Original Article

Fetal Liver Size and Hepatic Artery Doppler Study in Women with Late Intra Uterine Growth Restriction Versus Normal Pregnant Women

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ABSTRACT

Objectives: To assess the sizes of the fetal liver, the blood flow in the fetal hepatic artery, and other Doppler indices related to fetal blood vessels in instances of late intrauterine growth restriction (IUGR).

Methods: This study was conducted on a sample of 100 pregnant women who were at or beyond 32 weeks. It was an observational, analytical, and cross-sectional study. The subjects were categorized into two groups: Group 1 consisted of 50 pregnant women who experienced effects by IUGR. Group 2 (control group) consisted of 50 pregnant women who were not experiencing any complications.

Results: No statistically significant association observed between the weight of the fetus and the length of the liver. A strong and statistically significant association was found between symphysial fundal height (SFH) and estimated fetal weight (EFW) by ultrasonography in instances of IUGR. a significant reduction existed in the size of the liver in the IUGR group compared to the normal group, as shown by statistical analysis. A statistically significant decrease existed in hepatic artery Doppler indices.

Conclusion: Decreased size of the liver and hepatic arterial Doppler indices, such as PI and RI, can serve as reliable diagnostic tools for IUGR. SFH, in fetuses experiencing IUGR in comparison to normal instances, exhibited a significant correlation with EFW.

Key Words: Fetal, hepatic artery doppler, intra uterine growth restriction.

Received: 24 July 2024, **Accepted:** 8 January 2025

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ISSN: 2090-7265, 2025, Vol. 15

INTRODUCTION

Intrauterine growth restriction (IUGR) is a disorder characterized by the failure of the fetus to achieve its full growth potential. The condition affects a range of 3% to 10% of all fetuses[1], and has a high rate of mortality and morbidity, reaching approximately 80% in fetuses that go misdiagnosed and untreated[2]. Currently, the diagnosis is determined through the use of ultrasound to evaluate biometric data and estimate the weight of the fetus[3].The assessment of fetal hemodynamics is conducted using Doppler ultrasound and the determination of impedance indices in different fetal arteries[1]. Power Doppler is an effective instrument for assessing the blood vessels in both the placenta and the fetus[4]. A fetus affected by late IUGR is commonly observed to have a reduced 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, particularly their stores of liver glycogen, so a reduced liver size existed in addition to a decreased abdominal size[1].

Some authors say that the venous pressure in the fetal liver's circulation remains stable through reduced transport of umbilical blood to the right hepatic lobe and the subsequent expansion of the splenic and hepatic arteries [5].

Some authors have observed that a robust artery signal can occasionally be detected on the reverse channel during Doppler studies on ductus venosus (DV) flow in significantly growth-restricted fetuses[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.

This study aimed to assess the size of fetal liver, flow of blood in the hepatic artery of the fetus and additional foetal

DOI:10.21608/EBWHJ.2024.307217.1341

vascular Doppler markers in instances of late intrauterine growth restriction (IUGR).

METHODS

This observational cross-sectional, analytical work had been conducted on 100 pregnant women at or beyond 32 weeks attending to obstetrics and gynecology department at Tanta University hospital between January 2020 and April 2021. Subjects had been assigned into two groups: Group 1: A study group consisting of 50 pregnant women who got impacted by IUGR. Group 2: A control group consisting of 50 pregnant women in a normal state.

The sample size estimation[7,8] was conducted using the formula: no=Z2pq/B2, where no represents the original sample size. At a 95% confidence level, the value of Z is 1.96. p represents the proportion of the event in the population based on prior studies, with a value of 0.15 (indicating a prevalence of 4-7% for IUGR). q is equal to 0.07, and it is calculated as 1 minus p. The allowed bias for p in the sample is 0.05, denoted as B. The value of N was determined to be 100.

Cases were selected according to age range between 18 to 38 years, BMI (≥18-≤25) kg/m^2, 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 exposed to taking of history (personal, obstetric and family), examinations including vital signs, full obstetric examination, laboratory investigations and Ultra- sonographic 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 middle cerebral artery Doppler, umbilical artery Doppler, hepatic artery Doppler and ductus venosus Doppler.

Statistical Analysis

The data was analysed employing SPSS ver. 22.0. The data underwent testing for normality of distribution employing the Shapiro-Wilk test. The quantitative data were represented as the mean ±SD. A *p value* < 0.05 was considered statistically significant.

RESULTS

We compared between the IUGR and Normal groups according to pertinent data presented in, including (age, parity, BMI and calculated Gest. Age). A non- significant variation existed among 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. A statistically highly significant variation existed among both groups (Table 1).

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	IUGR	19	–	24	22.00	±	2.35	0.415	0.679
(Kg/m^2)	Normal	19	–	25	22.80	±	2.47		
Calculated	IUGR	32	–	35	33.30	±	1.074	1.757	0.082
G. Age	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)

We compared between IUGR and Normal groups according to SFH, and EFW in gm. We find that these parameters decrease in the IUGR group contrasted to the control group. A statistically highly significant variation existed among both groups. A highly positive statistically significant association existed among SFH and the EFW by ultrasonography in instances of IUGR. We compared the liver length Liver Length in mm between IUGR and Normal groups. A statistically highly significant variation existed among both groups. In the current study, the liver length measures were near to the 5th percentile of the reference value. No statistically significant association existed among weight of the fetus and length of the liver (Table 2).

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

* Intrauterine Growth Restriction (IUGR)

US of liver length in IUGR at GA 32W (Figure1)

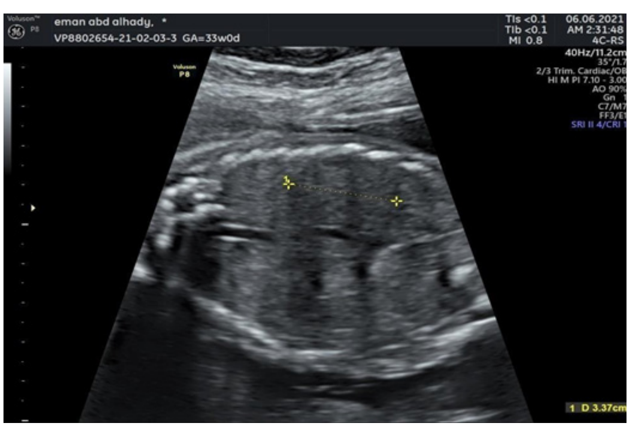

Fig. 1: US of liver length in IUGR at GA 32W

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 variation existed among IUGR and Normal groups ($p<0.01$). Comparing DV (PI) in both groups, showed a non-significant variation ($p>0.05$). 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 mentioned above in review (Table 3).

A statistically highly significant variation existed among the groups depending on Hepatic A (PI) and Hepatic A (RI); No statistically significant association existed among 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 IUGR	1.53 – 2.88	2.228±0.314	6.472	0.001*
ratio 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).

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 Normal	0. 5 – 0.58 0.55 – 0.75	0.471±0.069 0.674±0.045	17.363	0.001*
		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)

Umbilical artery Doppler in IUGR at GA 32 W (Figure2).

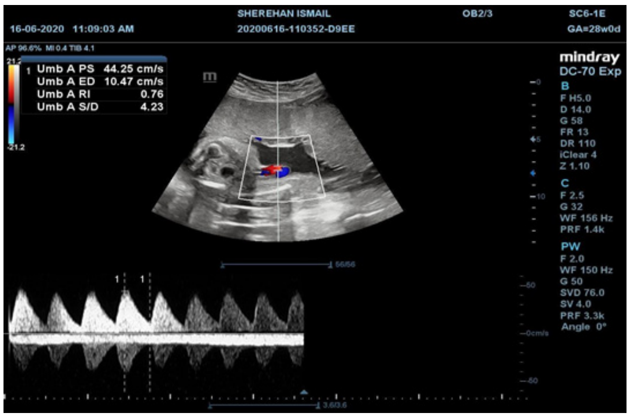

Fig. 2: Umbilical artery Doppler in IUGR at GA 32 W

Hepatic artery Doppler in IUGR at 32w (Figure 3).

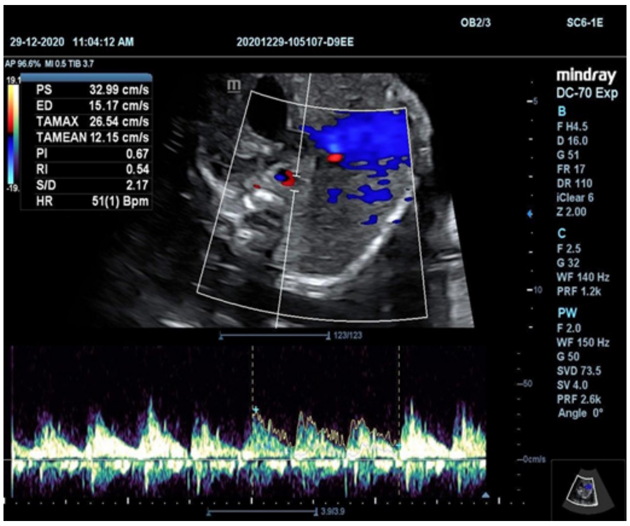

Fig. 3: Hepatic artery Doppler in IUGR at 32w

DISCUSSION

IUGR is a medical disorder characterized by a fetus that does not achieve its expected growth potential as defined by its genetic makeup[9]. Therefore, it is imperative to recognize these fetuses, initiate early monitoring during pregnancy, and promptly take medical actions to reduce the number of perinatal fatalities[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 liver size changes.

To enhance the diagnosis of FGR, a recommended technique is to utilize sequential ultrasound examinations. This is because the growth of fetuses is a dynamic process that necessitates several observations over time[11]. This was in line with the protocol of our study, where we repeated ultrasound after 2 weeks for confirmation. Comprehensive ultrasonography can be used to assess suspected IUGR by examining fetal biometry and identifying any potential fetal anomalies. Serial growth ultrasonography or abdominal circumference (AC) measures are the most accurate indicators of fetal growth in pregnancies with a high-risk factor[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). A statistically highly significant variation existed among both groups (p value<0.01). These findings were going in line with our work. Similar to our study findings, Yakout *et al*.[14] studied 50 IUGR versus 50 normal cases in the 2nd and 3rd trimesters. They studied four biometric measures: BPD, AC, HC and FL. The EFW 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 decreased in instances of IUGR in contrast to control group according to Campbell's formula[15].

Beune IM *et al*.[16] showed that EFW is a good screening ultrasonographic approach as it permits to evaluate the extent to which the size of the fetus deviates from a standard population. Specifically, it identifies fetuses that are considered SGA, defined as those with an EFW beneath the 10th percentile for their gestational age.

The present investigation found a substantial decrease in SFH measurements among instances with IUGR compared to the control group. According to the RCOG, it is suggested to determine the SFH every 2 weeks at antenatal appointments starting from 24 weeks of pregnancy. This practice has been found to enhance the accuracy of predicting SGA newborn[17].

The current study found a strong positive association among SFH and EFW by ultrasonography in instances of IUGR. This means that we can follow fetal growth clinically, as well as, by ultrasound.

In agreement with our study, Indraccolo U. *et al*.[18] studied IUGR cases at guest. age of 32-35 weeks and found was a positive association existed among the SFH and weight of fetal births. The diagnostic efficiencies of the SFH weren't significantly greater contrasted to the ultrasonography; and that clinical assessment of weight of the fetus in the 3rd trimester might be enhanced by combining it with ultrasonic data.

Morse K. *et al*.[19] conducted a systematic review of five studies, which revealed significant heterogeneity in the predictive accuracy of SFH measurements for identifying SGA infants. Marhatta N *et al*.[20] 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.

As reported in the ACOG[21,22], Fundal height, measured in centimeters between 24 and 38 weeks of pregnancy, is a reliable indicator of the gestational age. It is also used to identify cases of fetal growth that fall below or exceed the 10th percentile. If the precision of fundal height measurement is hindered due to obesity, ultrasound may serve as a more effective screening method. However, there is lot of discrepancies and there is no good evidence that these methods improve outcomes.

In the current work, a significant raise in umbilical indices, decrease in cerebral indices, and decrease in CPR existed in IUGR compared to normal cases. These changes denote the adaptive fetal hemodynamic changes. Vasodilation in the middle cerebral artery, indicated by lower PI, serves as an indicator of circulatory redistribution. These modifications indicated the brain's ability to prioritize its blood supply, as evidenced by higher Doppler indexes in the umbilical artery and decreased Doppler indices, resulting in greater cerebral blood flow. As the Doppler indexes were included into regular diagnostic procedures, their results were documented in several scientific publications and comprehensively explained in various resources and guidelines. It was observed that the impact of these indices got more pronounced as the severity of placental impairment rose[22,23].

The researchers determined that Doppler can effectively detect alterations in fetal circulation long before other monitoring techniques, hence enabling the identification of genuinely hypoxic fetuses[24].

There was a decreased DV indices (lowered resistance) in the IUGR contrasted 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 lowered, and it could be significant in sever degrees of IUGR.

Similar to our findings, Yakout *et al*.[14] observed cerebral vasodilation, as an indication of hypoxia, which was visualized as a decrease in MCA-PI. There were increased indices of umbilical artery and decreased indices of MCA, hence decreased cerebroplacental ratio.

Tongprasert F. *et al*.[25] 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 information on fetal liver length has various implications in clinical practice, including the assessment of growth of the fetuses in instances of IUGR.

In agreement of our study, Chang CH *et al*.[26] studied cases of IUGR and compared their fetal liver size versus normal cases. The study shown that utilizing 3-D ultrasound to evaluate the fetal liver may effectively distinguish between fetuses with FGR and those without. The fetal liver had a sensitivity of 97.6% in predicting FGR, along with a specificity of 93.6%. The predictive value of a positive test was 63%, while the predictive value of a negative test was 99.7%. The overall accuracy of the test was 94%.

In agreement of our study, Molina Giraldo *et al*.[27] studied 119 pregnant women at gest. age of 24 -34 weeks to assess the fetal liver in fetuses with IUGR, using 3-D US; (22 cases of IUGR and 97 normal cases). They found a significant reduction in liver volume in IUGR compared to normal case.

In our study, no significant association existed among the EFW and length of the fetal liver. 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*.[28] investigated the correlation between fetal liver volume (FLV) and EFW in 1847 normal fetuses between 20-41 gestational weeks 2-D US. The values of FLV showed a consistent and gradual rise as both EFW and GA increased. Significant associations were observed between FLV and GA, EFW and other biometric indicators ($p < 0.05$). The researchers determined that FLV, as measured by 2-D ultrasound, may be utilized to estimate the weight of the fetus.

Garcia-Flores J *et al*.[29] evaluated the value of fetal liver biometry for predicting 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. There was a strong correlation between birth weight and the measurements of liver diameters, area, and sectional volume. The multivariate model found that liver area volume had a substantial impact in predicting birth weight.

Torky H, *et al*.[30] used 3D- US to measure the FLV, head circumference, femur length, abdominal circumference, of 300 pregnant women attending at 20 weeks for anomaly scan and the measures were repeated between 34 and 40 weeks. A statistically significant positive relationship was observed between the volume of the fetal liver in the second trimester and birth weight. A strong association was observed between all measurements taken during the third trimester and the weight of the newborn at birth.

In the present work, a significant decrease PI, & RI existed in cases of IUGR versus the normal cases. Ebbing *et al*.[31] 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.

In agreement of our study, Samson *et al*.[32] studied 33 IUGR cases at gest. age 23 - 33 weeks and reported that an abnormal decreased HA- PI existed in 66% of the IUGR and in 24% of the normal fetuses. The observed changes in the hepatic artery blood flow in IUGR infants, as described in this study, are consistent with the changes observed in other important fetal organs, including the brain. These changes indicate a decrease in arterial hepatic vascular resistance and a rise in blood flow through the hepatic artery.

In their study, ebbing *et al*.[31] discovered evidence of changes in blood flow distribution in the abdomen. They observed that the splenic and hepatic arteries underwent vasodilation, resulting in a decrease in PI. This indicates that the liver received additional blood flow from the hepatic artery to compensate for decreased blood flow through the umbilical vein. Additionally, the spleen contributed more to the portal venous flow, which supplies blood to the liver sinusoids, when the distribution of umbilical venous flow to the right liver lobe was limited.

This buffer mechanism is hypoxia activated local release of adenosine; which is a local vasodilator[33]. This is diagnosed by Doppler as reduced vascular resistance and raised 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 liver' right lobe[4]. Fetal hypoxia triggers heightened sympathetic activity and constrictions in the portal hepatic vascular bed. This leads to a higher diversion of umbilical blood via the ductus venosus towards the heart, resulting in reduced distribution of umbilical flow to the liver[34]. 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 association between fetal hepatic artery and middle cerebral artery PI and RI was statistically non-significant.

Hepatic Doppler measures offer a chance to assess the degree of adaptation to low oxygen levels and the impact on a vital organ's blood flow and metabolism. They possess the ability for a more distinct clinical evaluation, as well as more comprehensive study investigating intrauterine pathways that are believed to have lasting impacts on health and disease.

CONCLUSIONS

Decreased size of the liver and hepatic arterial Doppler indices, such as PI and RI, can serve as reliable diagnostic techniques for IUGR. SGA, in fetuses experiencing IUGR in comparison to normal instances, exhibited a significant correlation with EFW.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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