Quantitative anatomy of the liver visceral surface in the human fetus

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Abstract

Background. Understanding liver growth is relevant in both determining the status of normative fetal development and prenatal detection of its disorders.

Objectives. This study attempted to examine age-specific reference intervals and the best-fit growth dynamics of the liver visceral surface for hepatic height, length, isthmic diameter, oblique diameters, circumferences of individual lobes, and total liver circumference.

Material and methods. Using anatomical, digital and statistical methods, the liver visceral surface was measured in 69 human fetuses of both sexes (32 males and 37 females) aged 18–30 weeks, derived from spontaneous abortions and stillbirths.

Results. The statistical analysis showed no sex differences. The best growth models mostly followed natural logarithmic functions, except for the length of the fissure for ligamentum teres hepatis and the length of fossa for gallbladder, which increased commensurately. Neither the length of fissure for ductus venosus nor the length of sulcus for inferior vena cava modeled the best-fit curves. The vertical-to-transverse diameter ratio of the liver was constant and averaged 0.75 ± 0.12 , while the isthmus ratio significantly altered from 0.78 ± 0.07 at 18–19 weeks through 0.68 ± 0.05 at 26–27 weeks to 0.72 ± 0.07 at 28–30 weeks of gestation.

Conclusions. With no sexual differences, the liver morphometric parameters increased either logarithmically (lengths of: transverse diameter, vertical diameter, right oblique diameter, left oblique diameter, isthmic diameter and porta hepatis, circumferences of: right lobe, left lobe, quadrate lobe, caudate lobe, and total liver circumference) or proportionately (length of fissure for ligamentum teres hepatis, length of fossa for gallbladder). The quantitative data of the growing liver may be relevant in both the ultrasound monitoring of fetuses and early detection of congenital liver anomalies.

Key words: liver, human fetus, size, visceral surface, growth dynamics

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Introduction

Liver size is a beneficial parameter in the diagnosis and monitoring of intrauterine growth retardation (IUGR), as well as in determining the status of fetal growth.^{1–4} Its abnormal size may result from maternal gestational diabetes, isoimmunization, intrauterine infections, heart malformations, tumors, some metabolic diseases, and either microsomia or macrosomia.^{5–9} The fetal liver is the very first organ to reveal an abnormal pregnancy.¹⁰ Reduction in liver size may be caused by IUGR, fetal erythroblastosis, anemia, thalassemia, and disturbances in the transport of oxygen with Bart's hemoglobin.^{11–14} According to Fleischer et al., liver size is a good indicator of clinical pregnancies complicated by serological conflicts.⁵ As a useful reference parameter for ultrasound examination, liver size provides us with quantitative and qualitative information concerning both liver structure and function.¹⁵ Both autopsy examinations and modern in utero imaging techniques provide suitable quantitative evidence about fetal growth and organ development.¹⁶ Knowledge on the normative liver growth is relevant in monitoring normal development and plays an essential role in prenatal detection of its malformations.¹⁷

To date, however, apart from anatomical research on the quantitative analysis of the fetal liver performed by Albay et al., no nomograms concerning its visceral surface have been computed.¹² Thus, in the present study we aimed to examine the liver visceral surface, as follows:

- age-specific reference intervals with respect to gestational age of the 15 linear hepatic dimensions (height, length, right and left oblique diameters, isthmus diameter, length of fissure for ligamentum teres hepatis, length of fissure for ductus venosus, length of fossa for gallbladder, length of sulcus for inferior vena cava, and length of porta hepatis, as well as circumferences of 4 individual lobes and total circumference);
- possible sex differences in the parameters studied;
- the best-fit growth curves for each morphometric parameter studied;
- the relative growth dynamics of the fetal liver (transverse-to-vertical diameter ratio, isthmus ratio).

Material and methods

The research material consisted of 69 human fetuses of both sexes (32 males and 37 females) aged from 18 to 30 weeks, of Caucasian ethnic origin (Table 1), collected at the Department of Normal Anatomy of our university (Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland). All samples had been gathered between the years 1989 and 1999 from spontaneous abortions or stillbirths, and then preserved in neutral formalin solution. Legal and ethical issues were approved by the University Research Ethics Committee (reference: KB 161/2013). Fetal

Table 1. Distribution of the fetuses examined

Fetal age [weeks]	Crown-rump length [mm]			n	Sex	
	median	min	max		males	females
18	139.5	131.0	143.0	4	3	1
19	152.5	145.0	155.0	6	4	2
20	161.0	159.0	167.0	7	3	4
21	175.0	170.0	180.0	7	5	2
22	185.5	181.0	190.0	6	1	5
23	199.5	195.0	204.0	6	4	2
24	212.0	205.0	214.0	10	2	8
25	215.0	215.0	220.0	5	2	3
26	233.0	225.0	233.0	3	1	2
27	240.5	235.0	242.0	4	2	2
28	253.0	247.0	253.0	7	1	6
30	264.0	263.0	265.0	4	4	0

For anatomists dealing with fetuses, the most objective information for establishing fetal ages is the crown-rump length, when compared to the known data of the beginning of the last maternal menstrual period or to ultrasonic measurements of head circumference, bi-parietal diameter, occipitofrontal diameter, abdominal circumference, and femur length.

age determination was based on the crown-rump length (CRL), known date of the 1st day of the maternal menstrual period, and the 5 fetal anthropometric measurements (head circumference, bi-parietal diameter, occipitofrontal diameter, abdominal circumference, and femur length) assessed by early 2nd trimester ultrasound scans.^{18–26} As a prerequisite, we excluded fetuses with chromosomal abnormalities or intrauterine growth restriction, as well as from multiple pregnancies, from diabetic mothers and those with severe infections.

Anatomical method

After having been fixed in 10% formalin solution for 12–24 months, fetuses were anatomically dissected through median and transverse laparotomy with the removal of the liver. Since no liver malformations were macroscopically perceived in the individuals studied, the examined sample could rightly be considered normal.

Digital image analysis

The visceral surface of each isolated liver with a millimeter scale was placed vertically to the optical lens axis, recorded with the use of a Canon 550D camera (Canon, Inc., Tokyo, Japan) and digitalized to TIFF images (Fig. 1). Next the morphometric measurements were performed using the digital image analysis system of NIS-Elements AR 3.0 (Nikon Corporation, Tokyo, Japan), with the greatest accuracy to the nearest 0.01 mm. In each specimen, the following 15 measurements in mm (Fig. 2 A–F) and 2 calculations on the visceral surface of the liver were performed:

Fig. 1. A screen of digital image analysis of NIS Elements AR 3.0 (Nikon Corporation, Tokyo, Japan) while assessing the transverse and vertical diameters

- transverse diameter of the liver, corresponding to the greatest horizontal distance of the liver between its right and left borderlines (Fig. 2 B);
- vertical diameter of the liver, corresponding to the greatest vertical distance of the liver between its superior and inferior borderlines (Fig. 2 B);
- isthmic diameter of the liver, corresponding to the shortest horizontal distance of the liver between its right and left borderlines (Fig. 2 B);
- right oblique diameter, corresponding to the longest oblique distance of the liver between its uppermost point of the right borderline to the lowermost point of the left borderline (Fig. 2 C);
- left oblique diameter, corresponding to the longest oblique distance of the liver between its uppermost point of the left borderline to the lowermost point of the right borderline (Fig. 2 C);
- length of fissure for ligamentum teres hepatis (Fig. 2 D);
- length of fissure for ductus venosus (Fig. 2 D);
- length of fossa for gallbladder (Fig. 2 D);
- length of sulcus for inferior vena cava (Fig. 2 D);
- length of porta hepatis (Fig. 2 D);
- circumference of right lobe (Fig. 2 E);
- circumference of left lobe (Fig. 2 E);
- circumference of quadrate lobe (Fig. 2 E);
- circumference of caudate lobe (Fig. 2 E);
- total liver circumference (Fig. 2 F);
- transverse-to-vertical ratio, corresponding to a quotient of the transverse diameter to the vertical diameter;
- isthmus ratio, corresponding to a quotient of the isthmus diameter to the vertical diameter.

Statistical analysis

All measurements were done by 2 independent researchers (M.P.A., M.B.). Each measurement was performed 3 times under the same conditions, but at different times, and then averaged. The differences between repeated measurements, as the intra-observer variation, were assessed by the one-way analysis of variance (ANOVA) test for paired data and post hoc Tukey's honest significant difference (HSD) test.¹⁷ Thus, in order to examine the inter-observer reproducibility, the intra-class correlation coefficients (ICC) were calculated. In the present study, we used the STATISTICA v. 10 (StatSoft Inc., Tulsa, USA) and PQStat v. 1.6.2. (PQStat Software, Poznań, Poland) programs to analyze all the numerical data. The studied fetuses were separated into 12 1-week intervals, not equally distributed with respect to the fetal age. Obviously, some 1-week intervals did not represent adequate samples, including either 4 (fetuses aged 18, 27 and 30 weeks) or 3 (fetuses aged 26 weeks) specimens only. As the initial step, the first 4 intervals (18–21 weeks), the successive 4 intervals (22–25 weeks) and the last consecutive 4 intervals (26–30 weeks) were aggregated. To examine possible sex differences, we used the Student's t-test for the following 3 age groups: 18–21 (n = 24), 22–25 (n = 27) and 26–30 (n = 18) weeks. The one-way ANOVA test for unpaired data and post hoc Tukey's honest significant difference (HSD) test were used for the 3 aforementioned age groups to check whether or not significant differences existed with age. Furthermore, to choose the best-fit curve for each parameter vs gestational age, the highest coefficient of determination (R^2) was selected, and then the linear or nonlinear regression

Fig. 2. Measurements of the fetal liver on its visceral surface in a female fetus aged 23 weeks (A)

B – transverse, vertical and isthmic diameters; C – right and left oblique diameters; D – lengths of fissure for ligamentum teres hepatis, fissure for ductus venosus, fossa for gallbladder, sulcus for inferior vena cava, and porta hepatis; E – circumferences of the liver lobes; F – total liver circumference.

analysis was computed. The relative liver growth was estimated as the transverse-to-vertical ratio and the isthmus ratio. A p-value <0.05 was considered statistically significant.

Results

No statistically significant differences were found in assessing both the intra-observer and inter-observer reproducibility of liver measurements ($p > 0.05$). As displayed in Table 2, the ICC calculated with respect to 2 independent observers were statistically significant ($p < 0.0001$) and of excellent reproducibility. The individual morphometric values obtained were characterized by the normality of distribution and homogeneity of variance. Due to this, quantitative variables were expressed as mean $\pm$ standard deviation (SD). The statistical analysis of numerical data showed no significant differences between male and female fetuses (Table 3). As a result, all individual parameters have been displayed aggregately for the entire sample (Tables 4–6).

The best growth models for the parameters studied along with their R^2 values were displayed in Table 7.

In order to objectify the obtained measurements in fetuses of different age, we calculated the relative growth of the liver as both the transverse-to-vertical diameter ratio and isthmus ratio. The transverse-to-vertical diameter ratio reached the value of 0.75 ± 0.12 , while the isthmus ratio significantly altered from 0.78 ± 0.07 at 18–19 weeks through 0.68 ± 0.05 at 26–27 weeks to 0.72 ± 0.07 at 28–30 weeks of gestation.

Table 2. Intra-class correlation coefficient (ICC) values for inter-observer reproducibility

Parameter	ICC (2,1)
Transverse diameter	0.999*
Vertical diameter	0.998*
Right oblique diameter	0.998*
Left oblique diameter	0.999*
Isthmic diameter	0.997*
Length of fissure for ligamentum teres hepatis	0.994*
Length of fissure for ductus venosus	0.986*
Length of fossa for gallbladder	0.995*
Length of sulcus for inferior vena cava	0.990*
Porta hepatis	0.979*
Right lobe circumference	1.000*
Left lobe circumference	1.000*
Quadrante lobe circumference	0.999*
Caudate lobe circumference	0.998*
Total liver circumference	1.000*

* statistically significant ($p < 0.0001$).

Table 3. Statistical analysis of fetal dimorphism

Parameter	18–21 weeks			22–25 weeks			26–30 weeks		
	male, n = 15		p-value	male, n = 9		p-value	male, n = 8		p-value
	mean	SD		mean	SD		mean	SD	
	female, n = 9	female, n = 16	female, n = 10	female, n = 10	female, n = 10	female, n = 10	female, n = 10	female, n = 10	female, n = 10
Transverse diameter	33.5	5.8	0.372	45.8	5.0	0.587	53.1	5.0	0.988
Vertical diameter	25.0	4.2	0.210	32.5	5.7	0.737	40.7	3.8	0.714
Right oblique diameter	32.6	4.7	0.110	43.9	5.8	0.958	52.1	4.6	0.175
Left oblique diameter	33.4	5.7	0.358	44.6	5.4	0.800	52.4	5.7	0.753
Isthmic diameter	19.5	3.8	0.466	23.7	4.6	0.791	29.2	5.5	0.501
Length of fissure for ligamentum teres hepatis	11.0	2.1	0.569	13.8	2.4	0.383	19.7	3.7	0.375
Length of fissure for ductus venosus	10.4	2.2	0.257	14.2	2.4	0.617	14.2	3.1	0.809
Length of fossa for gallbladder	12.3	2.4	0.500	16.6	4.0	0.501	22.7	1.2	0.460
Length of sulcus for inferior vena cava	10.2	2.6	0.566	14.1	2.5	0.835	14.4	3.0	0.883
Length of porta hepatis	5.1	1.0	0.631	8.3	1.2	0.156	9.2	1.1	0.703
Right lobe circumference	70.0	12.5	0.329	92.8	14.8	0.608	116.0	12.2	0.330
Left lobe circumference	68.1	15.2	0.366	89.0	12.5	0.538	114.7	19.1	0.635
Quadrante lobe circumference	38.4	6.2	0.920	52.8	10.1	0.115	61.2	6.7	0.906
Caudate lobe circumference	32.5	6.4	0.438	42.4	4.7	0.868	48.5	10.6	0.876
Total liver circumference	107.7	20.5	0.368	145.2	17.1	0.523	184.5	25.7	0.812

SD – standard deviation.

Table 4. Diameters of the growing liver in the human fetus

Age [weeks]	n	Diameter [mm]									
		transverse		vertical		isthmic		right oblique		left oblique	
		mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
18	4	29.64	6.21	21.51	3.84	15.82	2.63	29.02	5.10	29.56	4.92
19	6	32.04	2.32	23.48	4.14	18.64	3.11	31.82	2.33	30.72	3.43
20	7	35.22	4.25	27.69	3.83	21.37	3.36	35.64	5.66	36.50	4.68
21	7	37.87	5.93	28.79	3.14	21.84	3.04	36.63	3.66	37.78	5.40
18–21	24	34.27^(a)	5.42	25.93^(a)	4.52	19.90^(a)	3.67	33.87^(a)	4.99	34.27^(a)	5.61
22	6	40.02	2.99	29.16	5.14	21.94	4.67	39.19	3.56	40.02	2.99
23	6	44.45	3.71	33.70	4.25	23.60	3.83	43.59	4.83	44.45	3.71
24	10	45.05	3.51	33.67	6.38	24.50	3.15	44.15	3.31	45.05	3.51
25	5	51.89	2.47	35.86	6.98	26.34	6.75	49.21	2.03	51.89	2.47
22–25	27	45.07^(b)	4.95	33.08^(b)	5.95	24.07^(b)	4.43	43.86^(b)	4.68	45.07^(b)	4.95
26	3	48.99	0.21	36.92	2.56	27.07	0.17	49.37	3.48	45.07	2.69
27	4	52.77	6.92	39.36	3.61	25.39	2.23	47.44	6.55	47.05	6.58
28	7	54.00	9.22	41.18	4.79	29.03	3.40	50.38	2.79	52.13	7.30
30	4	54.73	5.68	42.17	3.50	31.42	7.07	54.64	2.95	55.84	4.76
26–30	18	53.05^(c)	6.93	40.29^(c)	4.09	28.43^(c)	4.30	50.50^(c)	4.44	51.82^(c)	6.26
(a) vs (b)		p < 0.001		p < 0.001		p < 0.01		p < 0.001		p < 0.001	
(a) vs (c)		p < 0.001		p < 0.001		p < 0.001		p < 0.001		p < 0.001	
(b) vs (c)		p < 0.001		p < 0.001		p < 0.01		p < 0.001		p < 0.01	

Means between the 3 age groups of 18–21, 22–25 and 26–30 weeks, marked by letters ^(a), ^(b) and ^(c) differ significantly (in bold). SD – standard deviation.

Discussion

Understanding the normative liver growth is crucial in both monitoring normal fetal development and prenatal detection of inherited faults. The present study intended to examine age-specific reference intervals and growth dynamics which are best-fit for the gestational age with respect to the linear dimensions of the liver measured on its visceral surface. Apart from that, we attempted to present their relative growth by introducing 2 liver ratios, namely the transverse-to-vertical diameter ratio and the isthmus ratio.

We considered the data obtained in the current examination to be both normative and factual. This statement results from the following 3 reasons. Firstly, the fetal sample presented neither explicit, extrinsic, nor intrinsic malformations. Secondly, the material under examination was comparable, because the fetuses had been immersed in formalin solution for 15–20 years. According to the professional literature, shrinkage in formalin did not exceed 1% with reference to any linear dimension of the liver.^{18–27} Furthermore, the size of the liver in situ was virtually unfettered by formalin solution, since some liver linear dimensions, i.e., height, as well as transverse and sagittal diameters, achieved in the present series, accurately corresponded with those obtained by Chang et al., when measuring in utero fetuses of the same age with the use of 3D-ultrasound.³ Thirdly, in order

to measure the liver parameters, an optimized digital image system (NIS-Elements AR 3.0.; Nikon) was used. It is noteworthy that digital image analysis is an objective method to quantitatively assess the growing liver. Notably, all the studied parameters were clearly defined, outlined by a cursor and so gauged.

The present study is the first to provide objective numerical information about the visceral surface of the growing liver in human fetuses at 18–30 weeks. Since the statistical analysis did not show any sexual differences in terms of the parameters studied, our findings have been displayed aggregately without regard to sex.

To date, however, only Albay et al., on the basis of autopsied human fetuses aged 9–40 weeks, provided algebraic data concerning the linear parameters on the hepatic visceral surface, volume and weight of the liver.¹² These authors found the liver width to increase from 39 ± 12 mm to 67 ± 11 mm in the period of 13–37 weeks. Their findings coincide with our results in the material under examination, at which the length of transverse diameter on the hepatic visceral surface increased from 29.64 ± 6.21 in a 18-week fetus to 54.73 ± 5.68 mm in a 30-week fetus. Also, in the fetuses aged 13–37 weeks, Albay et al. revealed an increase in liver height from 25 ± 8 mm to 41 ± 7 mm.¹² This parameter turned out to be equal to our liver vertical diameter, which increased from 21.51 ± 3.84 mm to 42.17 ± 3.50 mm. Of note, we found both the liver

Table 5. Lengths of the growing liver in the human fetus

Age [weeks]	n	Length [mm]									
		fissure for ligamentum teres hepatis		fissure for ductus venosus		fossa for gallbladder		sulcus for inferior vena cava		porta hepatis	
		mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
18	4	9.42	1.48	8.89	2.15	11.25	1.89	7.42	1.05	4.60	0.96
19	6	10.50	2.03	9.69	1.49	11.19	2.41	9.34	1.97	4.98	1.07
20	7	11.72	2.67	12.18	1.53	13.29	2.22	12.07	1.52	5.13	0.60
21	7	12.25	1.73	11.51	2.17	13.82	1.73	11.52	2.50	5.65	1.20
18–21	24	11.19^(a)	2.22	10.81^(a)	2.15	12.58^(a)	2.29	10.45^(a)	2.50	5.15^(a)	0.99
22	6	12.96	2.43	12.11	1.87	12.70	1.99	11.86	2.87	7.53	1.56
23	6	12.97	2.14	14.71	2.58	16.71	2.73	15.26	2.26	7.98	1.14
24	10	15.32	2.94	14.37	3.28	16.05	2.25	14.52	2.34	7.82	1.82
25	5	16.76	4.07	13.58	4.83	19.08	3.57	13.60	4.05	7.64	1.34
22–25	27	14.54^(b)	3.15	13.80^(b)	3.30	16.01^(b)	3.22	13.92^(b)	2.92	7.76^(b)	1.47
26	3	18.03	0.50	14.23	3.18	20.84	0.65	12.10	2.10	8.29	0.90
27	4	15.73	3.12	14.00	2.87	20.13	2.63	15.50	4.09	9.78	2.33
28	7	19.66	2.28	14.51	3.26	22.96	4.15	14.11	1.96	9.16	1.21
30	4	21.36	4.77	14.59	3.86	23.38	1.22	15.93	2.77	9.86	0.70
26–30	18	18.89^(c)	3.43	14.37^(b)	3.01	22.07^(c)	3.08	14.49^(b)	2.82	9.31^(c)	1.40
(a) vs (b)		p < 0.001		p < 0.01		p < 0.001		p < 0.001		p < 0.001	
(a) vs (c)		p < 0.001		p < 0.01		p < 0.001		p < 0.001		p < 0.001	
(b) vs (c)		p < 0.001		p > 0.05		p < 0.001		p > 0.05		p < 0.01	

Means between the 3 age groups of 18–21, 22–25 and 26–30 weeks marked by letters ^(a), ^(b) and ^(c) differ significantly (in bold). SD – standard deviation.

transverse and vertical diameters to grow in accordance with logarithmic functions. Apart from the aforementioned parameters on the hepatic visceral surface, Albay et al. examined the width of the right, left, quadrate, and caudate lobes, as well as the height of the quadrate and caudate lobes at 4 age ranges: 9–12, 13–25, 26–37, and 38–40 weeks of gestation.¹² However, we do not comment on these results, as we did not examine them at all.

According to Albay et al., porta hepatis did not alter its position with relation to the right and left hepatic borders.¹² Instead, with relation to the superior and inferior liver borders, porta hepatis shifted cephalad. In other words, the quadrate lobe lengthened more rapidly than the caudate one. To some extent, these results remain in line with our findings in the present study, because we have corroborated a greater increase in both the length of fissure for ligamentum teres hepatis and the length of fossa for gallbladder when compared to the lengths of fissures for both ductus venosus and inferior vena cava. As ascertained in the present study, an increase in length of both the fissure for ligamentum teres hepatis and fossa for gallbladder succeeded linearly. On the contrary, the lengthening of fissures for both ductus venosus and inferior vena cava proved to be unpredictable.

The lack of numerical information concerning the oblique diameters, isthmus and circumferences of the liver given in this paper limits our debate on this subject.

In order to match the best-fit model for a particular parameter of the growing liver, we initially computed different statistically significant regressions from logarithmic and square root functions through linear and quadrate functions to different polynomial functions. After that, we compared their R^2 values and finally selected the highest one. Eventually, in our study we discerned 2 disparate types of growth, presented by natural logarithmic and linear functions. A logarithmic increase indicates a gradual deceleration with age, while a linear increase is strictly commensurate. Natural logarithmic growths referred to: transverse diameter, vertical diameter, isthmus of the liver, right oblique diameter, left oblique diameter, length of fissure for ductus venosus, length of sulcus for inferior vena cava, length of porta hepatis, circumference of the right lobe, circumference of the left lobe, circumference of the quadrate lobe, circumference of the caudate lobe, and total liver circumference. On the other hand, only 2 liver parameters, i.e., length of fissure for ligamentum teres hepatis and length of fossa for gallbladder, grew linearly. The greatest R^2 values were typical of the following parameters: total liver circumference ($R^2 = 0.83$), transverse diameter ($R^2 = 0.77$), right oblique diameter ($R^2 = 0.77$), right lobe circumference ($R^2 = 0.76$), left lobe circumference ($R^2 = 0.74$), isthmus diameter ($R^2 = 0.74$), length of fossa for gallbladder ($R^2 = 0.74$), left oblique diameter ($R^2 = 0.72$),

and vertical diameter ($R^2 = 0.71$). The intermediate values of R^2 were typical of the length of porta hepatis ($R^2 = 0.68$), and the length of fissure for ligamentum teres hepatis ($R^2 = 0.64$) and quadrate lobe circumference ($R^2 = 0.64$). The lowest R^2 values were characterized by caudate lobe circumference ($R^2 = 0.58$). Because of a great inter-individual variability we did not manage to match any growth curves for the lengths of fissure for ductus venosus and of sulcus for inferior vena cava.

In the current study, we found no shape variation of the liver. In this aspect, our research does not correspond with the observations made by Albay et al., who perceived the 4 different shapes of the fetal liver: squared, trapezoid, rectangular, and triangular.¹² Furthermore, we observed no liver malformations, similarly to Haffajee et al. and Wang et al.^{28,29} These authors reported relevant cases of the fetal liver beyond week 17 with the gallbladder completely covered with hepatic parenchyma.

Table 6. Circumferences of the growing liver in the human fetus

Age [weeks]	n	Circumference [mm]									
		right lobe		left lobe		quadrate lobe		caudate lobe		total	
		mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
18	4	60.45	11.52	55.67	12.58	35.43	2.26	27.04	7.00	91.15	16.17
19	6	65.92	10.73	61.03	6.22	37.93	6.36	31.89	4.21	98.86	9.24
20	7	77.40	10.32	76.17	11.25	37.05	8.89	36.37	3.79	117.65	16.09
21	7	78.15	11.02	80.31	13.32	42.34	5.16	34.85	5.67	124.66	19.39
18–21	24	71.92^(a)	12.45	70.18^(a)	14.45	38.54^(a)	6.62	33.25^(a)	5.77	110.58^(a)	19.88
22	6	83.24	9.08	78.37	9.99	40.68	5.76	38.62	5.86	128.23	7.35
23	6	95.88	11.12	89.03	16.34	51.45	10.87	41.61	6.29	145.45	13.96
24	10	94.51	10.56	95.79	18.12	47.93	8.50	42.36	3.00	151.03	20.39
25	5	107.24	12.80	105.04	20.77	56.23	8.51	46.42	9.81	174.01	16.68
22–25	27	94.66^(b)	12.82	92.13^(b)	18.27	48.64^(b)	9.64	42.11^(b)	6.21	148.98^(b)	21.42
26	3	103.55	6.23	98.28	11.23	61.24	3.56	41.69	4.32	159.16	6.23
27	4	109.03	16.27	106.28	11.12	55.71	9.81	46.66	7.72	173.25	24.51
28	7	114.41	6.64	115.21	10.16	63.53	9.16	48.46	7.97	188.07	18.58
30	4	121.29	12.76	125.59	19.11	63.61	7.21	53.60	12.52	201.89	22.70
26–30	18	112.93^(c)	11.49	112.71^(c)	15.02	61.43^(c)	8.24	48.07^(c)	8.81	183.03^(c)	23.25
(a) vs (b)		p < 0.001		p < 0.001		p < 0.001		p < 0.001		p < 0.001	
(a) vs (c)		p < 0.001		p < 0.001		p < 0.001		p < 0.001		p < 0.001	
(b) vs (c)		p < 0.001		p < 0.001		p < 0.001		p < 0.05		p < 0.001	

Means between the 3 age groups of 18–21, 22–25 and 26–30 weeks marked by letters ^(a), ^(b) and ^(c) differ significantly (in bold). SD – standard deviation.

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

Parameter	Regression formula	R ² value	F	p-value
Transverse diameter	$y = -125.518 + 53.754 \times \ln(\text{Age}) \pm 4.198$	0.77	219.31	<0.001
Vertical diameter	$y = -98.969 + 41.840 \times \ln(\text{Age}) \pm 3.911$	0.71	161.85	<0.001
Right oblique diameter	$y = -110.111 + 48.557 \times \ln(\text{Age}) \pm 3.721$	0.77	227.02	<0.001
Left oblique diameter	$y = -117.329 + 50.964 \times \ln(\text{Age}) \pm 4.597$	0.72	169.75	<0.001
Isthmic diameter	$y = -53.900 + 24.693 \times \ln(\text{Age}) \pm 3.205$	0.74	80.01	<0.001
Length of fissure for ligamentum teres hepatis	$y = -8.733 + 0.996 \times \text{Age} \pm 2.513$	0.64	115.67	<0.001
Length of fossa for gallbladder	$y = -9.387 + 1.095 \times \text{Age} \pm 2.220$	0.74	184.09	<0.001
Porta hepatis	$y = -26.986 + 10.870 \times \ln(\text{Age}) \pm 1.115$	0.68	131.28	<0.001
Right lobe circumference	$y = -287.401 + 120.550 \times \ln(\text{Age}) \pm 10.003$	0.76	206.38	<0.001
Left lobe circumference	$y = -295.715 + 122.097 \times \ln(\text{Age}) \pm 10.450$	0.74	181.63	<0.001
Quadrate lobe circumference	$y = -144.413 + 61.299 \times \ln(\text{Age}) \pm 6.670$	0.64	116.44	<0.001
Caudate lobe circumference	$y = -100.827 + 45.013 \times \ln(\text{Age}) \pm 5.415$	0.58	86.16	<0.001
Total liver circumference	$y = -517.502 + 210.340 \times \ln(\text{Age}) \pm 13.714$	0.83	317.38	<0.001

F – critical value; R² – coefficient of determination.

Conclusions

The visceral liver surface reveals no sexual dimorphism in terms of its morphometric parameters.

The majority of the liver linear dimensions follow natural logarithmic functions, whereas the 2 linear dimensions (length of fissure for ligamentum teres hepatis, length of fossa for gallbladder) follow proportionately.

The transverse-to-vertical diameter ratio of the liver is relatively constant, while the isthmus ratio is unstable throughout the examined period.

The numerical data concerning the growing liver may be considered normative for particular fetal ages and relevant in both the ultrasound monitoring of in utero fetuses and early detection of inherited liver anomalies.

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