Original Article

Correlation of Foetal Liver Length with Gestational Age and Foetal Weight in Pregnant Nigerian Women

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Abstract

Background: This study aims to determine the relationship(s) of fetal liver length (FLL) to the gestational age, biometric parameters (BPD, FL, AC, HC), and fetal weight in third trimester pregnancies.
Methodology: This was a hospital-based cross-sectional study of 400 fetuses in normal third trimester pregnancies recruited from the Obstetrics and Gynaecology department of OAUTHC, Ile-Ife, Nigeria. The participants were between 20-45 years of age and their gestational ages ranged from 27-40weeks. The FLL, liver thickness and transverse diameter were measured on B-mode ultrasound. Fetal liver volume (FLV) was calculated using the ellipsoid formula. The expected gestational age (EGA) was determined from the date of the last menstrual period (LMP), early first-trimester crown-rump length (CRL), or early second-trimester biparietal diameter (BPD) ultrasound. The estimated gestational age (EGA) and EFW were calculated using computer-assisted analysis of ultrasound fetal biometrics.
Results: The mean height, weight and body mass index (BMI) of the participants were 1.62±0.08m, 72.07±13.26kg and 27±4.70kg/m^2 respectively. FLL had a linear relationship and a positive correlation with EGA and EFW. There was also a positive correlation between FLL and fetal biometrics, maternal weight, and BMI. Percentile distribution of FLL and FLV for the GA 27–40weeks was developed.
Conclusion: FLL could be used to predict GA in normal pregnancies especially when LMP is uncertain.
Keywords: Ultrasound; Pregnancy; Foetal Liver Length; Estimated Foetal Weight; Gestational Age.

Key Messages: Highlights the important relationship between fetal liver length, fetal liver volume, fetal weight, gestational age and maternal BMI. Additionally, since it is a local-based study, it compared the findings to similar studies in other environments showing areas of agreement and variability.

Introduction

The fetal liver is the earliest and the most severely affected organ when there is impairment of fetal growth in an abnormal pregnancy state like Rhesus (Rh) isoimmunisation, hemoglobin Bart's disease, maternal diabetes, intrauterine growth restriction (IUGR), twin-to-twin transfusion syndrome (TTTS) and Down's syndrome. It constitutes 10% of the total fetal body weight at the 10th week and accounts for 5% of the total body weight at birth. It

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is involved in extra-medullary hemopoiesis and glycogen storage in the fetus.

In-utero studies of fetuses, with both ultrasound and magnetic resonance imaging (MRI), have utilized fetal biometrics (BPD, FL, AC and HC), liver volume (LV), and liver length, to diagnose or rule out abnormalities of fetal growth. Ultrasound has been used more commonly because it is more readily available, less costly, and does not require the use of ionizing radiation.

The ultrasonic fetal liver length (FLL) correlates positively with gestational age and estimated fetal weight. It also correlates positively with fetal biometrics, and has been used as an additional measurement parameter in making the diagnosis of abnormal fetal growth in abnormal pregnancies.

The liver length and estimated fetal weight increase with fetal nutrition (an indicator of maternal nutrition) and maternal weight.

The FLV measured with two-dimensional (2D) ultrasound is comparable to the three-dimensional (3D) method, which is the recommended modality for ultrasound morphometric organ measurement. Since 2D ultrasound FLV also correlate positively with FL, HC, AC, and fetal weight, it can be used for gestational age estimation like 3D. Similarly, two-dimensional ultrasound estimated fetal weight correlates well with actual birth weight.

We embarked upon this study to assess the clinical relationship between FLL, gestational age and EFW in third-trimester pregnant women in our environment.

Subjects and Methods

This was a prospective, hospital-based, cross-sectional study conducted at the Department of Radiology Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife over twelve months.

We enrolled 400 pregnant women with normal pregnancies in their third trimester aged 20-45 years. They were recruited consecutively from the Obstetrics and Gynaecology Department of the hospital. Exclusion criteria included: subjects above 45 years (due to increased incidence of fetal abnormalities), hypertensive disease of pregnancy, diabetes mellitus (DM) and gestational diabetes, congenital anomalies, hydrops fetalis, abnormal fetal lie (which limits accuracy of FLL), multiple gestations, those uncertain of their last menstrual period (LMP) and without first-trimester ultrasound and patients who declined consent. We obtained verbal and written informed consent from all patients.

Patient's biodata such as age, parity, LMP, weight and height were obtained. Their medical records were also consulted where necessary.

All ultrasonographic examinations were performed using the Toshiba real-time diagnostic ultrasound machine Model TUS-F3D® equipped with a curvilinear probe frequency range of 2.5-5 MHZ.

The subjects were scanned in supine or semi decubitus position; slightly tilted to the left to prevent hypotension from vena cava compression. Routine obstetrics ultrasound was done and fetal biometrics (BPD, HC, AC, FL) were obtained using Hadlock's method. At the plane of AC (greatest transverse diameter of the abdomen, with liver, stomach, umbilical vein and the junction of the right and left portal veins visualised), measurement of transverse and anteroposterior diameters of the fetal liver was taken using Vinzileo's method (Figure 1). The probe was then longitudinally rotated to obtain a sagittal or coronal section, and then turned parallel to the aorta to obtain the cranio-caudal liver length (FLL) - measured from the dome of right hemi-diaphragm close to the heart to the tip of the right lobe (Figure 2) . Fetal liver volume was calculated using the ellipsoid formula: Length * Thickness * Transverse diameter * 0.52.

The estimated gestational age and fetal weight were calculated automatically by the ultrasound machine from the BPD, HC AC and FL using Hadlock's method.

The data were analysed using the Statistical Package for Social Sciences (SPSS) version 20.0 for windows (IBM Corp., Armonk, N.Y., USA). Data was represented using tables and charts as appropriate. Quantitative data were expressed as mean ± standard deviation (SD) or minimum and

maximum values, while categorical variables were summarized as frequencies.

Correlation analysis was done using Pearson's correlation for parametric data. Multiple regression analysis was done using FLL as the dependent variable and other fetal biometrics and maternal body mass index as predictor variables. Analysis of variance (ANOVA) was used to compare the relationship between the dependent and predictor variables. The significant value was $p \leq 0.05$. Post-hoc analysis was done to determine how statistically significant the positive correlations between FLL and all the categories of BMI were.

Results

Four hundred apparently healthy third-trimester pregnant subjects aged 20-45years were studied. The mean age was 30.93±4.82years with the highest percentile at the age range of 30-34years (34.2%). The mean height was 1.62±0.08m, while the weight was 72.7±13.26kg. BMI was 27.29±4.70.

Table 1 shows the normal distribution of mean and standard deviation values of FLL and FLV according to EGA, at 95% Confidence Interval (CI). The percentile chart of FLL and FLV values according to EGA is shown in Table 2.

There was a strong positive linear correlation between FLL and EGA ($r=0.756$, $p<0.05$) as well as other measured fetal biometrics (Table 3). Maternal BMI and weight also showed a significant positive correlation with FLL. Conversely, maternal height did not correlate with FLL.

A strong positive correlation was noted between FLV and other fetal biometrics. There was also a significant positive correlation between FLV and maternal parameters (BMI, weight and height).

The mean FLL was statistically significantly different across maternal BMI (Table 4). Post-hoc analysis revealed that the severely obese group did not show a significant positive relationship with FLL (Table 5).

To evaluate the relationship between FLL as the outcome or dependent variable and its association with other maternal and fetal parameters, regression analysis was performed and results are shown in Table 6. In Models I, maternal weight and BMI which correlated significantly with FLL were entered as independent variables. As highlighted in the table, maternal weight ($p=0.095$) and BMI ($p=0.367$) were not significant independent contributors to FLL, being responsible for just 5.8% of the variation observed in FLL (R2=0.058).

In Model II, the other fetal parameters which correlated significantly with FLL were entered together and they increased the multiple coefficient of determination by 0.564 (56.4%) i.e, from 0.058 in Model I to 0.622 in Model II. In this model, AC, EFW and maternal BMI remained significant independent contributors to FLL.

Table 1: Normal distribution of mean FLL and FLV at different EGA

Estimated gestational age	N	Fetal liver length			Fetal liver volume		
		Mean ± SD	95% C.I. for Mean		Mean ± SD	95% C.I. for Mean	
			Lower	Upper		Lower	Upper
27weeks	8	3.39 ± 0.23	3.21	3.59	24.30 ± 6.77	18.65	29.96
28weeks	15	3.66 ± 0.33	3.48	3.85	31.78 ± 7.12	27.83	35.72
29weeks	21	3.91 ± 0.47	3.69	4.12	38.14 ± 6.21	35.31	40.96
30weeks	16	4.20 ± 0.40	4.06	4.49	44.43 ± 6.73	40.84	48.01
31weeks	24	4.27 ± 0.43	4.02	4.38	43.64 ± 10.40	39.25	48.03
32weeks	29	4.48 ± 0.53	3.88	4.28	43.35 ± 11.76	38.87	47.82
33weeks	27	4.70 ± 0.43	4.53	4.87	57.97 ± 14.38	52.28	63.66
34weeks	28	4.81 ± 0.31	4.68	4.93	60.68 ±14.24	55.16	66.21
35weeks	64	4.71 ± 0.57	4.57	4.85	60.50 ± 15.99	56.51	64.49
36weeks	52	5.01 ± 0.42	4.89	5.13	78.65 ± 17.28	73.84	83.46
37weeks	46	5.10 ± 0.49	4.95	5.24	80.55 ± 19.31	74.82	86.28
38weeks	37	5.48 ± 0.51	5.31	5.65	100.42 ± 22.82	92.81	108.02
39weeks	26	5.60 ± 0.51	5.39	5.81	94.79 ± 22.09	85.87	103.72
40weeks	7	6.02 ± 0.21	5.82	6.21	122.58 ± 16.69	107.15	138.01
Total	400	4.75 ± 0.74	4.68	4.82	66.14 ± 27.09	63.48	68.81

Table 2: Percentile chart of FLL and FLV values by EGA

EGA	Fetal liver length			Fetal liver volume		
	5th	50th	95th	5th	50th	95th
27weeks	3.01	3.40	4.39	13.50	22.97	40.32
28weeks	3.27	3.63	4.77	21.57	33.27	49.09
29weeks	3.13	4.10	5.10	24.94	36.61	52.32
30weeks	3.70	4.20	4.85	33.01	44.83	61.09
31weeks	3.57	4.14	4.99	26.28	45.07	61.83
32weeks	2.92	4.12	4.80	21.67	43.19	61.49
33weeks	3.69	4.73	5.50	37.12	56.06	92.09
34weeks	4.21	4.79	5.53	37.93	59.72	93.12
35weeks	3.56	4.77	5.63	35.33	59.15	91.66
36weeks	4.30	5.01	5.74	52.87	79.92	117.37
37weeks	4.76	5.19	5.79	47.98	78.62	118.64
38weeks	4.25	5.46	6.30	49.24	101.88	148.85
39weeks	4.60	5.56	6.61	68.03	87.09	137.11
40weeks	5.79	6.08	6.26	90.22	124.38	132.86

Table 3: Pearson correlation between estimated and measured parameters

	Estimated Fetal Weight		Estimated Gestational Age		Fetal Liver Length		Fetal Liver Volume	
	r	*p*	r	*p*	r	*p*	r	*p*
Maternal Height	0.120*	0.017	0.105*	0.035	0.048	0.335	0.122*	0.015
Maternal Weight	0.165**	0.001	0.125*	0.012	0.236**	<0.05	0.274**	<0.05
Body Mass Index	0.104*	0.038	0.070	0.160	0.226**	<0.05	0.222**	<0.05
Biparietal Diameter	0.941**	<0.05	0.954**	<0.05	0.735**	<0.05	0.746**	<0.05
Head Circumference	0.877**	<0.05	0.903**	<0.05	0.674**	<0.05	0.678**	<0.05
Abdominal Circumference	0.983**	<0.05	0.970**	<0.05	0.744**	<0.05	0.770**	<0.05
Femur Length	0.439**	<0.05	0.462**	<0.05	0.359**	<0.05	0.355**	<0.05
Estimated Fetal Weight	1		0.980**	<0.05	0.769**	<0.05	0.800**	<0.05
Estimated Gestational Age	0.980**	<0.05	1		0.756**	<0.05	0.773**	<0.05
Fetal Liver Volume	0.800**	<0.05	0.773**	<0.05	0.892**	<0.05	1	

**Correlation is significant at the 0.05 level
r = Correlation coefficient

Table 4: Mean FLL according to BMI group

	N	Mean	Std. Deviation	F	*p*
< 24.9	122	4.4801	0.68376	8.875	<0.05
25 - 29.9	198	4.8509	0.72305		
30 - 34.9	50	4.9779	0.78870		
> 35	30	4.7933	0.63075		
Total	400	4.7494	0.73429		

F = ANOVA (Analysis of variance)

Table 5: Post-hoc (Tamhane) analysis of BMI statistical significance

(I) BMI GROUP	(J) BMI GROUP	Mean Difference	Std. Error	*p*
< 24.9	25 - 29.9	-.37074*	.08045	<0.05
	30 - 34.9	-.49777*	.12757	.001
	35 - 39.9	-.31320	.13074	.117
25 - 29.9	<24.9	.37074*	.08045	<0.05
	30 - 34.9	-.12703	.12281	.887
	35 - 39.9	.05754	.12610	.998
30 - 34.9	<24.9	.49777*	.12757	.001
	25 - 29.9	.12703	.12281	.887
	35 - 39.9	.18457	.16032	.827
35 - 39.9	<24.9	.31320	.13074	.117
	25 - 29.9	-.05754	.12610	.998
	30 - 34.9	-.18457	.16032	.827

*Significant at p < 0.05

Table 6: Regression Analyses for the association between FLL and other parameters

Independent Variables	B	Std. Error	t	*p* value	95% CI for B	R2
Model I						**0.058**
(Constant)	3.734	.213	17.538	.000	3.316 – 4.153	
Maternal Weight	.009	.005	1.675	.095	-0.002 – 0.019	
Body Mass Index	.014	.015	.902	.367	-0.016 – 0.043	
Model II						**0.622**
(Constant)	2.240	1.072	2.089	.037	0.132 – 4.347	
Biparietal Diameter	.113	.111	1.020	.308	-0.105 – 0.332	
Head Circumference	-.004	.022	-.173	.863	-0.047 – 0.039	
Abdominal Circumference	-.078	.037	-2.097	.037	-0.151 – 0.005	
Femur Length	.008	.017	.458	.647	-0.026 – 0.042	
Estimated Fetal Weight	.835	.212	3.945	<0.05	0.419 – 1.251	
Estimated Gestational Age	.034	.044	.762	.446	-0.054 – 0.121	
Maternal Weight	-.003	.003	-.869	.386	-0.010 – 0.004	
Maternal Body Mass Index	.032	.010	3.337	.001	0.013 – 0.052	

FLL: Fetal Liver Length
R2 = Coefficient of determination

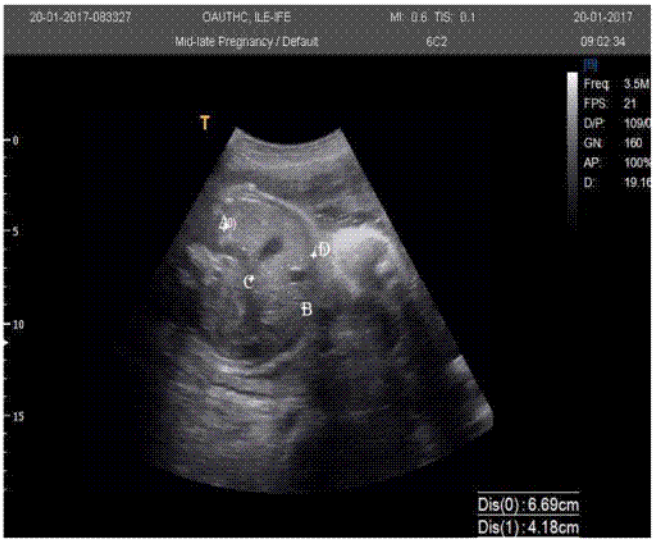

Figure 1: Transverse B-mode ultrasound scan of foetal abdomen showing measurements of antero-posterior AP (thickness) Diameter represented by AB and the transverse diameter represented by CD at plane of abdominal circumference measurement.

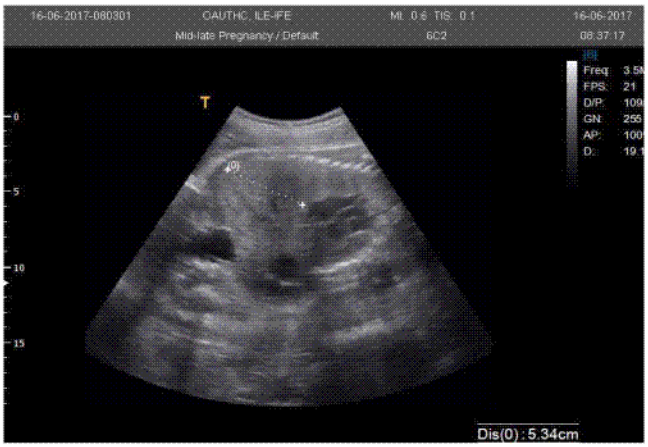

Figure 2: Longitudinal B-mode ultrasound scan of foetal abdomen showing measurement of FLL (cephalo-caudal length) indicated by the calipers, from the dome of right hemi-diaphragm close to right cardiac border to the caudal end of right lobe of the liver in the coronal plane.

Discussion

Reliable information on gestational age is important for assessment and monitoring of fetal size and growth, as early detection of abnormal fetal growth may help to reduce associated morbidity and mortality. Maternal obesity is associated with both short-term and long-term adverse maternal and fetal outcomes such as postpartum weight retention, metabolic syndrome and obesity in the offspring.

The growth of the liver is a measure of fetal wellbeing and maternal nutritional status during pregnancy. Sonographic measurement of FLL has been described previously in the literature and it has been suggested that FLL measured using Vinzileos *et al.*'s technique may be a useful adjuvant in the determination of gestational age, and also in detecting IUGR or macrosomia in the fetus.

This study showed that FLL and FLV increase with EGA, EFW and other fetal biometric measurements, as has been reported in other studies . It was also observed that both FLL and FLV had a positive linear relationship with EGA, EFW and other biometrics. This was in agreement with the studies done by Agwu*et al.* and Chiegwu *et al.* in Nigeria as well as in various parts of the world .

The mean FLL with corresponding EGA in this study was similar to that of Murao *et al.* . They also found a significant difference between the control and IUGR fetuses. They made a recommendation of cut-off values of FLL for IUGR, based on the sensitivity and specificity of their test tool, <43mm at 33weeks and <53mm at 40 weeks, respectively. Their recommendation was that a < 5% percentile FLL for EGA should raise the suspicion of IUGR while a > 95% should be suspicious for fetal macrosomia.

The mean FLL and FLV in this study were 4.75±0.73cm and 66.14±0.65cm^3, respectively. The FLL showed a strong positive linear correlation with EGA and EFW (r=0.756, r=0.769 with p< 0.0001 respectively). This is comparable to the findings of Vintzileos *et al.* (r=0.86) , Murao *et al.* (r=0.93) and Tongprasert *et al.* (r=0.94) . Similarly, FLV showed a strong positive linear correlation with EGA and EFW (r= 0.773, r=0.800 with p< 0.0001, respectively). This is similar to the findings of Agwu *et al.* (r=0.98) and Chiegwu et al. (r^2=2.242).

The values of our FLL percentile chart were slightly higher than those of Phatihattakorn *et al.* and Tongprasert *et al.* in Thailand. This difference could be due to racial and environmental factors. Our FLV chart is also slightly higher than that of Agwu *et al.* , and this could be attributed to the fact that about 60% of subjects in this study were in the overweight BMI category.

In this study, FLL showed a strong positive linear correlation with fetal biometrics (BPD, HC, AC and FL). This is similar to the findings of Murao *et al.* in Japan for BPD and FL, and Vintzileos *et al.* as well as Anderson *et al.* (R^2=0.77). Similarly, FLV showed a strong positive linear correlation with BPD, HC, AC, and FL. This is also similar to the findings of Agwu *et al.* .

The BMI showed a significant positive linear correlation with FLL and FLV in this study. This is similar to the findings of Mackic *et al.* (r=0.33, p<0.001) , and Perovic *et al.* (r=0.59, p<0.001) . However, post-hoc analysis showed that FLL did not show any significant correlation with the severely obese BMI group (Table 5). Pearson correlation also showed that maternal weight has a significant positive correlation with FLV but did not show significant correlation with FLL.

Conclusion

FLL has a positive linear relationship with EGA, EFW and fetal growth parameters, and can be used along with other fetal growth parameters with increased accuracy for predicting gestational age (GA) in normal pregnancy especially when patient is not sure or does not know her LMP. An abnormal FLL for the corresponding GA should raise the suspicion of a fetal or maternal disease condition.

The nomogram developed can be used to calculate the GA with increasing accuracy. The percentile chart can also be used to detect IUGR and fetal macrosomia when combined with other fetal parameters.

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