Sonographic determination of liver size in healthy newborns, infants and children under 7 years of age*

Determinação do tamanho do figado de criancas normais, entre 0 e 7 anos, por ultrassonografia

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Abstract OBJECTIVE: The present study was aimed at sonographically determining the liver size in healthy newborns, infants and children under 7 years of age, correlating results with age, sex, height, body weight and body mass index. MATERIALS AND METHODS: A total of 584 healthy children subdivided into 11 age groups were evaluated with measurements of the left lobe craniocaudal diameter at the midsternal line, and the craniocaudal diameter of the right lobe posterior surface at the midclavicular line. The following tests were utilized for statistical analysis: a) Pearson's correlation coefficient (correlation study); b) non-paired Student's t-test (comparison of measures between sexes); c) nonlinear regression models (nomograms). RESULTS: The liver size presented a progressive growth from the birth up to the age of 7, proportionally lower than the body growth, in correlation with age, height and body weight (r > 0.70). Correlation with the body mass index was not observed (r < 0.11). There was no significant difference in liver size between male and female individuals. CONCLUSION: Liver size was sonographically determined in healthy children under the age of 7 by means of a standardized method, demonstrating a strong correlation with age and anthropometric indicators. Nomograms demonstrate the typical variations of the liver size in the population evaluated with a different growth pattern for each hepatic lobe.

Keywords: Liver; Liver size; Biometry; Child; Ultrasonography.

OBJETIVO: Determinar o tamanho do fígado de crianças normais, entre 0 e 7 anos de idade, por ultrassonografia, correlacionando os valores obtidos com: idade, sexo, estatura, peso corporal e índice de massa corpórea. MATERIAIS E MÉTODOS: Foram examinadas 584 criancas saudáveis, subdivididas em 11 grupos etários, sendo medidos o diâmetro crânio-caudal do lobo esquerdo, na linha médio-esternal, e o diâmetro crânio-caudal da superfície posterior do lobo direito, na linha hemiclavicular. Na análise estatística foram aplicados: a) coeficiente de correlação de Pearson (estudo de correlação); b) teste t de Student não-pareado (comparação das medidas entre os sexos); c) modelos de regressão não linear (nomogramas). RESULTADOS: O tamanho hepático apresentou aumento progressivo, do nascimento aos 7 anos de idade, proporcionalmente menor que o crescimento corporal, correlacionado com idade, estatura e peso corporal (r > 0.70), não havendo correlação com índice de massa corpórea (r < 0,11). Não se observou diferença consistente das medidas hepáticas em relação ao sexo. CONCLUSÃO: Valores do tamanho do fígado de crianças normais (entre 0 e 7 anos) foram determinados mediante aplicação de técnica padronizada, verificando-se forte correlação com a idade e indicadores antropométricos. Nomogramas demonstram as variações normais do tamanho hepático na população estudada, com crescimento diferenciado para cada lobo.

Unitermos: Fígado; Tamanho do fígado; Biometria; Criança; Ultrassonografia.

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INTRODUCTION

Hepatomegaly is a frequent clinical finding in children, and may be caused by intrinsic liver diseases or by systemic alterations⁽¹⁾, and in case of clinical suspicion, ultrasonography (US) is generally the method of choice for starting diagnostic investigation in pediatric patients. Biometry studies in children by means of US, however, propose different methods^(1–15), none of them with consensus acceptance.

In a previous study⁽¹⁶⁾ the authors have standardized an easy and reproducible ultrasonographic biometry method for utilization in the pediatric age range^(16,17) based on the measurement of the hepatic length in two longitudinal planes. The singular aspect of such technique lies in the proposition of intrahepatic anatomical repairs in association with external orientation lines and the introduction of a new parameter for measurement of the right hepatic lobe, resulting in higher accuracy in the definition of section planes and the measurements themselves.

The present study is aimed at determining the liver size in healthy children in the age range between 0 and 7 years, by applying the technique described by Rocha et al. (16), and correlating the results with the following variables: age, height, body weight, body mass index and sex.

MATERIALS AND METHODS

Casuistic

Between April 2003 and April 2005, a cross-sectional study with measurements of children livers by B-mode ultrasonography was developed. The sample included 584 children whose parents or guardians signed a term of free and informed consent. Among these children, 301 were girls (51.54%) and 283 boys (48.46%) aged from 0.23 months (7 days) to 83.8 months (6 years, 11 months and 25 days) (mean = 42.2 months).

The project was approved by the Ethics Committee for Analysis of Research Projects (Comissão de Ética para Análise de Projetos de Pesquisa – CAPPesq) of Board of Clinical Directors of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HC-FMUSP). The children were referred by the following institutions related with Universidade de São Paulo:

- a) Liga de Puericultura do Instituto da Criança (Childcare League of the Children's Institute) (ICr) of HC-FMUSP (32 children);
- b) General Pediatrics Ambulatory (AGEP) of Hospital Universitário da Universidade de São Paulo (HU-USP) (18 children):
- c) Day care unit of HC-FMUSP (248 children);
- d) Municipal School for Children (EMEI) "Prof. Antonio Branco Lefèvre" located in the HC-FMUSP Complex (286 children);

The selected children population determined the age range covered by the study. The children were divided into groups according to age, as follows:

- group 1: 0 to 2 months and 29 days (n
 32; 13 girls, 19 boys);
- group 2: 3 to 5 months and 29 days (n34; 19 girls, 15 boys);
- group 3: 6 to 8 months and 29 days (n42; 17 girls, 25 boys);
- group 4: 9 to 11months and 29 days (n
 36; 21 girls, 15 boys);
- group 5: 12 to 17 months and 29 days (n = 32; 18 girls, 14 boys);
- group 6: 18 months to 23 months and 29 days (n = 36; 20 girls, 16 boys);
- group 7: 2 years to 2 years, 11 months and 29 days (n = 34; 19 girls, 15 boys);
- group 8: 3 years to 3 years, 11 months and 29 days (n = 48; 23 girls, 25 boys);
- group 9: 4 years to 4 years, 11 months and 29 days (n = 70; 47 girls, 23 boys);
- group 10: 5 years to 5 years, 11 months and 29 days (n = 111; 53 girls, 58 boys);
- group 11: 6 years to 6 years, 11 months and 29 days (n = 109; 51 girls, 58 boys);

All the children were weighted, measured and evaluated by a pediatrician. Weight and height were recorded and compared with the weighted stature standard of the National Center of Health Statistics (NCHS) 2000 USA.

Subsequently to the clinical evaluation, the US scans were performed. All the children were examined by the same professional, an experienced radiologist specialized in US.

Exclusion criteria: Exclusion criteria were the following: a) children with altered

clinical or US examinations; b) children bearing any chronic or acute diseases.

Inclusion criteria: All the children with ages up to 6 years, 11 months and 29 days, whose parents authorized the participation in the research, until the minimum number of individuals for each age range was achieved.

Method

Children assisted in the Childcare League of The Children's Institute of ICr/HC-FMUSP were submitted to US scan in the Division of Diagnostic and Therapeutic Support of the Institute, with a Logic 7 unit (General Electric Medical Systems; Milwaukee, USA) and an Apogee 800 Plus unit (ATL Inc.; Bothell, USA), utilizing convex, multifrequency 2–10 MHz and 2–7 MHz transducers, respectively.

Children assisted in the AGEP of HU-USP underwent US scan in the Imagenology Division of HU-USP, with a conventional US equipment model SSA 270-A (Toshiba; Tokyo, Japan), utilizing a convex, multifrequency, 3–7 MHz transducer.

The children enrolled at EMEI underwent US scan with a portable Logiq Book unit (General Electric Medical Systems; Milwaukee, USA), utilizing a convex, multifrequency 3-7 MHz transducer.

The equipment settings were standardized according to the protocol for pediatric abdomen.

The examinations were performed with the children in the supine position, with the upper limbs extended along the body, and extended lower limbs, without any support under the head, and without any preparation or sedation. The transducer was positioned below the costal cage, with longitudinal orientation, in orthogonal position relative to spine plane.

Measurements of the liver were based on external orientation lines in correlation with intra- and extrahepatic anatomic repairs (Figure 1).

The following measurements were performed: a) craniocaudal diameter in the midsternal line (CCMSL), through a horizontal line parallel to the abdominal wall, extending from the diaphragmatic surface to the lower hepatic border; b) craniocaudal diameter of the posterior surface of the liver on the hemiclavicular line (CCPHCL),

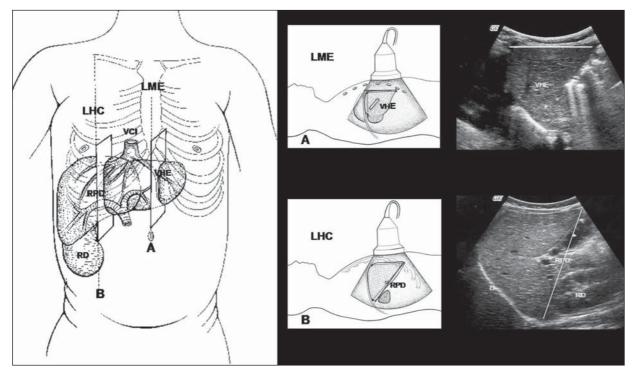


Figure 1. Schematic representation and photographic documentation of a ultrasonography study, showing the section planes and reference points for liver measurements. Section plane A established by the midsternal line (LME) and Section plane B established by the hemiclavicular line (LHC). Intra-hepatic anatomic repairs: left hepatic vein (VHE) in section plane A and cross section of right portal branch (RPD) in section plane B, where one uses the diaphragm (DIAF) with intra-abdominal extra-hepatic repair. VCI, inferior vena cava; RD, right kidney; LC, caudate lobe (modified from Rocha et al.⁽¹⁶⁾).

through an oblique line traced between the upper extremity and the lower hepatic border.

Statistical analysis

The measurements were correlated with age, height and weight of the children evaluated, with the Pearson's correlation coefficient. The non-paired Student's *t* test was utilized for comparing measurements between the female and male groups. The significance level utilized was 0.05.

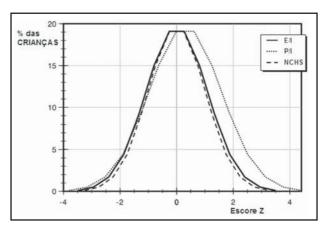
Normality curves for liver size, as a function of age and the anthropometric variable with highest correlation coefficient, were elaborated by means of non-linear regression models, utilizing the Curve Expert 1.3 software.

RESULTS

Of the 584 children included in the sample, 301 were girls (51.54%0 and 283 were boys (48.46%), aged between 0.23 months (7 days) and 83.8 months (6 years, 11 months and 25 days) (mean = 42.2 months, median = 47.2 months).

Figure 2. Sample profile in relation to anthropometric indicators: frequency distribution curve in relation to the Z score, compared with the expected Z score distribution, based on the NCHS 2000 reference. S/A, height to age; W/A, weight to age.

The sample profile in terms of anthropometric indicators is very close to the expected distribution standard, according to the reference curve of the NCHS 2000 (Figure 2). The height/age curve practically matches the expected distribution, while the weight/age curve shows a small deviation to the right as compared with the reference curve, indicating a trend towards overweight in the target population of this study.



Analysis of correlation between liver measures, age, anthropometric indicators (height and weight) and body mass index

The correlation analysis showed a positive and significant correlation between the liver measures, age, height and body weight, with high correlation coefficients (r > 0.70), while for the body mass index, the correlation coefficients were close to zero (r < 0.11) for measures of both lobes (Table 1).

Table 1 Correlation of liver measures and age, height, body weight and body mass index (n = 584).

	CCMSL	CCPHCL	
Age	r = 0.75 p = 0.000	r = 0.80 p = 0.000	
Height	r = 0.80 p = 0.000	r = 0.85 p = 0.000	
Weight	r = 0.74 p = 0.000	r = 0.82 p = 0.000	
Body mass index	r = 0.038 p = 0.365	r = 0.107 p = 0.009	

CCMSL, craniocaudal diameter in the midsternal line; CCPHCL, craniocaudal diameter of the posterior surface of the liver on the hemiclavicular line; r, Pearson's correlation coefficient, p, probability of significance.

Comparison of liver measures between the female and male groups by age

The comparison of CCMSL and CCPHCL between the female and male groups in the different age ranges demon-

strated small but significant difference in three of them (p > 0.05), with higher values for the boys (Figure 3):

In the age groups 3 and 10 (6 to 9 months and 5 to 6 years, respectively) a

significant difference was observed between sexes with respect to the CCPHCL measure (p = 0.006 and p = 0.009, respectively).

In age group 8 (3 to 4 years) there was significant difference between sexes with respect to CCMSL measure (p = 0.004).

Comparison of liver measures in the different age ranges

Both the left hepatic lobe and the right hepatic lobe presented progressive increase in size with aging (Figure 4).

The average of CCMSL measures ranged from 3.41 cm in neonates to 6.91 cm in children between 6 and 7 years of age (Table 2).

The mean CCPHCL ranged from 6.61 cm in neonates to 10.94 cm in children between 6 and 7 years of age (Table 3).

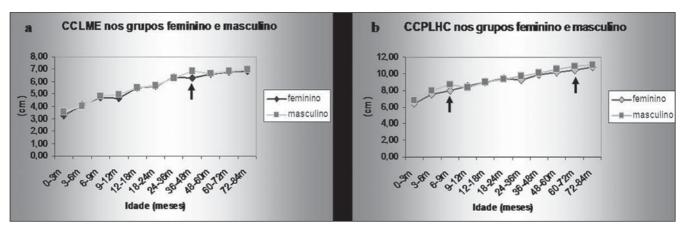


Figure 3. Graphical representation of the comparison between mean CCMSL (a) and CCPHCL (b) in the female and male groups by age.

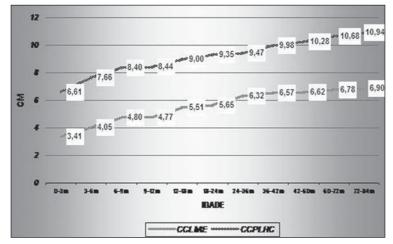


Figure 4. Graphical representation of right and left hepatic lobes tabulated mean CCPHCL and CCMSL measures in the different age groups.

Nomograms

Nomograms of size of left and right hepatic lobes according to age (Figures 5 and 6) and height (Figures 7 and 8) were established by means of non-linear regression models. The curves selected were those that more closely matched the data, with higher correlation coefficients, smaller errors and with an evolution pattern compatible with the biologic phenomenon.

DISCUSSION

The present study relied on a large sample of healthy children. It is known that, in population studies, the high number of

Table 2 Mean, standard deviation, median and minimum and maximum values for measurements of craniocaudal diameter in the midsternal line in the different age groups.

Age (months)	n	Mean	Standard deviation	Median	Minimum	Maximum	_
0 to 3	32	3.41	0.55	3.27	2.48	4.91	
3 to 6	34	4.05	0.77	4.04	2.83	5.50	
6 to 9	42	4.80	0.65	4.88	3.20	6.27	
9 to 12	36	4.77	0.70	4.74	3.40	6.03	
12 to 18	32	5.51	0.62	5.40	4.49	6.87	
18 to 24	36	5.65	0.77	5.53	3.77	6.91	
24 to 36	34	6.32	0.83	6.23	4.91	7.78	
36 to 48	48	6.57	0.71	6.60	5.15	8.28	
48 to 60	70	6.62	0.69	6.58	5.20	8.56	
60 to 72	111	6.79	0.87	6.85	4.61	8.86	
72 to 84	109	6.91	0.85	6.87	3.90	9.34	

Table 3 Mean, standard deviation, median, minimum and maximum values for measurements of craniocaudal diameter of the posterior surface of the liver on the hemiclavicular line, in the different age groups.

Age (months)	n	Mean	Standard deviation	Median	Minimum	Maximum
0 to 3	32	6.61	0.57	6.62	4.76	7.50
3 to 6	34	7.66	0.72	7.75	5.80	9.09
6 to 9	42	8.40	0.91	8.32	6.35	10.14
9 to 12	36	8.44	0.69	8.42	6.56	9.61
12 to 18	32	9.00	0.78	8.95	7.38	10.83
18 to 24	36	9.35	0.74	9.20	7.83	11.17
24 to 36	34	9.47	0.74	9.37	8.14	11.28
36 to 48	48	9.98	0.67	10.02	7.87	11.53
48 to 60	70	10.28	0.79	10.30	8.67	12.24
60 to 72	111	10.68	0.85	10.69	8.75	13.09
72 to 84	109	10.94	0.87	10.89	9.19	13.33

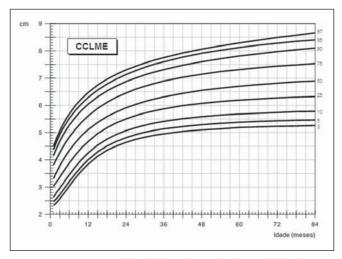


Figure 5. Percentile curves (3, 5, 10, 25, 50, 75, 90, 95 and 97) of left hepatic lobe size, represented by the CCMSL diameter, according to age.

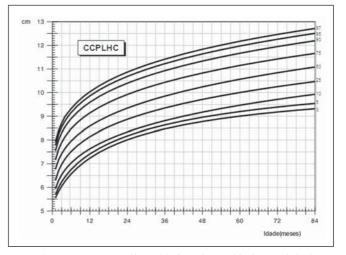
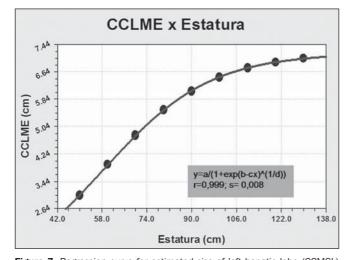


Figure 6. Percentile curves (3, 5, 10, 25, 50, 75, 90, 95 and 97) of right hepatic lobe, represented by the CCPHCL diameter, according to age.



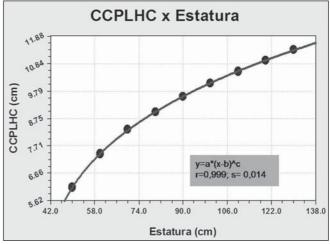


Figure 8. Regression curve for estimated right hepatic lobe size (CCPHCL) according to height.

sample elements decreases the standard error of the estimated value in the research⁽¹⁸⁾. The US studies for determination of the liver size variability in healthy children usually utilized as a reference in the ultrasonography practice were based on smaller samples^(5–8,12–14).

In spite of being a sample of convenience, the present sample presents as favorable characteristics, racial diversity, similar number of boys and girls, and the prevalence of average socioeconomic background, thus assuring a minimal risk for malnutrition in this group, allowing the inclusion of small but healthy children (below the 3rd percentile in NCHS weighted growth curves). One also opted for the inclusion of children overweight (above the 97th percentile of the reference curve), since no relevant clinical or anatomic correlation was found between liver size and body mass index (r < 0.11), indicating that overweight does not represent an influencing factor on the hepatic dimensions.

The liver size in the selected children population presented a continuous and progressive increase from birth to 7 years of age. The increase in dimensions was observed in both hepatic lobes, however in a distinctive manner. The left hepatic lobe, represented by the CCMSL parameter, presented an accelerated growth in the first three years of life, and after that a practically inexpressive growth, with decreasing yearly increments (≤ 0.25 cm). The right hepatic lobe, represented by the CCPHCL parameter, presented a gradual, progressive and significant growth, from birth to 7 years of age, with a faster growth in the first 9 months of life (increments around 1.0 cm per quarter), and progressive growth, however with smaller increments in the subsequent age groups.

The growth pattern observed in the present study corresponds to the expected standard, with a higher rate in the first years of life, following the somatic growth, which is more accelerated in this age group¹⁹⁾. The differentiated growth of each lobe was also expected, as embryology and anatomy studies describe a progressive disproportion of hepatic lobe dimensions, with a relative reduction of the left hepatic lobe, from the intrauterine period until after birth⁽²⁰⁾. The body growth was propor-

tionally larger than the hepatic growth in the studied age groups, with an average increase in height of 125.5%, while the hepatic left lobe grew 103.5% and the right hepatic lobe grew 71%.

The measurements of the liver presented a positive and significant correlation with age, height and body weight, in agreement with results found in literature (2,3,5-8,12,13,15,21-25). The height was the variable that presented the highest correlation coefficients for both parameters for liver size evaluation (r = 0.80 for CCMSL and r =0.85 for CCPHCL). The analysis of correlation between the mean hepatic diameter measures and the variables age and body weight also evidenced high and very close coefficients: r = 0.75 for CCMSL and r =0.80 for CCPHCL, in relation to age, and r = 0.74 for CCMSL and r = 0.82 for CCPHCL, in relation do weight.

The differences found between the hepatic measure averages in relation to sex, were not constant amongst the several age groups, therefore it was not possible to characterize a differentiated growth pattern for boys and girls, and not even a trend. In spite of being statistically significant, these measures variations in relation to sex were punctual and small in absolute values, therefore being inexpressive from a clinical point of view. Thus, in agreement with other authors (2,6,8,11,12,22,23,26), the authors believe that such finding in not consistent enough to justify the construction of different reference tables for both sexes.

The normal liver size values in the sample evaluated presented great variation, in all age groups, and in both measured diameters. Similar results are found in the several hepatic biometry studies reviewed, particularly stressed by Konuş et al. (12). A possible explanation for the wide spectrum of values for the normality range of liver size may lie in the complex and variable morphology of the organ.

The liver size variation values based on age for the children included in the present study, were presented in the form of: a) percentile curves, with high degree of adjustment (r=0.98 for CCMSL and r=0.99 for CCPHCL); b) tables showing means, minimum and maximum values and the standard deviations by age group. The tables are practical for use in the routine of

the sonographist. On the other hand, the curves allow the precise determination of values in the class intervals of the tables. Ancillary normality curves as a function of height were also established, to contemplate the evaluation of children with growth deficit, for whom the tables as a function of age were not appropriate.

The comparison between the liver size values in the population of healthy children of the present sample with those obtained in studies with children populations from other countries could only be made in an approximate manner, as each study applies different methods both in what refers to the measurements, as well as in data processing

The variation in size of the left hepatic lobe was similar to that in other populations^(5,12). However, with respect to the right hepatic lobe, the mean measures of the present study were significantly larger, in all age groups, when compared to those determined in other studies (5,12). This can be explained by the difference in size between the measured hepatic surfaces: the posterior surface in the present study and the anterior surface in those of other authors. The length of the posterior hepatic surface is clearly larger than that the anterior surface, its size being affected, to a certain extent, by the anteroposterior hepatic diameter. The authors believe that the utilization of CCPHCL as a parameter to estimate the dimensions of the right hepatic lobe has the potential of representing both alterations of the longitudinal axis size as well as, indirectly, alterations in the anteroposterior axis. Additionally, this measurement allows the simultaneous assessment of the morphological characteristics of the right lobe (surface and inferior border), which constitutes an additional factor in favor of the adoption of this parameter.

FINAL CONSIDERATIONS

The method applied in the present study aims at defining with higher accuracy the referential for determination of hepatic measurements, with the expectation of contributing to the improvement of the technique to increase the reliability of US, minimizing the factor operator dependence.

The determination of the liver size in healthy children by means of US was yet to be made in our environment. The results obtained reflect a very small fraction of the children population in our region, and rigorously they should not be extended as a reference standard. However, they do constitute a starting point for a future population study, ideally covering the entire pediatric age group.

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