To Establish A Correlation Between Liver Morphometric Parameters With Gestational Age

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Abstract

Background: During most of the prenatal period, the liver occupies a large portion of the abdomen, playing a key role in the development of functional organs. The left and right lobes of the liver show a linear increase in size from 18 – 41 weeks of gestational age. We can utilize this fact to assess the gestational age. The normal range of the fetal liver's length is useful for identifying and monitoring hepatomegaly of fetuses in diabetes mothers.
Objective: The objective of the study was to correlate the vertical, transverse, and sagittal diameter of the liver with the gestational age (GA) of the fetus.
Methods: This study was conducted on 131 formalin-fixed fetuses with the gestational age ranging from 12 to 36 weeks in the Department of Anatomy of D Y Patil medical college in the collaboration with OBGY Department of D Y Patil Hospital, Nerul, Navi Mumbai (from July 2020 to December 2022). The liver was dissected and measurements of the vertical, transverse, and sagittal diameter of the fetal liver were taken with the help of vernier caliper.
Results: From this study, we calculated the mean value and standard deviation of the vertical, transverse, and sagittal diameters of the fetal liver. The value of which is 28.19±8.55 mm, 42.01±10.47 mm, and 19.32±5.56 mm respectively for the total sample size. Calculation of the vertical, transverse, and sagittal diameter of the liver was found to be highly significant.
Conclusion: This study concluded that there is a significant correlation between the vertical, transverse, and sagittal diameter of the fetal liver with the gestational age. It is crucial to make the right preoperative diagnosis if needed after birth.

Key Words: Fetus, Diameters of liver, Gestational age.

Introduction:

During most of the prenatal period, the liver occupies a large portion of the abdomen, playing a key role in the development of functional organs. At 6 weeks, it transforms into a hematopoietic organ and produces hemopoietic cells. At around 8 weeks, It starts to synthesize biochemical molecules including albumin, bile, glycogen, and fetal-specific proteins that are crucial for development. Understanding fetal liver growth and evaluating fetal physiology and well-being both depend greatly on how well the fetal liver is growing. Laparoscopy reveals a surprisingly high prevalence of congenital liver abnormalities (19.3% of patients).[1-4] Since the liver is the first organ to be impacted by intrauterine growth retardation, it should be helpful in identifying the issue early. There is, however, little information available regarding ways to evaluate the size of the liver in the fetus in utero.[5]
Murao et al [6] according to them, the left and right lobes of the liver grew linearly between 18 and 41 weeks. Furthermore, Murao et al [7] observed a strong association between the liver size and other indicators used to monitor fetal growth between the 19th week and term, and they came to the conclusion that we can utilize liver size to evaluate fetal growth as well. Roberts AB et al [8], Presented evidence that the height of the fetal liver was 12% greater in

diabetic pregnancies, at 18 weeks and over, compared to non-diabetic pregnancies, and they made the conclusion that understanding the normal range of the fetal liver length is helpful for diagnosing and monitoring gestational diabetes and hepatomegaly. Usually, the estimated liver volume and length are employed as measures to assess liver growth.[9] Unusual prenatal growth noticeably affects the fetal liver. Direct ultrasonic measurement of the right lobe of the liver in utero has been found to be more helpful and significant in clinical practice than indirect measurement of abdominal circumference. Because of this, the size of the fetal liver as measured by three-dimensional ultrasonography is crucial for assessing the state of fetal growth, nutrition, and maturity, and in particular for the early detection and monitoring of both fetal micro- and macrosomia. It is observed that the foetal liver's size is typically decreased in intrauterine growth retardation, whereas an increase in size is a reliable sign of fetal macrosomia, Rh isoimmunization, erythroblastosis, Hb Bart's disease, congestive heart failures, and intrauterine infections. Despite the widespread use of MRI and 3D ultrasound all over the world, a conventional autopsy is still the gold standard for evaluating fetal organs quantitatively. As a result, from a clinical point of view, physically acquired development curves and visceral measurements are equally important to consider as ultrasonic measurements. Earlier, We were unable to locate thorough information about liver growth dynamics in relation to its length, transverse, and sagittal diameters in the medical literature.[10,11,12]

Materials and Methods:

This study was conducted on 131 human fetuses (40 females and 91 males) formalin-fixed fetuses with the gestational age ranging from 12 to 36 weeks in the Department of Anatomy D Y Patil medical college in the collaboration with OBGY Department of D Y Patil Hospital, Nerul , Navi Mumbai. The study was carried out for a period of two and a half years (from July 2020 to December 2022). The fetuses were collected soon after delivery of spontaneous miscarriages & therapeutic legal abortions with the families' consent. The history of the fetus was collected from the labour ward of the OBGY Department of D Y Patil Hospital. After that, fetus was preserved in 10% formalin for 10 days in the research lab of the department of anatomy. After approval from the institutional Ethics Committee for Biomedical and health research D. Y. Patil school of medicine, Navi Mumbai, fetuses were separated into 6 groups, Group A aged <12 weeks, Group B (13-16 weeks), Group C (17 - 20 weeks), Group D (21- 24 weeks), Group E (25-28 weeks) and Group F (>28 weeks). Vernier caliper was used to measure the morphometric parameters in this study. The abdomen was dissected through a transverse incision that went from the umbilicus to the mid-axillary line on either side and two vertical incisions that ran from the costal arch to the iliac crest on either side of the mid-axillary line. The liver and surrounding organs were visible (Fig. 1). The liver was pulled out after cutting the hepatic ligaments, abdominal diaphragm, inferior vena cava, and structures at the porta hepatis. Cases having a deformity or anomaly were excluded from the study. Length, Transverse and sagittal diameters of the liver were dissected and measurements of all diameters were taken with the help of Vernier Caliper. Transverse diameter in mm, corresponding to the greatest horizontal distance of the liver, from its right to the left border, measured in the anterior projection (Fig. 2). Length in mm, corresponding to the greatest vertical distance of the liver, from its superior to inferior border on the right lobe, measured in the anterior projection (Fig. 3). Sagittal diameter in mm, corresponding to the greatest sagittal distance of the liver, from its anterior to posterior border on the right lobe, measured in the superior projection (Fig. 4). Using the SPSS statistical tool, the means of the parameters with respect to gestational age, sex, and groups were calculated. All parameters were statistically significant (p-value <0.05).

Fig. 1: Liver in situ of male fetus

Fig. 3: Showing Measurement of Vertical diameter of Fetal liver

Fig. 2: Showing Measurement of Transverse diameter of Fetal liver

Fig. 4: Showing Measurement of Sagittal diameter of Fetal liver

Results:

Table 1: Classification of fetal samples based on their group, gestational age and gender

Group	Gestational Age	Male (n=91)	Female (n=40)	Total (n=131)
A	Up to 12 weeks	06	00	06
B	13-16 weeks	04	03	07
C	17-20 weeks	28	18	46
D	21-24 weeks	40	14	54
E	25-28 weeks	11	04	15
F	>28 weeks	02	01	02

Table 2: Descriptive statistics of the measured parameters (Mean and SD) of each group

Parameters	Gestation age											
	Up to 12 wks.		13 to 16 wks.		17 to 20 wks.		21 to 24 wks.		25 to 28 wks.		>28 wks.	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD

Vertical diameter of Rt. liver lobe (mm)	16.24	4.28	19.99	5.58	23.74	5.30	31.07	5.72	36.10	7.59	48.35	17.02
Width of the liver (mm)	29.84	13.94	32.68	13.02	37.67	6.43	44.46	6.86	48.91	7.50	76.19	10.87
Thickness of liver (mm)	12.60	6.25	13.85	6.17	17.27	4.41	21.38	4.45	22.07	5.14	26.32	8.55

Table 3: Descriptive statics and Pearson's correlation coefficients (r) and p-value show statistically significant correlation for all the measured parameters

Parameter	Mean and SD (Total sample)	r value	r^2 value	p - value
Vertical diameter of Rt. liver lobe (mm)	28.19±8.55	0.716	0.512	p<0.0001
Width of liver (mm)	42.01±10.47	0.692	0.478	p<0.0001
Thickness of liver (mm)	19.32±5.56	0.533	0.284	p<0.0001

Table 4: Pearson's correlation between fetal liver parameters

Parameter	Vertical diameter of Rt. liver lobe (mm)	Width of liver (mm)	Thickness of liver (mm)
Vertical diameter of Rt. liver lobe (mm)	1	0.785	0.762
Width of liver (mm)	0.79	1	0.779
Thickness of liver (mm)	0.76	0.779	1

Table 5: Post-hoc test in fetal liver parameters within the groups

Parameter	a-b	a-c	a-d	a-e	a-f	b-c	b-d	b-e	b-f	c-d	c-e	c-f	d-e	d-f	e-f
Vertical diameter of Rt. liver lobe (mm)	-3.75	-7.5	-14.83	-19.86	-32.11	-3.75	-11.1	-16.1	-28.36	-7.33	-12.36	-24.6	-5.03	-17.28	-12.25
Width of liver (mm)	-2.85	-7.84	-14.63	-19.07	-46.35	-4.99	-11.8	-16.2	-43.51	-6.79	-11.24	-38.5	-4.45	-31.73	-27.28
Thickness of liver (mm)	-1.25	-4.67	-8.79	-9.47	-13.72	-3.42	-7.54	-8.22	-12.47	-4.11	-4.8	-9.05	-0.69	-4.93	-4.25

Table 6: Mean (in mm) and standard deviation of the fetal liver parameters according to gender in different gestational age groups. (M- Male, F- Female, SD- Standard Deviation)

	Gestation age									
	≤ 12 wks.	13 to 16 wks.		17 to 20 wks.		21 to 24 wks.		25 to 28 wks.		>28 wks.
	M	M	F	M	F	M	F	M	F	M
Parameters	Mean & SD	Mean & SD	Mean & SD	Mean & SD	Mean & SD	Mean & SD	Mean & SD	Mean & SD	Mean & SD	Mean & SD

Vertical diameter of Rt. liver lobe (mm)	16.243±4.28	21.96± 5.93	17.36 ±4.75 2	23.34 ±5.75	24.35 ±4.59	30.72± 5.95	32.05 ±5.08 5	35.92 3±8.7 6	36.59± 3.47	53.19±20.94
Width of liver (mm)	29.83±13.94	36.675 ±11.12	27.36 ±15.7 7	37.22 5±7.4 2	38.37 ±4.60 5	44.37± 6.98	44.7± 6.73	49.18 ±7.99	48.15± 6.96	82.36±2.77
Thickness of liver (mm)	12.59±6.25	15.885 ±5.34	11.12 6±7.2 12	17.12 2±4.7 36	17.49 ±3.96	21.2±4. 27	21.89 ±5.03	21.5± 5.44	23.62± 4.494	27.33±11.83

Table 7: The best-fit regression formulas for the fetal liver

Parameter	Regression Formula
Vertical Diameter (mm)	Y=-2.431+(1.503×GA in weeks)
Transverse diameter (mm)	Y= 5.712+(1.781×GA in weeks)
Sagittal Diameter (mm)	Y=4.48+(0.728×GA in weeks)

Classification of fetal samples based on their groups, gestational age, and gender are shown in Table 1. The GA of the fetuses in this study ranged from 12 to 36 weeks. The CRL ranged from 128.3 mm to 278.4mm. This study was conducted on 131(91 males and 40 females) fetuses. All received fetuses were divided into 6 groups, Group A aged <12 weeks, Group B (13-16 weeks), Group C (17 - 20 weeks), Group D (21- 24 weeks), Group E (25-28 weeks) and Group F (>28 weeks). The mean and standard deviation of CRL is 192.30±38.46 mm for total fetuses. Whereas, CRL is 163.83±39.48 mm, 156.17±16.34 mm, 168.59±56.53, 206.14±30.45 mm, 229.64±32.88 mm, and 261.38±27.75 mm at groups A, B, C, D, E, and F respectively.

Descriptive statistics of the measured parameters (Mean and SD) of each group are shown in Table 2. Descriptive statics and Pearson's correlation coefficients (r) and p values show statistically significant correlation for all the measured parameters are shown in Table 3. Pearson's correlation between fetal liver parameters is shown in Table 4. Post-hoc tests in fetal liver parameters within the groups are shown in Table 5. The mean (in mm) and standard deviation of the fetal liver parameters according to gender in different gestational age groups are shown in Table 6. The best-fit regression formulas for the fetal liver are shown in Table 7.

Discussion:

Tracking healthy fetal development and spotting genetic problems prior to conception requires an understanding of typical liver growth. The current study sought to better understand the relationship between gestational age and the linear dimensions of the liver as measured on its visceral surface by examining growth dynamics and age-specific reference intervals.

In the present study, we observed that the vertical diameter of the liver is (16.243±4.28mm, 21.96±5.93 mm, 23.34±5.75mm, 30.72±5.95mm, 35.923±8.76mm, and 53.19±20.94mm) in male at group - A, B, C, D, E, and F respectively. The vertical diameter of the liver in females is (17.36±4.752 mm, 24.35±4.59 mm, 32.05±5.085 mm, 36.59±3.47 mm, and 38.67 mm) in the group- B, C, D, E, and F respectively. The transverse diameter of the liver in males is (29.83±13.94 mm, 36.675±11.12 mm, 37.225±7.42 mm, 44.37±6.98 mm, 49.18±7.99 mm, and 82.36±2.77 mm) at group-A, B, C, D, E, and F respectively. Whereas Transverse diameter in females observed that 27.36±15.77 mm, 38.37±4.60 mm, 44.7±6.73 mm, 48.15±6.96 mm, and 63.84 mm in group- B, C, D, E, and F respectively. We found highly significant correlations between vertical diameter, transverse diameter, and sagittal diameter with gestational age ($p<0.0001$).

A study by Soner A et al[9] and Mirghani H et al[11] showed that the study on the development of the liver during the fetal period, divided the fetus into 4 groups (1st trimester, 2nd trimester, 3rd trimester, and full-term) respectively. The vertical diameter (height) of the fetal liver was 13 ± 2 mm, 25 ± 8 mm, 41 ± 7 mm, and 47±8 mm at 1st, 2nd, 3rd trimester, and full-term respectively. Whereas the vertical diameter was 32 ±12 mm in the total sample. The transverse diameter (width) of the liver was 19 ± 3 mm, 39 ± 12 mm, 67 ± 11mm, and 82 ± 9 mm at 1st, 2nd, 3rd trimester, and full-term respectively. 51 ± 20 mm was the transverse diameter of the total sample. The sagittal diameter of fetus was 11 ± 1 mm, 18 ± 5 mm, 26 ± 5 mm, and 31 ± 8 mm in all groups. Whereas at total sample sagittal diameter was 22 ± 8mm, the observation of this study is differ from our study.

In a study conducted by Michal S and Monika P et al [12] on Three-dimensional growth dynamics of the liver in the human fetus, according to them vertical diameter (Liver length) were 19.51 ±1.02, 20.64±3.24, 26.79 ± 4.05, 25.95 ±3.35, 27.91±6.40, 32.89 ±5.34, 31.13 ±4.14, 35.53±6.08, 31.47±2.51, 36.81±6.5 and 33.51± 3.80 mm from 18, 19, 20,…. 30 weeks respectively. The transverse diameter was 29.44± 3.73, 30.43± 1.65, 34.08± 4.25, 37.55 ±6.15, 39.62± 3.00, 43.27± 4.45, 44.40 ±4.24, 50.83 ±2.51, 47.78 ±1.06, 50.63± 5.92, 50.81± 9.52 and 53.13 ± 5.31 mm individual each week from 18 to 30 weeks respectively. Sagittal diameter of the liver was (22.97 ± 3.79, 26.44± 3.17, 29.57 ± 4.68, 31.25 ± 3.54, 31.78 ± 1.74, 36.71 ± 3.16, 38.34 ± 2.89, 39.60 ± 4.37, 44.14 ± 4.17, 38.48 ± 5.33, 45.94 ± 6.01 and 43.22 ± 5.49) at individual gestational weeks 18 to 30 respectively, this study is not similar with our study.
Monika P et al [13] assessed the quantitative anatomy of the liver's visceral surface in a human fetus (2018). In terms of gestational ages, the obtained fetuses were categorized as group 18-21 weeks, group 22-25 weeks, and group 26-30 weeks, whereas each group is separated into male and female. According to them, the mean value and Standard deviation Transverse diameter were (33.5± 5.8mm, 45.8± 5.0mm, 53.1± 5.0mm) in males and (35.6± 4.7 mm, 44.7± 5.0 mm, 53.0± 8.4mm) in female. Vertical diameter (25.0± 4.2 mm, 32.5± 5.7mm, 40.7±3.8 mm) in males and (27.4±4.9, 33.4±6.2mm, 40.0±4.5) in females respectively. The transverse to vertical diameter ratio reached the value of 0.75 ±0.12mm, this study is similar to our study.
A study by Kavita M et al [14], observed the Length, Width of caudate and quadrate lobe at 12-36 weeks GA. The fetuses that were retrieved were divided into five groups based on gestational ages: group A (12-16 weeks), group B (17–21 weeks), group C (22–26 weeks), group D (27–31 weeks) and group E (32-36 weeks). According to them, the vertical diameter was (1.9± 0.4cm, 3.0±3.0 cm, 3.6±0.8 cm, 4.0± 1.2 cm, 5.8±1.6 cm) in males and (7.4±10.9 cm and 3.2±0.9 cm) in female at group B, C respectively. They observed transverse diameter of the liver was (2.5± 0.6 cm, 4.1±0.5 cm, 4.2±0.4 cm, 5.2± 1.1 cm, 5.8±2.0 cm) in males and (1.7±0.4 cm at group B 1.6±0.6 cm at group C) in Female Respectively. The sagittal diameter of the fetal liver was 1.1± 0.3 cm, 1.5±0.3 cm, 1.5±0.3 cm, 1.7± 0.3 cm, 2.3±0.3 cm in males whereas 1.7±0.4 cm and 1.6±0.6 cm in female at B & C group respectively, this study is similar to our study.
Monika P et al [15] assessed the morphometric study of the diaphragmatic surface of the liver in human fetuses. In terms of gestational ages, the obtained fetuses were categorized as group-a 18-21 weeks, group-b 22-25 weeks, and group-c 26-30 weeks. The vertical diameter of the liver was 23.50±4.40, 31. 21±5.67 and 34.93±5.65 mm at group-a, b, and c respectively. All groups are statistically significant except group- c (p–value 0.93), this study is highly correlated with our study.
A study by Fuanglada T et al [16] conducted a study on the Normal Length of the Fetal Liver from 14 to 40 Weeks of Gestational Age. The estimated 5th, 50th, and 95th percentile ranges of liver length at each gestational week were the best fit by the linear regression model. According to them, Fetal liver length was gradually increased with GA is fitted with the equation as follows: Liver length (mm) = 1.61(GA, week) 2 6.75 (r2 5 0.94, $p < 0.001$). Hepatomegaly in Hb Bart's disease-affected fetuses may manifest as early as in the late first trimester since anemia, which is a frequent issue in Southeast Asia, typically manifests in the early stages of gestation. Thus, it is crucial that the nomogram contains fetuses in the early second trimester. In advanced hydrops fetalis, which is brought on by fetal anemia, hepatomegaly is visible. However, despite the fact that the typical hydropic alterations brought on by Hb Bart's illness are more likely to manifest after 20 weeks, our experience of perinatal Although typical Hb Bart's disease hydropic alterations are most likely to appear after 20 weeks, our experience with pregnancy. To the best of our knowledge, no research on the relationship between liver size and Hb Bart's disease during the first trimester of pregnancy has been published. Even though they only covered a small number of patients at 18 to 22 weeks of gestation, certain investigations have demonstrated that the liver length can accurately and specifically identify afflicted pregnancies in fetuses with Rh is immunization.

Conclusion:

This study concluded that there is a significant correlation between the vertical, transverse, and sagittal diameter of the fetal liver with the gestational age. However length, transverse, and sagittal diameters of the fetal liver do not demonstrate sex differences. The quantitative information on the developing liver can be regarded as typical for specific fetal ages and is pertinent to both the ultrasound monitoring of in-utero fetuses and the early detection of inherited liver defects. It is crucial to make the right preoperative diagnosis since it will aid the surgeon in organizing biliary procedures or Porto systemic anastomoses.

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