



Fetal Liver Size, Hepatic Artery Doppler Study in Late Intra Uterine Growth Restriction

Ali Farag Ali^{1*}, Magdy Hassan Hussein Balaha¹, Ahmed El Sayed El Halwagy¹ and Mohamed Mohsen El Namori¹

¹*Obstetrics and Gynecology Department, Faculty of Medicine, Tanta University, Tanta, Egypt.*

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2021/v33i1731041

Editor(s):

(1) Dr. Ashish Anand, GV Montgomery Veteran Affairs Medical Center, University of Mississippi Medical Center, William Carey School of Osteopathic Medicine, USA.

Reviewers:

(1) G. Krishna Kumar, JIPMER, India.

(2) Anwar Farooq Muslim Al Taie, University of Baghdad, Iraq.

(3) Sabah Abdellatif Hussein Ali Beza, Cairo University, Egypt.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/71952>

Original Research Article

Received 01 June 2021

Accepted 05 August 2021

Published 06 August 2021

ABSTRACT

Background: Intrauterine growth restriction (IUGR) is a condition in which the fetus does not reach its growth potential. It is well known that a fetus affected with late IUGR has smaller abdominal size. The aim of the study is to evaluate the fetal liver size, fetal hepatic artery blood flow and other fetal vascular Doppler indices in cases of late IUGR.

Methods: This observational analytical, cross-sectional study was carried out on 100 pregnant women at or above 32 weeks. Participants were divided into two groups: Group 1 (study group): 50 pregnant women as study group who were affected with IUGR. Group 2 (control group): 50 normally pregnant women as control group.

Results: There was no statistically significant correlation between fetal weight and liver length. There was a positive highly statistically significant correlation between symphysial fundal height and the estimated fetal weight by ultrasound in cases of IUGR. There was a statistically significant decrease in the liver size in IUGR compared to the normal group. There was a statistically significant reduced hepatic arterial Doppler indices.

Conclusions: Reduced liver size and hepatic arterial Doppler indices (PI, RI) can be valid diagnostic methods in IUGR. SFH, in fetuses suffering from IUGR when compared to normal cases, was correlated with EFW.

*Corresponding author: E-mail: ali.sanad923@gmail.com;

Keywords: Fetal; hepatic artery Doppler; late intra uterine growth restriction; IUGR.

1. INTRODUCTION

Intrauterine growth restriction (IUGR) is a condition in which the fetus does not reach its growth potential. It affects 3%–10% of all pregnancies [1], with morbidity and mortality rates close to 80% in fetuses who are undiagnosed and therefore untreated [2]. At present, the diagnosis is made by ultrasonography evaluation of biometric parameters and estimation of fetal weight [3].

Fetal hemodynamic evaluation is performed by Doppler ultrasonography and analysis of impedance indices in various fetal vessels [1]. Power Doppler is a useful tool for evaluating both the placental and the fetal vascular tree [4].

It is well known that a fetus affected with late IUGR has smaller abdominal size. This might partly be due to decreased subcutaneous fat and decreased liver size. The liver size is observed to have smaller size than normal. Some authors describe that is because of consuming energy reserves by fetuses with late IUGR, especially their liver glycogen stores, so there is a reduced liver size as well as a decreased abdominal size [1].

Some authors say that, the venous pressure in the fetal liver circulation is maintained with decreased distribution of umbilical blood to the right hepatic lobe and compensatory vasodilation of the hepatic and splenic arteries [5].

During Doppler study on ductus venosus (DV) flow in severely growth-restricted fetuses some authors find that, a strong arterial signal can sometimes be recorded on the reverse channel [6].

The liver affection whether the parenchyma, glycogen storage or vasculature in intra uterine growth restricted fetuses is still in the phase of many future studies.

The aim of the study is to evaluate the fetal liver size, fetal hepatic artery blood flow and other fetal vascular Doppler indices in cases of late intrauterine growth restriction (IUGR).

2. PATIENTS AND METHODS

This observational analytical, cross-sectional study was carried out on 100 pregnant women at

or above 32 weeks attending to obstetrics and gynecology department at Tanta University hospital in the period from January 2020 till April 2021. Participants were divided into two groups: Group 1 (study group): 50 pregnant women as study group who were affected with IUGR. Group 2 (control group): 50 normally pregnant women as control group.

Sample size estimation [7,8] was done based on the formula: $no = Z^2pq/B^2$, where: no is initial sample size. Z equals 1.96 if we use 95% Confidence level. p is the percentage of the phenomena in population from the previous studies, $p = 0.15$ (IUGR prevalence is 4-7%), $q = 0.07$, and $q = 1 - p$. B is the accepted bias for p in the sample = 0.05. N was calculated to be 100.

Cases were selected according age range between 18 to 38 years, BMI ($\geq 18 - \leq 25$) kg/m², singleton pregnancy, viable fetus and hypertension disorders “gestational hypertension, preeclampsia and chronic essential hypertension”. Women who were morbidly Obese, multiple pregnancies, fetal anomalies, DM with pregnancy renal or hepatic diseases, vascular diseases other than hypertension and Rh incompatibility were excluded.

After taking informed written consent the recruited were subjected to the following: History taking (personal, obstetric and family), examinations including vital signs, full obstetric examination, laboratory investigations and Ultrasonographic scanning which was done twice in fetuses affected with IUGR; at time of examination and confirmatory 2 weeks later to be sure from our Doppler measurement stability. The scanning was used to measure fetal biometry for estimated weight measurement (EFW), liver size estimation and C. Doppler studies including umbilical artery Doppler, middle cerebral artery Doppler, ductus venosus Doppler and hepatic artery Doppler.

2.1 Statistical Analysis

The data was analyzed using and SPSS ver. 22.0. Data were tested for normal distribution using the Shapiro Walk test. Quantitative data were expressed as mean \pm SD. A p value < 0.05 was considered statistically significant.

3. RESULTS

We compared between the IUGR and Normal groups according to pertinent data presented in, including (age, parity, BMI and calculated Gest. Age). There was a non- significant difference between the groups. We compared BPD, FL, and AC between IUGR and Normal groups according to their week estimation. The HC/AC ratio was also measured. There was statistically highly significant difference between both groups (Table 1).

We compared between IUGR and Normal groups according to Symphysial fundal height, and

estimated fetal weight in gm. We find that these parameters decrease in IUGR group compared with the control group. There was statistically highly significant difference between both groups. There was highly positive statistically significant correlation between Symphysial fundal height and the estimated fetal weight by ultrasound in cases of IUGR. We compared the liver length Liver Length in mm between IUGR and Normal groups. There was statistically highly significant difference between both groups. In the current study, the liver length measures were near to the 5th percentile of the reference value. There was no statistically significant correlation between fetal weight and liver length (Table 2).

Table 1. Comparison of the pertinent data and analysis of ultrasound biometry data between the IUGR and Normal groups

			Range	Mean	±	S. D	t. test	p. value
Age	IUGR	18	– 38	28.16	±	5.66	0.844	0.401
	Normal	19	– 37	27.24	±	5.24		
Parity	IUGR	0	– 4	1.62	±	1.01	0.412	0.681
	Normal	0	– 3	1.54	±	0.93		
BMI (Kg/m ²)	IUGR	19	– 24	22.00	±	2.35	0.415	0.679
	Normal	19	– 25	22.80	±	2.47		
Calculated G. Age	IUGR	32	– 35	33.30	±	1.074	1.757	0.082
	Normal	32	– 35	33.70	±	1.199		
BPD	IUGR	30w	– 35w	32.30	±	1.21	4.371	0.001*
	Normal	30w	– 38w	33.88	±	2.15		
FL	IUGR	25w	– 34w	28.64	±	2.08	12.884	0.001*
	Normal	30w	– 39w	34.10	±	2.16		
AC	IUGR	26w	– 34w	28.58	±	1.98	13.998	0.001*
	Normal	31w	– 39w	34.28	±	2.09		
HC/AC	IUGR	1.25	– 1.5	1.33	±	0.050	19.571	0.001*
	Normal	1.0	– 1.17	1.09	±	0.058		

* Intrauterine Growth Restriction (IUGR), Body mass index (BMI), Biparietal diameter (BPD), Femur length (FL), Abdominal Circumference (AC), Head Circumference (HC)

Table 2. Analysis of the estimated fetal weight and the symphysial fundal height in IUGR & normal group

		Range	Mean ± S. D	t. test	p. value
Estimated Fetal Weight (gram)	IUGR	1200 – 1580	1405 ± 80	20.008	0.001*
	Normal	2100 – 3500	2605 ± 416		
Symphysial fundal height (cm)	IUGR	24 - 33	27.10 ± 2.11	17.605	0.001*
	Normal	31 – 38	34.20 ± 1.92		
Symphysial fundal height					
Estimated Fetal Weight			r	0.887	
			P	< 0.01**	
Liver length (mm)	IUGR	29 – 35	31.4 ± 0.15	26.88	0.001*
	Normal	38 – 48	40.5 ± 0.19		
Liver Length					
Estimated Fetal Weight			r	0.083	
			P	0.565	

* Intrauterine Growth Restriction (IUGR)



Fig. 1. US of liver length in IUGR at GA 32W

We compared UMA (PI &RI), MCA (PI &RI), Cerebroplacental ratio and Ductus venosus in IUGR and normal groups. Except for the DV, other parameters showed a statistically highly significant difference between IUGR and Normal groups ($p < 0.01$). Comparing DV (PI) in both groups, revealed a non-significant difference ($p > 0.05$). From the findings in tables, records of our study showed that all IUGR cases were in stage I according to Barcelona classification or

stage II according to San Paulo classifications as mention above in review (Table 3).

There was statistically highly significant difference between the groups according to Hepatic A (PI) and Hepatic A (RI); There was no statistically significant correlation between fetal hepatic artery and middle cerebral artery (Table 4).

Table 3. Analysis of Doppler data including the UMBA (PI, RI), MCA (PI, RI) and Cerebroplacental ratio, in IUGR and Normal groups

		Range	Mean ± S. D	t. test	p. value
UMA (PI)	IUGR	1.14 – 1.32	1.21±0.57	23.099	0.001*
	Normal	0.82 – 1.1	0.927±0.058		
UMA (RI)	IUGR	0.71 – 0.81	0.747±0.023	43.221	0.001*
	Normal	0.48 – 0.58	0.531±0.027		
MCA (PI)	IUGR	1.1– 1.9	1.518±0.213	4.440	0.001*
	Normal	1.3 – 2.1	1.714±0.229		
MCA (RI)	IUGR	0.66 – 0.72	0.681±0.016	23.169	0.001*
	Normal	0.75 – 0.85	0.795±0.031		
Cerebroplacental ratio	IUGR	1.53 – 2.88	2.228±0.314	6.472	0.001*
	Normal	1.36 – 2.53	1.858±0.255		
DV (PI)	IUGR	0.42 – 1.35	0.862±0.209	0.794	0.429
	Normal	0.34 – 1.32	0.899±0.254		

* Umbilical Artery (UMA), Ductus Venosus (DV), Middle Cerebral Arterial (MCA), Pulsatility Index (PI), Resistive Index (RI)

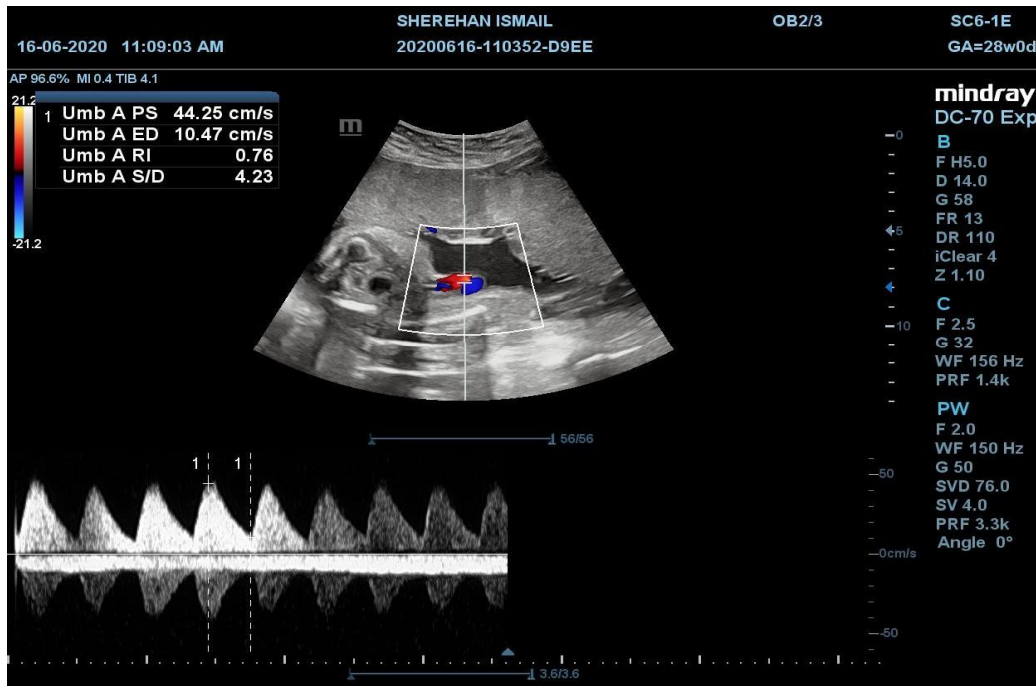


Fig. 2. Umbilical artery Doppler in IUGR at GA 32 W

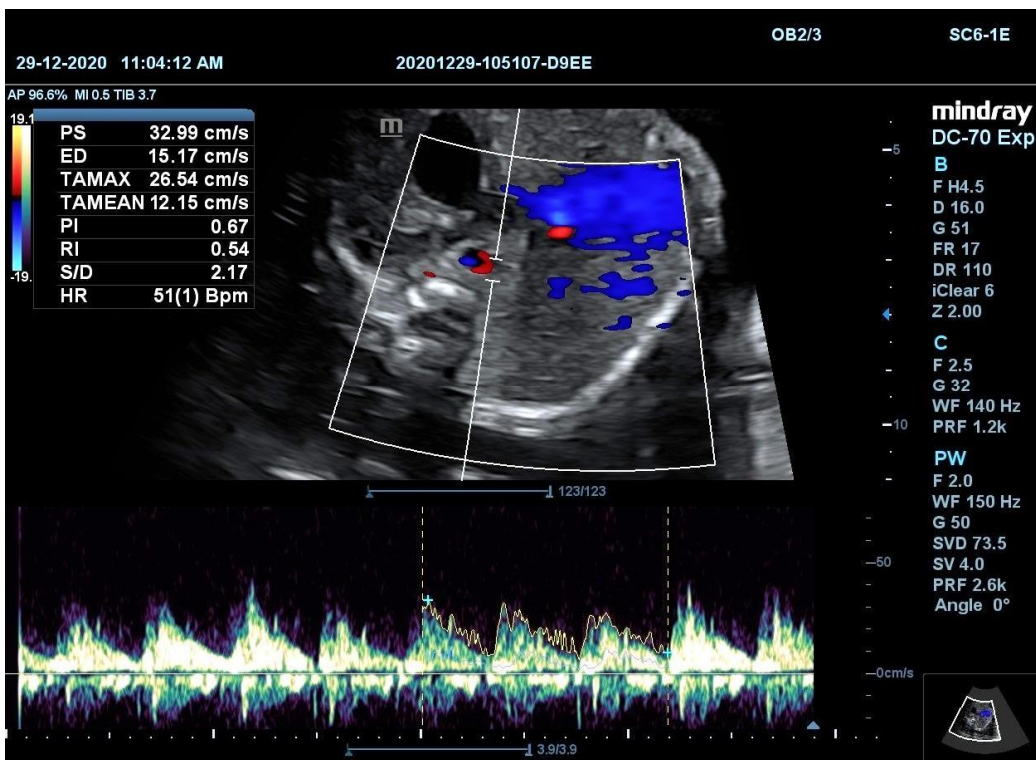


Fig. 3. Hepatic artery Doppler in IUGR at 32w

Table 4. Analysis of Doppler data of the Hepatic Artery in IUGR & Normal groups

		Range	Mean ± S. D	t. test	p. value
Hepatic A (PI)	IUGR	0.49 – 0.88	0.725±0.089	22.092	0.001*
	Normal	0.97 – 1.45	1.260±0.147		
Hepatic A (RI)	IUGR	0.5 – 0.58	0.471±0.069	17.363	0.001*
	Normal	0.55 – 0.75	0.674±0.045		
Middle cerebral artery					
Hepatic A (PI)		r		0.014	
		P		0.461	
Hepatic A (RI)		r		0.237	
		P		0.079	

* Intrauterine Growth Restriction (IUGR), Pulsatility Index (PI), Resistive Index (RI)

4. DISCUSSION

Intrauterine growth restriction (IUGR) is a pathological condition that refers to a fetus that fails to reach his/her genetically predetermined growth potential [9]. Thus, it is necessary to identify these fetuses, begin early antenatal surveillance and implement prompt obstetric measures to decrease perinatal mortality [10].

The research problem was the fully unseen issue of hepatic affection in cases of IUGR; and whether there was a vascular liver sparing in cases of late IUGR. This study hypothesized that the change in fetal body weight in late IUGR, might be also associated by hepatic venous and arterial vascular changes; as well as the liver size changes.

As fetal growth is a dynamic process, and its assessment requires at least two observations separated in time, an intuitive approach to improve the diagnosis of FGR is the use of serial ultrasound evaluations [11]. This was in line with the protocol of our study, where we repeated ultrasound after 2 weeks for confirmation. Suspected IUGR could be evaluated by detailed ultrasound to identify fetal anomalies in addition to biometry. In high-risk pregnancies, serial growth ultrasound or abdominal circumference (AC) measurements are the best predictors of fetal growth [12].

El-Sayed et al. [13] who compared 26 cases of IUGR with 26 normal cases; at Gest. age 27 - 37 weeks. They utilized the trans cerebellar diameter and other biometric diameters (BPD, HC, AC and FL). There was a statistically highly significant difference between the two groups (p value<0.01). These results were going in line with our study.

Similar to our study findings, Yakout et al. [14] studied 50 IUGR versus 50 normal cases in the second and third trimesters. They studied four biometric measures; BPD, HC, AC and FL. The estimated fetal weight in IUGR cases were less than the values in normal cases and they reported a highly significant reduction in IUGR group.

In the present study, the EFW was significantly lower in cases of IUGR in comparison with control group according to Campbell's formula [15].

Beune IM et al. [16] showed that EFW is a good screening ultrasonographic approach as it allows to assess the deviation of the fetal size from a reference population defining empirically as small for gestational age (SGA), those fetuses with the EFW below the 10th percentile for the gestation.

In the current study, SFH was significantly lower in cases of IUGR in comparison with control group. The RCOG reported that the Serial measurement of symphysis fundal height (SFH) every 2 weeks is recommended at each antenatal appointment from 24 weeks of pregnancy as this improves prediction of a SGA neonate [17].

In the present study, there was a significant positive correlation between symphyseal fundal height and the estimated fetal weight by ultrasound in cases of IUGR. This means that we can make follow fetal growth clinically, as well as, by ultrasound.

In agreement of our study, Indraccolo U. et al 146. (2008) studied IUGR cases at gest. age of 32-35 weeks and found that there was a positive correlation between the SFH and fetal birth

weight. The diagnostic effectiveness of the SFH was not significantly higher than the ultrasound; and that clinical evaluation of fetal weight in the 3rd trimester could be improved if it is taken along with the ultrasound scanning data [18].

Morse K. et al. [19] conducted a systematic review of five studies, and highlighted the wide variation of predictive accuracy of SFH measurement for a SGA infant. Marhatta N et al, (2017) conducted a comparative study at Gest. age >20 weeks; as regard sonographic and clinical data. They evaluated the SFH, ultrasound biometry and Doppler to evaluate fetal growth. There was a decreased SFH in IUGR cases [20].

As reported in the ACOG (2013, 2021), fundal height measured in centimeters (24–38 weeks of gestation) approximates the gestational age and is used to screen for fetal growth less than or greater than the 10th percentile. If the accuracy of fundal height is compromised because of obesity, ultrasonography may be a better screening modality. However, there is lot of discrepancy and there is no good evidence that these methods improve outcomes [21,22].

In the present study, there were a significant raise in umbilical indices, decrease in cerebral indices, and decrease in CPR in IUGR compared to normal cases. These changes denote the adaptive fetal hemodynamic changes. Vasodilation in the middle cerebral artery (reduced PI) is a marker of circulatory redistribution. These changes denoted the brain sparing; with increased Doppler indices in the umbilical artery and lowered Doppler indices, allowing for more cerebral blood flow. As these Doppler indices became part of the routine workup, the findings were published in many literatures and well explained in some resources and guidelines; where the effect increased with the degree of placental compromise [22,23].

Anjum S, and Lakshmi T.S. (2019) investigated 110 high risk pregnant women with US for growth, AFI, Doppler studies of UMA and MCA, NST, BPP. Abnormal Doppler indices in Umbilical artery were the initial Doppler abnormality in majority of the cases. The finding of AEDF/REDF in Umbilical artery is an ominous sign, associated with adverse perinatal outcome and high perinatal loss. They concluded that Doppler can help to identify the fetal circulation changes well in advance of other surveillance tests, thus identify the truly hypoxic fetus [24].

In a recent study, Veerabathini M. al, (2020) conducted an observational study on 50 IUGR cases and 50 normal cases, at Gest. age > 28 w. They found that there was increased umbilical artery Doppler indices and decreased MCA Doppler indices, hence a decreased cerebroplacental ratio. There was a statistically highly significant difference between IUGR and normal cases [25].

There was a decreased DV indices (lowered resistance) in the IUGR compared to the normal group, however, it was statistically non-significant. This lowered resistance is also expected in cases of IUGR to allow for more oxygenated blood to be shifted to the heart. With advancement of the IUGR severity, more oxygenated blood shift is needed, hence, the resistance may be more lowered and it could be significant in sever degrees of IUGR.

Similar to our findings, Yakout et al. [14] observed cerebral vasodilatation, as a marker of hypoxia, which was visualized as a reduction in MCA-PI. There was increased indices of umbilical artery and decreased indices of MCA, hence decreased cerebroplacental ratio.

Tongprasert F. et al. [26] studied fetal liver length as an indicator of liver size at different gestational ages of 14 - 40 weeks and reported significant fetal liver volume changes with different gestational age. This normative data of fetal liver length had several applications in clinical practice such as in evaluation of fetal growth in cases of intrauterine growth restriction.

In agreement of our study, Chang CH et al. [27] studied cases of IUGR and compared their fetal liver size versus normal cases. They showed that measurement of the fetal liver by 3-D US can differentiate fetuses with from those without FGR. The sensitivity of fetal liver in predicting FGR was 97.6%, with specificity 93.6%, predictive value of positive test 63%, predictive value of negative test 99.7% and accuracy 94%.

In agreement of our study, Molina Giraldo et al, (2019) studied 119 pregnant women at gest. age of 24 -34 weeks to assess the fetal liver in fetuses with intrauterine growth restriction, using 3-D US; (22 cases of IUGR and 97 normal cases). They found significant reduction in liver volume in IUGR compared to normal cases [28].

In our study, there was no significant correlation between the estimated fetal weight and fetal liver length. Hence, we could not speculate that liver size as evaluated by the liver length, could be used as an indicator for fetal body weight. The reason was not understood. As a possibility, we thought of different pathogenesis; liver size is affected by its lowered blood supply, while fetal body weight (other organs) reflects changes in their blood supply, and diminished hepatic products. Hence, the effect may be less in the liver in our included cases.

Chiegwu HU et al (2014) investigated the relationship between fetal liver volume (FLV) and, estimated fetal weight (EFW) in 1847 normal fetuses between 20-41 gestational weeks 2-D US. There was a steady linear increase in values of FLV with increasing EFW and GA. Strong positive correlations were found between FLV and EFW, GA and other biometric parameters ($p < 0.05$). They concluded that fetal liver volume by 2-D US could be used to estimate fetal weight [29].

Garcia-Flores J et al. [30] evaluated the value of fetal liver biometry to predict birth weight in gestational diabetes using 3D- US between 32 and 34 weeks and all data were stored for post-acquisition processing with a specific software. All the hepatic diameters, area and sectional volume demonstrated significant association with birth weight. In multivariate model, liver area volume gave significant values for predicting birth weight.

Torky H, et al. (2017) used 3D- US to measure the fetal liver volume, head circumference, abdominal circumference and femur length, of 300 pregnant women attending at 20 weeks for anomaly scan and the measures were repeated between 34 and 40 weeks. They reported a statistically significant positive correlation between second trimester fetal liver volume and birth-weight. A significant correlation was found between all third trimester measurements and birth weight [31].

In the current study, there was a significant decrease PI, & RI in cases of IUGR versus the normal cases. Ebbing et al, (2009) studied IUGR cases at gest. ages >22 weeks in comparison with normal cases. They found significant decrease in hepatic artery PI, indicating vasodilation in this artery in response to hypoxia in cases of IUGR. This was similar to the results in the current study [32].

In agreement of our study, Samson et al, (2009), studied 33 IUGR cases at gest. age 23 - 33 weeks and reported that there was an abnormal decreased HA- PI in 66% of the IUGR and in 24% of the normal fetuses. These changes were similar to those reported for other vital fetal organs, such as the brain, and they suggested that there is a lower arterial hepatic vascular resistance and, consequently, an increased hepatic artery blood flow in IUGR fetuses [33].

Ebbing et al., (2008) found also signs of arterial redistribution of blood flow in the abdomen; vasodilation of the hepatic and splenic arteries (reduced PI) suggests a compensatory hepatic arterial contribution directly to hepatic sinusoid blood flow and an increased splenic contribution to portal venous flow to the sinusoids, when umbilical venous flow and distribution to the right liver lobe is low [32] This buffer mechanism is hypoxia activated local release of adenosine; which is a local vasodilator [34]. This is diagnosed by Doppler as reduced vascular resistance and increased blood flow in the fetal hepatic and splenic arteries. This effect was observed in our study.

In cases of IUGR, fetal hypoxia will affect the liver and splanchnic area, especially for the right lobe of the liver [4]. Fetal hypoxia induces increased sympathetic tone and constriction in the portal hepatic vascular bed. This causes increased shunting of umbilical blood through the ductus venosus to the heart and less umbilical flow distribution to the liver [35]. This effect showed a non-significant value in our studied IUGR cases. This might be due to the stage of the IUGR in our included cases (Barcelona stage I).

In the current study, the correlation between fetal hepatic artery and middle cerebral artery PI and RI was statistically non-significant.

Hepatic Doppler measurements provide an opportunity to grade adaptation to hypoxia and compromise of a hemodynamic and metabolic important organ. They carry the potential for a more differential clinical assessment, but also more detailed research addressing intrauterine mechanisms with assumed long-term effects on health and disease.

5. CONCLUSIONS

Reduced liver size and hepatic arterial Doppler indices (PI, RI) can be valid diagnostic methods

in IUGR. SFH, in fetuses suffering from IUGR when compared to normal cases, was correlated with EFW.

CONSENT

As per international standard or university standard, participant's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ahmad N, Greenaway S. Anaesthesia for inguinal hernia repair in the newborn or ex-premature infant. *BJA Educ.* 2018;18: 211-7.
2. Walker SM. Pain after surgery in children: clinical recommendations. *Curr Opin Anaesthesiol.* 2015;28:570-6.
3. Bosenberg A. Benefits of regional anesthesia in children. *Paediatr Anaesth.* 2012;22:10-8.
4. Rosenberg PH. Future of regional anaesthesia. *Acta Anaesthesiol Scand.* 2005;49:913-8.
5. Tran TM, Ivanusic JJ, Hebbard P, Barrington MJ. Determination of spread of injectate after ultrasound-guided transversus abdominis plane block: a cadaveric study. *Br J Anaesth.* 2009;102: 123-7.
6. Johns N, O'Neill S, Ventham NT, Barron F, Brady RR, Daniel T. Clinical effectiveness of transversus abdominis plane (TAP) block in abdominal surgery: a systematic review and meta-analysis. *Colorectal Dis.* 2012;14:e635-42.
7. Tulgar S, Selvi O, Senturk O, Serifsoy TE, Thomas DT. Ultrasound-guided erector spinae plane block: indications, complications, and effects on acute and chronic pain based on a single-center experience. *Cureus.* 2019;11.
8. Figueras F, Gratacós E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. *Fetal Diagn Ther.* 2014;36:86-98.
9. Lees CC, Stampalija T, Baschat A, da Silva Costa F, Ferrazzi E, Figueras F, et al. ISUOG Practice Guidelines: diagnosis and management of small-for-gestational-age fetus and fetal growth restriction. *Ultrasound Obstet Gynecol.* 2020;56:298-312.
10. Hirsch L, Melamed N. Fetal growth velocity and body proportion in the assessment of growth. *Am J Obstet Gynecol.* 2018;218:S700-S11.e1.
11. AIUM practice guideline for the performance of obstetric ultrasound examinations. *J Ultrasound Med.* 2010;29:157-66.
12. Skovron ML, Berkowitz GS, Lapinski RH, Kim JM, Chitkara U. Evaluation of early third-trimester ultrasound screening for intrauterine growth retardation. *J Ultrasound Med.* 1991;10:153-9.
13. El-Sayed YAE, Mohamed MES, Abdel Salam WA, Soliman RRI. Assessment of Transcerebellar Diameter Accuracy in Detection of Gestational Age in Third Trimester in Cases of Intrauterine Growth Restriction. *The Egyptian Journal of Hospital Medicine.* 2021;82:426-32.
14. Yakout AE-SA-S, Zakaria M, El-Monaem A, Mohammed Saeed A. Role Of Middle Cerebral Artery and Ductus Venosus Doppler in Evaluation of Intrauterine Growth Restriction. *Al-Azhar Medical Journal.* 2021;50:1047-58.
15. Campbell S, Wilkin D. Ultrasonic measurement of fetal abdomen circumference in the estimation of fetal weight. *Br J Obstet Gynaecol.* 1975;82:689-97.
16. Beune IM, Bloomfield FH, Ganzevoort W, Embleton ND, Rozance PJ, van Wassenaer-Leemhuis AG, et al. Consensus Based Definition of Growth Restriction in the Newborn. *J Pediatr.* 2018;196:71-6.e1.
17. Coomarasamy A, Fisk N, Gee H, Robson S. Investigation and management of the small for gestational age fetus. 2002.
18. Indraccolo U, Chiocci L, Rosenberg P, Nappi L, Greco P. Usefulness of symphysis-fundal height in predicting fetal weight in healthy term pregnant women. *Clin Exp Obstet Gynecol.* 2008;35:205-7.
19. Morse K, Williams A, Gardosi J. Fetal growth screening by fundal height

- measurement. *Best Pract Res Clin Obstet Gynaecol.* 2009;23:809-18.
20. Pourali L, Ayati S, Tavakolizadeh S, Soleimani H, Teimouri Sani F. Clomiphene citrate versus letrozole with gonadotropins in intrauterine insemination cycles: A randomized trial. *Int J Reprod Biomed.* 2017;15:49-54.
 21. American College of Obstetricians and Gynecologists CoPBO, Society for Maternal-Fetal Medicine Publications Committee. Fetal Growth Restriction: ACOG Practice Bulletin, Number 227. *Obstet Gynecol.* 2021;137:e16-e28.
 22. American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics SfM-FMPC. ACOG Practice bulletin no. 134: fetal growth restriction. *Obstet Gynecol.* 2013;121:1122-33.
 23. Novac MV, Iliescu DG, Tudorache S, Manolea M, Meetescu RE, Vrabie S, et al. Ultrasound Evaluation of Fetal Biometry and Doppler Parameters in the Third Trimester of Pregnancy Suspected of Intrauterine Growth Restriction. *Curr Health Sci J.* 2018;44:23-8.
 24. Ozeren M, Dinç H, Ekmen U, Senekayli C, Aydemir V. Umbilical and middle cerebral artery Doppler indices in patients with preeclampsia. *Eur J Obstet Gynecol Reprod Biol.* 1999;82:11-6.
 25. Manoj Kumar Veerabathini SSM, Nilanjan Mukherjee, Aavula Adarsh, B. Arun Kumar, Girendra Shankar. Role of Colour Doppler in Evaluation of Intrauterine Growth Retardation. *IJCMSR.* 2020;5.
 26. Tongprasert F, Srisupundit K, Luewan S, Tongsong T. Normal length of the fetal liver from 14 to 40 weeks of gestational age. *J Clin Ultrasound.* 2011;39:74-7.
 27. Chang CH, Yu CH, Ko HC, Chen CL, Chang FM. Predicting fetal growth restriction with liver volume by three-dimensional ultrasound: efficacy evaluation. *Ultrasound Med Biol.* 2006;32:13-7.
 28. Molina Giraldo S, Alfonso Ayala DA, Arreaza Graterol M, Perez Olivo JL, Solano Montero AF. Three-dimensional Doppler ultrasonography for the assessment of fetal liver vascularization in fetuses with intrauterine growth restriction. *International Journal of Gynecology & Obstetrics.* 2019;144:260-4.
 29. Chiegwu H, Okafor I, Ohagwu C, Ogbu S, Udoh B, Ugwuanyi D, et al. Relationship of Fetal Liver Volume with Estimated Fetal Weight and Gestational Age: A 2-Dimensional Ultrasonographic Study of Normal Nigerian Fetuses. *International Journal of Medicine and Medical Sciences.* 2014;47:1476.
 30. Garcia-Flores J, Cruceyra M, Cañameres M, Garicano A, Nieto O, Tamarit I. Predictive value of fetal hepatic biometry for birth weight and cord blood markers in gestational diabetes. *Journal of Perinatology.* 2016;36:723-8.
 31. Haitham Torky MH, Mourad Kamel, Mohammad Salah Eldin, Hossam Eldin Hussein, Diaa Abdelhalim. The Egyptian formula a new formula for prediction of fetal birth weight using liver volume measured by three-dimensional ultrasound (VOCAL system). *MOJ Womens Health.* 2017;4:25-8.
 32. Ebbing C, Rasmussen S, Godfrey KM, Hanson MA, Kiserud T. Redistribution pattern of fetal liver circulation in intrauterine growth restriction. *Acta Obstet Gynecol Scand.* 2009;88:1118-23.
 33. Samson J, De Leon-Luis J, Meyer N, Santolaya J, Uhlmann R, Mari G. 378: Hepatic artery Doppler in IUGR fetuses. *American Journal of Obstetrics & Gynecology.* 2009;201:S146.
 34. Ebbing C, Rasmussen S, Kiserud T. Fetal hemodynamic development in macrosomic growth. *Ultrasound Obstet Gynecol.* 2011;38:303-8.
 35. Tchirikov M, Schlabritz-Loutsevitch NE, Hubbard GB, Schröder HJ, Nathanielsz PW. Structural evidence for mechanisms to redistribute hepatic and ductus venosus blood flows in nonhuman primate fetuses. *Am J Obstet Gynecol.* 2005;192: 1146-52.

© 2021 Ali et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<https://www.sdiarticle4.com/review-history/71952>