Syndrome), hypoglycemia, cerebral palsy, Polycythemia, NEC (Necrotizing Enterocolitis) and IVH (Intraventricular hemorrhage). Accurate monitoring and on time intervention are important in preterm fetuses and outcome of pregnancy (Morris et al., 2011; Sharma, Shastri, and Sharma, 2016; AB. 2018). In the high risk pregnancies, the results of umbilical artery (UA) Doppler sonography can determine the placental insufficiencies, such as (IUGR) or pregnancy hypertensive disorders. Multiple observational studies show high sensitivity and prognostic accuracy of UA Doppler for FGR fetal compromise (Heidweiller-Schreurs et al., 2018; Khanduri et al., 2013). The result of a Cochrane review shows that UA Doppler velocimetry in placental insufficiency, Reduces the risk of mortality and obstetrical interventions during pregnancy (AB. 2018; Heidweiller-Schreurs et al., 2018). The most common IUGR fetuses care is the biophysical profile (BPP) and non stress test (NST). These tests are not sensitive enough to predict bad out comes in IUGR pregnancy. in this case the Doppler identification of abnormal vascular resistance patterns is useful to terminate of pregnancy with minimal complications, such as pre-eclampsia, intrauterine growth restriction, and perinatal mortality (3, 6) (AB. 2018; Sharbaf et al., 2018). It is not important to identify a small fetus, but is important to identify a "fetus in danger"(AB. 2018). Doppler examination provides an assessment of the hemodynamic status and blood flow of the main fetus blood vessels. The study of umbilical artery is the easiest way to Optimize the efficacy of diagnosis in fetal compromise and placental-insufficiency (Maulik et al., 2010; Aditya et al., 2016; Lecarpentier et al., 2013). Therefore, UA Doppler technique becomes a standard for antenatal management of IUGR (Lecarpentier et al., 2013). Doppler velocimetry parameters obtained at perivesical umbilical artery (PVUA) site of the umbilical artery is significantly higher, more feasible and easier to perform, than other sites (Khare, Paul, and Konje 2006). On the other hand, differences in Doppler results show, a meaningful reduced resistance from abdominal to placental end as a fact, there is a vast variation in Doppler waveform along the umbilical artery. It is usual for two operators to obtain completely different waveforms from the same subject during the same examination. The common clinical practice site, the free loop (FL) site, has the minimum reproducible results on the base of insonation site. The most reproducible waveform patterns and indices belongs to The placental insertion (PL), abdominal insertion (AI) and PVUA because of their fixed anatomical positions (Khare, Paul, and Konje 2006).The noticeable point is the fact that perivesical site is reliable for calculating UA PI (pulsatility index)

more than a free-loop and the end of the umbilical cord. It is potentially important for the severe growth retardation in mono amniotic twins (Bruner et al., 1994). This study is design to determine the correlation between free loop and perivesical Doppler indices and FGR pregnancy outcome.

2. MATERIALS AND METHODS

This prospective study was performed at Imam Khomeini Hospital, affiliated with Tehran University of Medical Sciences in 2018-2019. Ethical certification was obtained from the Institutional Review Board of Tehran University of Medical Sciences. Each patient is participated in the study with a written consent. The sampling carried out by random choosing of 50 singleton fetuses with restricted intrauterine growth in gestational age of 26 to 38 weeks. The IUGR fetuses is defined by fetal Weight <10% for the gestational age according to Hadlock-3 formula and impaired umbilical arterial Doppler either in free loop or perivesical sites. All pregnancies were calculated based on an accurate crown-rump length between 8 and 12 weeks. Exclusion criteria included Pregnancies with multiple gestations, congenital anomalies, mothers with underlying illness (diabetes, high blood pressure, ischemic heart disease, kidney disease and autoimmune diseases and smoking) and Mothers not willing to participate in the study. The data is collected by the Philips Affiniti 70 ultrasound color Doppler machine with convex 5 MHz probe by a single operator, machine, and method. The settings of Power were at B / 92 MW / cm2 spatial maximum temporal mean intensity. (7.5 MHz) was set for wall filter and the frequency of the pulse repetition was 5 MHz and the persistence was at middle. The insonation angle was less than 60° or equal, and Doppler studies performed during fetal apnea. In the first step, the fetal bladder was recognized in the coronal section with gray scale. Then the color mode turned on to identify the PVUA arteries, in the location, where the vessels followed along the side walls of the bladder, Doppler waveforms were measured. In the next step, the scale was placed on the vessel, making sure that the size of the sample was large enough to interrogate all the waveforms of the velocity. It is needed at least, four complete cardiac cycles for the measurement of Doppler Indices. Tracing the waveform and generating several indices, were performed by an automated system. In this study; we used resistance index (RI), pulsatility index (PI), and systolic/diastolic ratio (S/D) for analysis. Doppler Indices of Both umbilical arteries in the site of PVUA were measured and the mean of them was used for analysis. Since the detection of two arteries in other sites was clearly difficult, just one umbilical artery Doppler was measured. The mentioned procedure was carried out for free-loop site too. All pregnant women received standard prenatal care such as BPP and NST throughout the study. The results of the last Doppler (3-7 days before delivery) were evaluated with the outcome of pregnancy including, birth weight, gestational age at delivery, number of hospitalization days in NICU, APGAR score, neonatal mortality, termination method of pregnancy, termination reasons, atrial blood gas (figure 1 & 2).

This study was approved by ethical committee of Tehran University of Medical Sciences and received ethical code as IR.TUMS.IKHC.REC.1397.306.

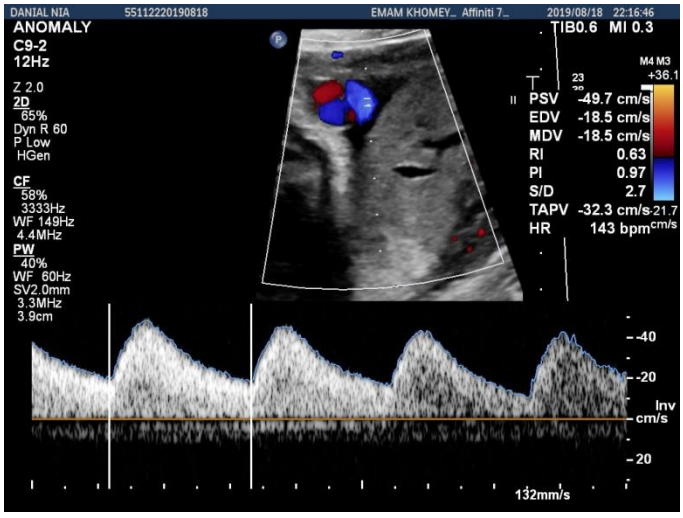

Figure 1 free loop doppler

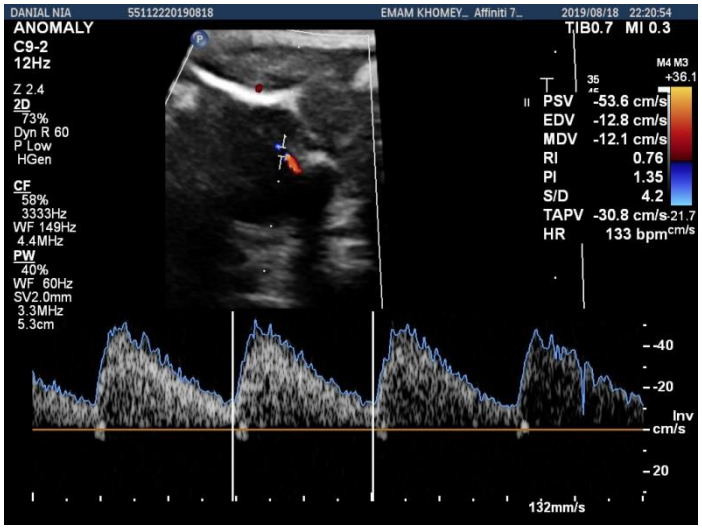

Figure 2 Perivesical umbilical artery Doppler

Statistical analysis

In this study, The SPSS-v22 software was used to analyze the information. The quantitative variables were reported by (mean ± SD) and qualitative variables were reported as frequencies and percentages. Correlation analysis was performed by the Pearson test. Quantitative data analysis was performed by independent t-test, ANOVA; generalized linear model and for non-normal quantitative variables Chi-Square were used. The P value of < 0.05 was as significant difference level.

3. RESULTS

Fifty pregnant women were participated in the study. The mean gestational age at the time of delivery was 34.3 weeks (based on 8-12 weak gestational age by ultrasound), and the average birth weight of newborns was 1846.5 grams. Frequencies of characteristic are shown in Table 1.

Table 1 Frequencies of characteristic factors

Frequencies	Gestational age	birth weight	Duration of hospitalization in NICU
Mean (min,max)	34.3(26-38)	1846.5(510-3200)	11.3(0-91)
Std.Deviation(SD)	4.1	647.4	18.1

In this study sixty-eight percent had normal umbilical artery pH, and 24% had acidosis. About 32% of newborns had Apgar score <7 at 5 min and 68% had normal one. According to delivery mode, sixteen percent of pregnant women had normal delivery and 84% cesarean section. The frequency of fetal death was 16 %(8 cases). Seventy percent (35 cases) of newborns were admitted to NICU, but others did not need the admission. of pregnancy termination was done in 46 %(23 cases) for gestational age over 37 weeks, 18% (9 cases) due to fetal distress, 32 %(16 cases) preeclampsia and 2 %(cases) were terminated for other reasons (table 2).

Table 2 Umbilical artery Doppler indices

Frequencies	Free-loop (S/D)	Free-loop (RI)	Free-loop (PI)	Perivesical (S/D)	Perivesical (PI)	Perivesical (RI)
Mean(min,max)	3.6 (1.52,6.9)	0.68 (0.30,0.89)	1.24 (0.11,201)	4.1 (2.1,7.2)	1.5 (0.9,4.4)	0.95(0.14,8)
Std.Deviation	1.11	0.11	0.40	1.13	0.52	1.10

Pregnant women were divided to 4 groups base on gestational age: group 1(lower than 32 weeks), Group 2(32-34 weeks), group 3(34-36), Group 4 (36-38 weeks).

In Doppler ultrasonography, only the umbilical artery free-loop S/D (systolic/diastolic) ratio had a significant difference between gestational age groups (p value: 0.05). Fetuses were divided in to 4 groups Based on their birth weight: less than 1000 grams, 1000-

1500 grams, 1500-2000 grams, more than 2000 gram. There was not any significant difference between free-loop and perivesical Doppler indices in 4 groups (table 3 & chart 1).

Table 3 Doppler indices frequencies base on gestational age

Gestational age group	Umbilical artery (S/D)	Umbilical artery (RI)	Umbilical artery(PI)	Perivesical artery (S/D)	Perivesical artery (PI)	Perivesical artery (RI)
Group 1(<32 weeks)						
Mean	4.7	0.685	1.21	4.57	1.46	1.45
Std. deviation	1.14	0.1038	0.424	1.246	0.306	2.29
Group 2(32-34 weeks)						
Mean	5.04	0.796	1.63	5.02	1.72	0.76
Std. deviation	1.19	0.062	0.17	1.30	0.336	0.418
Group 3(34-36 weeks)						
Mean	3.15	0.60	1.06	3.92	1.76	0.80
Std. deviation	1.50	0.184	0.355	1.45	1.12	0.34
Group 4(36-38 weeks)						
Mean	3.45	0.6922	1.24	3.92	1.44	0.8383
Std. deviation	0.668	0.071	0.42	0.84	0.27	0.36
all Group						
Mean	3.64	0.68	1.24	4.19	1.53	0.95
Std. deviation	1.11	0.112	0.40	1.131	0.52	1.10

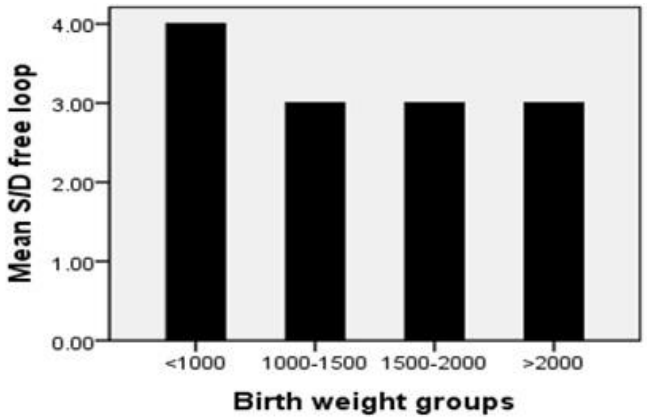

Chart 1 frequency of mean S/D free loop in birth weight groups

There was not any significant difference in Doppler indices of free loop and perivesical artery between the group which had Apgar score <7 at 5 min and normal Apgar. There was not any significant difference in Doppler indices of free loop and perivesical artery between the group which had normal & abnormal umbilical artery PH and also for different weight groups. There was significant difference in prevesical RI value between fetal death (Mean: 2.85, SD: 3.61) & alive (Mean: 0.8, SD: 0.33) groups (p value: 0.001). In the NICU admission group, free loop S/D had significant difference with none admitted one (p value: 0.007). The mean and sd of S/D ratio in NICU admission was 3.5, 1.01 and 3.7, 1.3 in non-admitted respectively (chart 2). According to the Results obtained in this study, there were significant differences between gestational age (GA) groups and these parameters:

A. NICU admission (Pvalue: 0.008); the lower gestational age needed more NICU admission; in group 1(lower than 32-weeks gestational age), all (100%) of them admitted to NICU; so the lower gestational age, needs more NICU admission

B. umbilical artery PH (Pvalue: 0.0001); the lower gestational age showed lower umbilical artery PH;

C. Apgar score (Pvalue: 0.0001); the lower gestational age had correlation to lower Apgar;

D. fetal death (Pvalue: 0.0001); fetal death decreased while gestational age increased.

There was no significant relationship between mode of delivery and gestational age. IN the General Linear Model analysis (regression multi variant) showed that GA groups had significant difference between S/D ratio (Pvalue: 0.21), RI value (0.013) of free loop and perivesical S/D ratio (0.031). Normal and acidotic groups had significant difference between *Perivesical* RI. Birth weight groups has different S/D ratio in *perivesical* umbilical artery. IN the fetal death group have significantly different *perivesical* RI value. There is 70 percent correlation between S/D ratio in free loop and perivesical umbilical artery. There is 30 percent correlation between PI value in free loop and perivesical umbilical artery. There is 90 percent correlation between estimated fetal weight by sonography and neonatal accurate weight.

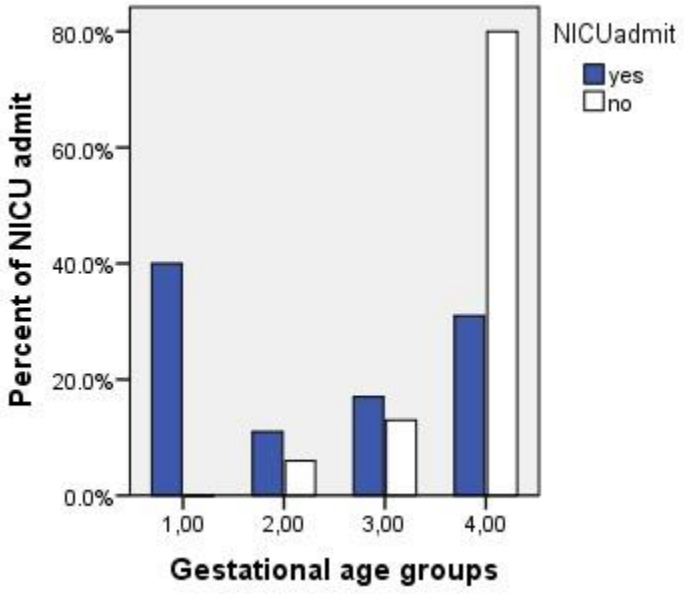

Chart 2 frequency of percentage of NICU admission base on birth weight groups

4. DISCUSSION

As measured by Doppler, a falling gradient in impedance from the PVUA to the free loop sites of the umbilical cord was detected according to the study of MANJIRIKHARE in 2006. Also our results show the similar pattern (mean free loop S/D: 3.6 and PVUA S/D: 4.1)(Khare, Paul, and Konje 2006). The free loop insonation site have a better sensitivity than other sites so Although differences in Doppler indices from the PVUA site and free loop of the cord have been reported(Bruner et al. 1994) to the best of our knowledge, in this study free loop S/D ratio have 70% correlation to PVUA S/D ratio .

The abdominal and PL(Placental site) sites were the most difficult to assay and PVUA measurement is the easiest and most reproducible to obtain, also there is a potentially relationship between PVUA and free loop, so we can utilize PVUA site instead of free loop in the sonography follow up. The quality of the FL waveforms was occasionally affected by not only the adjacent artery interference but by minor maternal and fetal movements. So getting PVUA vessel Doppler is more accurate because of getting it close to zero in most cases (Khare, Paul, and Konje, 2006; Bruner et al., 1994). On the other hand, the FL site is the most commonly used in clinical practice, as it is technically easier to obtain, sampling could be from very disparate sites, so it is likely to have a significant inter- and intra-observer variability. Bruner et al., suggested that the reduction in S/D ratio from the fetal to the placental site of insonation resulted more from a decrease in the peak systolic maximum velocity than from an increase in the diastolic velocities (Bruner et al., 1994). Now in this study it is obvious that the mean of S/D ratio in PVUA site is clearly more than the free loop site. Our findings of varying Doppler waveform patterns and indices at the two sites of the umbilical artery have significant importance for clinical practice. By the abnormality in the umbilical artery Doppler, the site of sampling will be an effective parameter in determining the degree of abnormality and also the timing of delivery. It seems that it is necessary for clinicians to consider a reference point for PVUA umbilical artery Doppler. According to mentioned reference, clinicians can have a more accurate will comparisons of results, consistency in interpretation and so the uniform clinical application.

The other PVUA site benefit is in cases of mono-amniotic twins where the assessment of individual fetuses can be undertaken surely, severe growth restriction with severe oligohydramnios or anhydramnios or ruptured membranes with associated oligohydramnios (AB. 2018; Lecarpentier et al., 2013; Lewkowitz et al., 2019). In this study we performed umbilical artery Doppler in

50 high-risk pregnancy women, this helped us to predict fetal morbidity and mortality in the abnormal umbilical artery Doppler group. A significant fall in S/D ratio and RI value of umbilical artery as gestational age increases. In 2018 Rashmi showed that the abnormal umbilical artery velocimetry have a shorter diagnosis of abnormal Doppler to delivery interval, decreased birth weight, early delivery, increased NICU admissions and duration of stay there and with low Apgar scores than those with normal Doppler (AB. 2018). These results were obtained in IUGR fetuses with impaired Doppler velocimetry similar to Rashmi study outcomes. Also we show that the higher umbilical artery RI value group had more fetal death rate than the ones. Many studies recommend that Doppler studies of velocity waveforms of the umbilical artery are more useful to detect IUGR prone fetuses for than sonographic estimation of fetal weight, so it is very important to do it with most accuracy to diagnose high risk fetuses. results showed that there was a significantly increased incidence of neonatal death and duration of admission for NICU care in preterm SGA (small for gestational age) infants with impaired umbilical artery as the same as our results (Sharma, Shastri, and Sharma 2016). In Rashmi study the S/D ratio and RI value of umbilical artery was significantly higher in those fetuses that had Apgar <7 than those who had Apgar >7, as the same we measured PVUA RI value high in the Apgar<7 group. This shows a higher umbilical vascular resistance in PVUA and therefore, a decreased placental perfusion in those who had birth Apgar<7 (Sharma, Shastri, and Sharma 2016).

In Rashmi study, the mean S/D ratio of umbilical artery was 2.95 in those fetuses which were not NICU admitted as compared to 3.14 in those who transferred to NICU in the normal umbilical artery Doppler group. Similarly mean S/D ratio of PVUA umbilical artery was 4.07 in those fetuses which were not NICU admitted; on the other hand NICU admitted fetuses had 4.25 (Sharma, Shastri, and Sharma 2016). Doppler technology provides us the chance for repetitive noninvasive monitoring in IUGR pregnancies. The most important prognostic factors related to the adverse outcome in the management of IUGRs are Gestational age (at diagnosis and at delivery) as the same we show in this study (Bansal et al., 2016).

5. CONCLUSION

UA Doppler parameters are various in the different area. Free loop S/D ratio has 70% correlation to PVUA S/D ratio. PVUA is potentially reproducible in IUGR. Fetuses and sonography follow up to accurate time for delivery. The most important prognostic factors related to the adverse outcome in the management of IUGRs are Gestational age and also we can conclude that Perivesical artery Doppler especially in multiple pregnancies proved the fix point to compare fetal status and assess the pregnancy outcome. Because of lower sample size in this study, it is recommended to perform this study in multiple pregnancies and in large-scale participants.

Conflict of interest

There is no financial or other conflict of interest.

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