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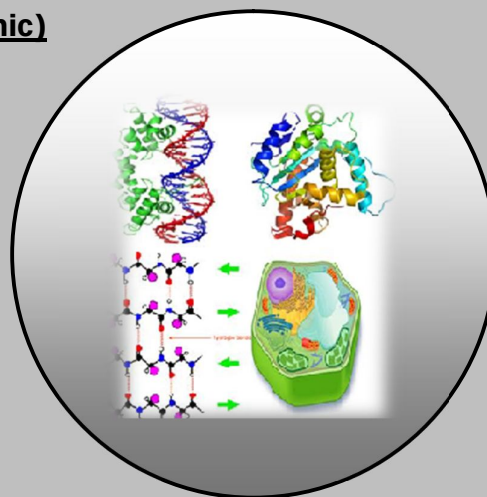
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Sonographic Measurement of Liver Dimension in Healthy Nigerian Subjects: An Intra- and Inter- Observer Reproducibility Study

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ABSTRACT

The liver is vulnerable to a wide variety of metabolic, toxic, microbial, circulatory and neoplastic insults and a reproducible measurement of its dimensions is essential for initial diagnosis and follow-up management.

This study tested the intra-observer and inter-observer reproducibility of sonographic measurements of liver dimension using the mid-clavicular line as the sectional plane.

This study showed a high intra-observer reproducibility which is however dependent on the level of experience. Intra- observer reproducibility was higher than the inter-observer reproducibility which is an indicative of greater consistency of measurements within an observer. Using Pearson's correlation coefficient (r) or intra-class correlation coefficient (r_1), the study showed that inter-observer agreement for the second measurements made by both examiners (A_2 & B_2), was found to be higher than for the first measurements (A_1 & B_1) and the average measurements by the examiners (A_{av} & B_{av}).

The study showed that the mean of the average measurements made by both examiners for the antero-posterior dimension of liver was 11.73 ± 0.70 cm in apparently healthy female subjects within the age range of 18years and 59years. Furthermore, the value of 0.5cm ($S.D=0.45$) should be used as correction factor for the error margin associated with the sonographic measurement of liver in the antero-posterior diameter.

The authors recommend that in taking measurement using ultrasound, three measurements should be gotten after which the average of the last two measurements will be used.

Keywords: Sonography, Measurement, Liver, Reproducibility, Nigerians and Observer.

INTRODUCTION

The liver is vulnerable to a wide variety of metabolic, toxic, microbial, circulatory and neoplastic insults (Kumar et al, 2004) and hence the determination of liver dimension is essential for clinical diagnosis (Niederau et al, 1983). Hepatic enlargement is an index of liver disease (Rosenfield and Schneider, 1973) and so the possibility of obtaining an estimate of the liver dimension is generally considered to be very important in several pathological situations such as cirrhosis and hepatitis. Assessment of liver dimension is also a standard procedure in both the pre- and post- treatment assessment of liver diseases. Determination of hepatic size is a prognostic marker of fulminant hepatic failure (Gupta et al, 2008). Ultrasound is commonly used in initial assessment of patients with liver diseases to determine further investigation. Hepatic size can be assessed by physical means (palpation), percussion and also with radiological imaging tools which is a way of differentiating normal liver from diseased liver (Gupta et al, 2008). In using this imaging modality (Ultrasound) for evaluation of hepatic dimension, the cranio-caudal span and the anterior-posterior diameter at the mid-clavicular line are used as Sectional planes. The best sectional plane with less error margin is the mid-clavicular line (Kratzer et al, 2003; WHO, 2005; Rosenfield and Schneider, 1973; Niederau et al, 1983). The variation in measurement procedure has led to error associated with repeated measures by an observer and also between and amongst observers.

In order to develop a protocol for sonographic assessment of liver dimensions, specific landmark and definitions are required to be developed and tested for consistency and reproducibility with the same operators and between operators. To the best of our knowledge, none of these studies has considered the reproducibility of measurements by a single radiographer (Observer A) or between and a trainee radiographer (Observer B). Paucity of qualified radiographers in Nigeria has created avenues for student radiographers to undertake clinical duties with minimal supervision. The lack of evidence concerning reproducibility studies of sonographic measurements limits widespread use of such measurements in research studies and clinical applications (Bailey, 1997).

This study is aimed at testing the intra-observer and inter-observer reproducibility of sonographic measurements of liver dimension using the mid-clavicular line as the sectional plane for the procedure.

MATERIAL AND METHODS

The study involved the sonographic measurement of the antero-posterior dimension of the liver in female adults. The subjects (apparently healthy) were scanned by two (2) observers (an experienced radiographer and a graduating student radiographer to assess intra-observer and inter-observer reproducibility using a standard protocol. Thirty (30) apparently healthy female subjects between the age range of 18years and 59years (mean $\pm$ S.D= 28.7 $\pm$ 8.77) were recruited in this study. The adequacy of the statistical power was based on a similar study by Alcazar and Zornoza (2001) on intra-observer and inter-observer reproducibility in trans-vaginal ultrasonographic measurement of endometrial thickness in which 30 asymptomatic female volunteers were evaluated. Exclusion criteria included history of hepatic diseases e.g. cirrhosis, jaundice and hepatitis and pregnancy.

In line with Helsinki declaration, approval for the study was obtained from the human research Ethics committee of Holy Rosary Maternity and Radiological Centre Water- Side, Ose, Onitsha in Anambra State. The subjects' consents were obtained prior to the scanning.

A basic protocol was adopted and replicated for each subject. Accordingly, each volunteer was laid supine on the ultrasound couch. Acoustic gel was liberally applied over the right upper quadrant (RUQ). A dedicated Siemens Sonoline- 250 ultrasound machine made in Hungary with 3.5 MHz sector transducer (Probe) was used for this study. The time gain compensation (TGC) was set such that the liver parenchyma appeared homogenous in echogenicity throughout its depth. Transverse plane scan through the inter-costal and sub-costal spaces as well as slow rocking movement was done to obtain the best visualization of the liver. The antero- posterior (A.P) dimension was measured in arrested inspiration at the mid-clavicular line (Niederau et al, 1983). The results of the dimension of the liver by one (1) observer were blinded to the other observer. Below is a line drawing showing how the antero-posterior (A.P) measurement was taken during transverse scan:

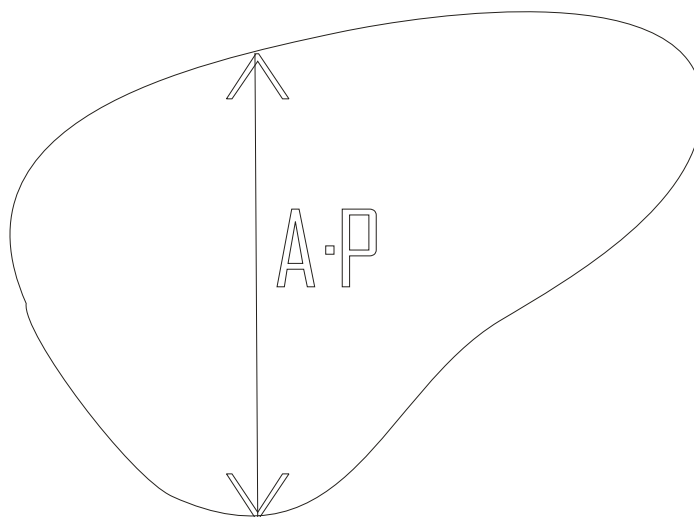


Fig.3. A line diagram showing the AP Measurement of the liver

Statistical Analysis was conducted using statistical package for social sciences (SPSS) version 14.0 (SPSS INC, Chicago, Illinois, USA). The measurements were evaluated to determine if they are normally distributed (Gaussian distribution) using 3 sigma rule ($\text{mean} \pm 3\text{SD}$). Both descriptive (mean, range, standard deviation, skewness and kurtosis) and inferential statistics (using both Pearson's correlation coefficient and intra-class correlation coefficient) were done using significance level of $P < 0.05$ was used as criterion. According to the guidelines suggested by Portney and Watkins (2000) on how characterize Pearson's reliability coefficient: when r is between 0.00 and 0.24 it indicates little or no degree of relationship; when r is between 0.25 and 0.49, it indicates a fair degree of relationship; when r is between 0.5 and 0.74, indicates a moderate to good degree of relationship; when r is between 0.75 and 1.00, indicates a good to excellent degree of relationship.

In addition, using the scheme of Landis and Koch (1977), we characterized intra-class reliability coefficient values as: slight (0.0-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80), and almost perfect (0.81-1.00). The coefficients are defined as variance/ co-variance ratios and range from 0 to 1 with higher values indicating consistency and reproducibility in repeated antero-posterior measurement of the liver.

RESULTS

Table. 1. Individual paired measurements by Observer A and by Observer B.

PATIENT	Observer (A)		Observer(B)	
	1 st measurements (cm)	2 nd measurements (cm)	1 st measurements (cm)	2 nd measurements (cm)
1	10.7	10.6	11.2	10.7
2	13.3	13.5	13.5	13.3
3	10.9	11.0	11.8	11.8
4	10.8	11.0	11.5	12.2
5	11.0	11.1	11.5	11.8
6	12.0	12.2	12.1	12.1
7	9.8	10.0	11.5	11.3
8	11.8	11.7	11.7	12.0
9	10.4	10.6	11.7	11.2
10	11.0	11.2	11.5	11.7
11	10.4	10.3	10.3	10.4
12	11.3	11.4	12.2	11.5
13	12.4	12.6	12.4	12.6
14	11.9	12.0	12.0	12.1
15	12.6	12.6	12.6	12.4
16	12.0	12.0	11.6	11.7
17	10.4	10.6	10.8	10.8
18	13.0	13.0	12.2	12.1
19	13.0	13.0	13.3	13.1
20	10.6	10.7	11.7	11.5
21	11.4	11.4	11.6	11.8
22	11.5	11.5	12.2	12.2
23	11.0	11.1	12.5	12.7
24	11.6	11.6	11.7	11.8
25	12.2	12.4	11.7	12.0
26	11.9	11.9	12.0	12.4
27	11.7	11.7	11.3	11.5
28	11.8	11.8	12.4	12.5
29	10.8	10.7	12.5	12.0

Table. 2. Descriptive statistics of subjects' age and measurements obtained by the two observers.

	Range		Mean	Standard Deviation	Skewness	Kurtosis
	Minimum	Maximum				
Age (yrs)	18.00	59.00	28.70	8.77	1.97	4.62
A1 (cm)	9.80	13.30	11.52	0.88	0.19	-0.58
A2 (cm)	10.00	13.50	11.59	0.87	0.29	-0.52
A av (cm)	9.90	13.40	11.55	0.87	0.24	-0.56
A1-A2 (cm)	-0.20	0.10	-0.07	0.11	0.04	-1.38
B1 (cm)	10.30	13.50	11.91	0.65	0.17	1.23
B2 (cm)	10.40	13.30	11.92	0.65	-0.26	0.41
B av (cm)	10.35	13.40	11.92	0.63	-0.02	1.06
B1-B2 (cm)	-0.70	0.70	-0.02	0.31	0.43	0.38
Mean av (cm)	10.35	13.40	11.73	0.70	0.24	0.18
B av- A av (cm)	-0.85	1.55	0.31	0.61	0.32	0.06

Key: A1= first measurements by Experienced Radiographer

A2= second measurements by Experienced Radiographer

A av= average of the measurements by Experienced Radiographer

A1-A2= differences between the first and second measurements by Experienced Radiographer

B1= first measurements by Graduating Student

B2= second measurements by Graduating Student

B av= average of the measurements by Graduating Student

B1-B2= differences between the first and second measurements by the Graduating Student

Mean av= mean of both average measurements by Experienced Radiographer (A av) and Graduating student (B av).

B av- A av= differences between the average measurements (B av) and (A av).

Table 2 shows the mean of the subjects age was 28.7 ± 8.77 years. The mean of the average measurements by the Observer A (A av) is 11.55 ± 0.87 cm (9.90 – 13.40cm) and the mean of the differences between the first and second measurements by the experienced (A1-A2) is -0.07 ± 0.11 cm (-0.20 – 0.10cm). Also, the mean of measurements by the observer B (B av) is 11.92 ± 0.63 cm (10.35 – 13.40cm) and the mean of the differences between the first and second measurements by the Observer B (B1-B2) is -0.017 ± 0.305 cm (-0.70 – 0.70cm). The mean of both average measurements by the Observer B (mean av) is 11.73 ± 0.70 cm (10.35 – 13.40cm) and the mean of the differences between the average measurements by Observer A and B (B av – A av) is 0.31 ± 0.61 cm (-0.85 – 1.55cm). The measurements are normally distributed (Gaussian response) with respect to degree of skewness & kurtosis and also for the 3 sigma rule (mean $\pm$ 3SD) to have contained all the values.

Figures A: showing the plots of the differences between measurements against their mean for Observer A (fig. A), Observer B (Fig. B) and for the average measurements for both observers (fig. C).

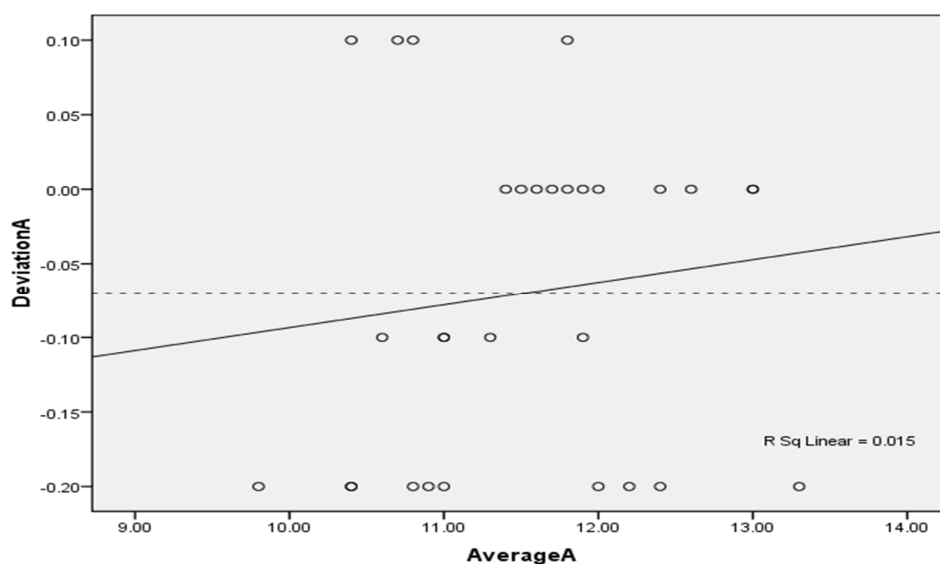


Figure A. plot of the differences between measurements (deviation A) against the average A for observer A. The dotted line shows the mean of deviation A while the thick line shows the line of best fit.

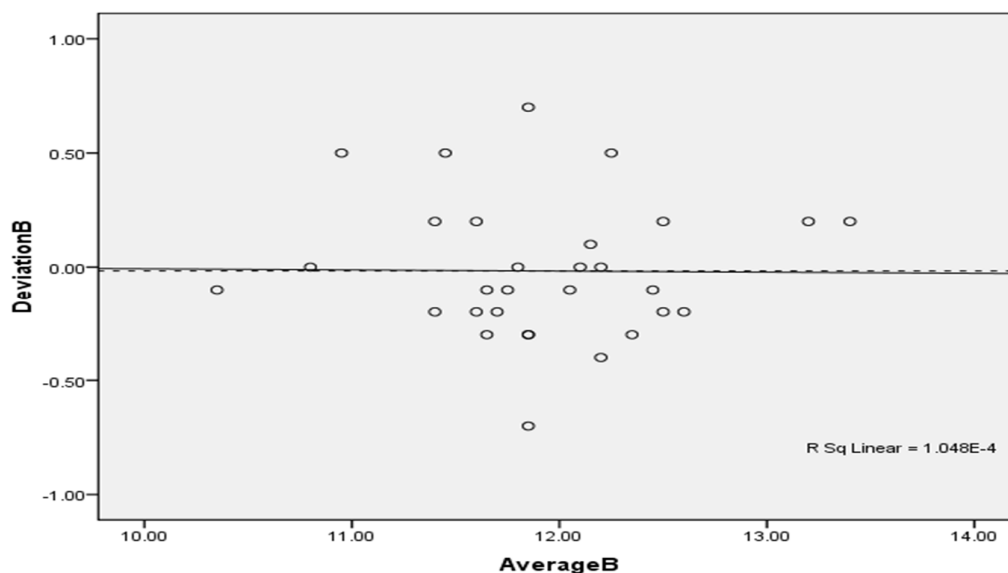


Figure B. plot of the differences between measurements (deviation B) against the average B for the second observer. The dotted line shows the mean of deviation B while the thick line shows the line of best fit.

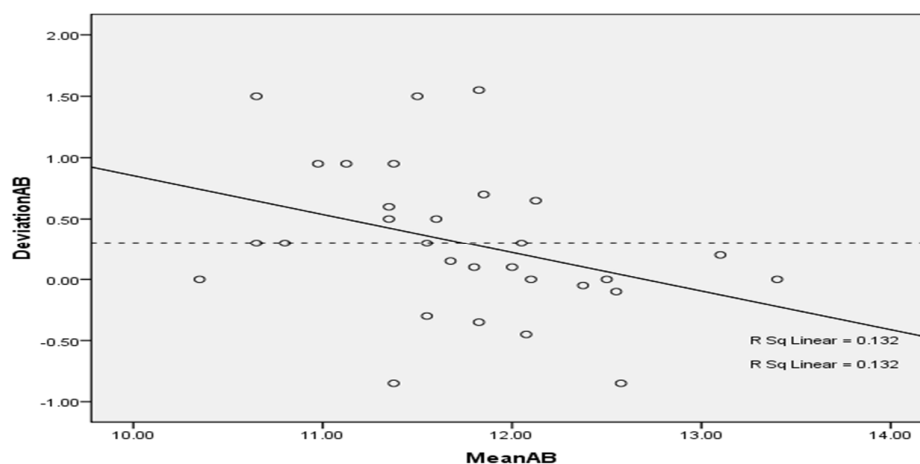


Figure C. plot of the differences between measurements (deviation AB) against the mean AB for the average measurements for both Observers. The dotted line shows the mean of deviation AB while the thick line shows the line of best fit.

Explicitly, figures A – C show the plots of the differences between measurements against their mean for Observer A (fig. A), Observer B (fig.B) and between observers (fig. C). Each scatter plot has dotted line showing the mean of the differences in measurements for each observer and between observers; and the thick line showing the line of best fit. The limits of agreement which indicate how far apart measurements were likely to be for most subjects for the measurements can be calculated with this relation: mean of the difference $\pm (1.96S.D)$ as described by Bland and Altman (1986).

Table. 3. Pearson's and Intra-class correlation coefficients and their P-values within observer and between observers.

	Pearson correlation coefficient (r)			Intra-class correlation coefficient (r ₁)		
	r	P-value	Grade	r ₁	P-value	Grade
Intra-observer A (A ₁ & A ₂)	0.993	0.000 (S)	Good to excellent	0.993	0.000 (S)	Almost perfect
Intra-observer B (B ₁ & B ₂)	0.890	0.000 (S)	Good to excellent	0.890	0.000 (S)	Almost perfect
Inter-observer (A ₁ & B ₁)	0.689	0.000 (S)	Moderate to good	0.660	0.000 (S)	Substantial
Inter-observer (A ₂ & B ₂)	0.763	0.000 (S)	Good to excellent	0.733	0.000 (S)	Substantial
Inter-observer (A _{av} & B _{av})	0.737	0.000 (S)	Moderate to good	0.701	0.000 (S)	Substantial

S= significant

INTERPRETATION AND DISCUSSION

Intra-observer reproducibility

The Pearson's correlation coefficient for reproducibility of intra-observer A (A_1 & A_2) was $r = 0.993$ which shows a good to excellent relationship as categorized by Portney and Watkins (2000). The intra-class correlation for reproducibility of intra-observer A was $r_1 = 0.993$ which shows an almost perfect reproducibility as categorized by Landis and Koch (1977). Pearson's correlation coefficient for the graduating student's intra-observer reproducibility (B_1 & B_2) was noted to show a good to excellent relationship ($r = 0.893$) and the intra-class correlation coefficient also showed an almost perfect relationship ($r_1 = 0.893$). The intra-observer agreement for the experienced sonographer was found to be higher than the intra-observer agreement for the graduating student.

Inter-observer reproducibility

The inter-observer agreement for the first measurements by both the Observers A and B (A_1 & B_1), for the second measurements by both observers (A_2 & B_2) and for the average measurements by the observers (A_{av} & B_{av}) using Pearson's correlation coefficient ($r_{A_1 \& B_1} = 0.689$, $r_{A_2 \& B_2} = 0.763$, $r_{A_{av} \& B_{av}} = 0.737$) at a p value of 0.000. A_1 & B_1 and A_{av} & B_{av} showed moderate to good relationship while A_2 & B_2 showed a good to excellent relationship as described by Portney and Watkins (2000). Intra-class correlation coefficient ($r_1_{A_1 \& B_1} = 0.660$, $r_1_{A_2 \& B_2} = 0.733$, $r_1_{A_{av} \& B_{av}} = 0.701$) at a p value of 0.000 showed a substantial agreement as described by Landis and Koch (1977). The inter-observer agreement for the second measurements (A_2 & B_2) was found to be higher than the inter-observer agreement for the first measurements (A_1 & B_1) and the inter-observer agreement for the average measurements (A_{av} & B_{av}). From table 3 also, the values for intra-observer reproducibilities using either Pearson's or intra-class correlation coefficient were the same but in inter-observer agreement, intra-class correlation coefficient appeared more conservative (less) than the Pearson's correlation coefficient. The mean of absolute differences for the first and second measurements by the experienced Radiographer was 0.24 ± 0.19 cm, that for the first and second measurements by the graduating student was 0.097 ± 0.084 cm and for average measurements by both the experienced and the graduating student was 0.50 ± 0.45 cm. The mean absolute differences for the average measurements should be adopted as the correction factor for these measurements since it encompasses both for the experienced and the graduating student.

Measurement of liver size is important in the diagnosis and management of liver diseases. Liver size can be estimated by physical means and radiological imaging tools (Gupta et al, 2008). The physical means (palpation and percussion) is inaccurate because it either under- or over-estimates the size of liver (Gupta et al, 2008); this could be as result of Reidel's lobe been present. Evaluation with radiological imaging tools include conventional radiography, ultrasound, computed tomography, magnetic resonance imaging, scintigraphy (Lomas, 2008). Moreover, conventional radiography, computed tomography and scintigraphy involve ionizing radiation which is not recommended in follow-up examinations; MRI does not utilize ionizing radiation but is very expensive. Ultrasound is a useful, most widely utilized, economical and safest imaging tool in the assessment and measurement of liver. The cranio-caudal span and the antero-posterior diameter at the mid-clavicular line (midpoint between the right lateral margin of the liver and the xiphoid) are used as the sectional planes for measurements. The antero-posterior diameter was used in the present study.

In spite of the wide clinical importance in the measurement of liver size, clinical studies to the best of our knowledge dealing with the reproducibility of the method are scanty.

Results in this study showed that the intra-observer agreement for the experienced radiographer ($r_A=0.993$, $r_1A=0.993$) was found to be higher than the intra-observer agreement for the graduating student ($r_B=0.893$, $r_1B=0.893$). The inter-observer reproducibility for the second measurements made by both experienced sonographer and a graduating student ($r_{A_2 \& B_2}=0.763$, $r_1A_2 \& B_2=0.733$) was higher than the inter-observer reproducibility for the first measurements by both the experienced and the inexperienced observers ($r_{A_1 \& B_1}=0.689$, $r_1A_1 \& B_1=0.660$) and the inter-observer reproducibility for the average measurements ($r_{A_{av} \& B_{av}}=0.737$, $r_1A_{av} \& B_{av}=0.701$). In addition, the average measurements for both the experienced and inexperienced have a mean (mean of the measurement) of 11.73 ± 0.70 cm. The range for the average measurements by both observers ($A_{av} \& B_{av}$) was between 9.80 cm and 13.40 cm and also the mean of the absolute differences for the average measurements by both experienced and inexperienced observers was found to be 0.5 cm (S.D=0.45) which was adopted as the correction factor in this study. The intra-observer reproducibility for the experienced radiographer was higher than the intra-observer reproducibility for the graduating student which is similar with the findings in related previous works: Alcazar and Zornoza (2001) on trans-vaginal measurement of the endometrial thickness, an intra- and inter-observer reproducibility by Mighlor et al (2004) on evaluation of ultrasound measurements of central corneal thickness; and by Paternot et al (2009) on intra- and inter-observer analysis in the morphological assessment of early stage embryos using multi-level images. In their works, the largest reproducibility was recorded in the experienced observer and they were of the opinion that reproducibility varies with level of experience. They also opined that training is needed notwithstanding that the reproducibility for the inexperienced observer might be high in order to yield more homogenous clinical results.

The inter-observer reproducibility was found to be lower than the intra-observer reproducibility which is in agreement with the conclusion by works conducted by Alcazar et al (2001), Paternot et al (2009) and Mighlor et al (2004). The higher value of intra-observer reproducibility than inter-observer reproducibility indicates great consistency and better reproducibility of these measurements. To optimize accuracy, the aim is to demonstrate 'almost perfect' intra-observer reliability and substantial inter-observer reliability according to the classification by Landis and Koch (1977). Eliasziw et al (1994) suggested the use of intra-class coefficient values of 0.8 and 0.6 as target standard of accuracy for intra-observer and inter-observer reproducibilities. The target values were met by values obtained in this study (Table 3). The researchers were of the opinion that training is highly needed to increase inter-observer reproducibility and decrease inter-observer variability. With respect to this finding, it would be preferable to have the same examiner perform all investigations of a given patient but it would seem impossible for outpatients, so training is highly needed to decrease inter-observer variability and achieve skill because ultrasound is primarily operator dependent. The inter-observer reproducibility for the second measurements made by the experienced and the inexperienced observers was found to be higher than the inter-observer reproducibility for the first measurements and the inter-observer reproducibility for the average measurements by both observers.

Hence, the authors suggest that since inter-observer reproducibility for the average measurements is higher than the inter-observer reproducibility for first measurements, obtaining 3 measurements and taking the mean values of the last two measurements will obviously reduce variability. The mean of the average measurements of the liver dimension by the two observers in antero-posterior diameter was found to be 11.73 ± 0.70 cm. This measurement is similar to the value of ≤ 11.3 cm given by Niederau et al (1983) as the normal antero-posterior (A.P) dimension of the liver. The similarity is obviously due to the Gaussian nature of the liver dimensions which statistically will permit the use of moderate sample size as against large sample size for the establishment of nomograms. A sample size of ≥ 30 is large sample and in view of the normal distribution pattern of liver dimensions, this sample and mean value of 11.73 ± 0.70 cm can be adopted as the normal range in line with Lyapunov central limit theorem. In addition, the mean of the absolute differences between the average measurements of the experienced (A_{av}) and the graduating student (B_{av}) was gotten to be 0.5 cm (S.D=0.45). This is congruent with a previous study by Alcazar and Zornoza (2001). The mean absolute difference of 0.5 cm (S.D= 0.45) which is the mean of the absolute difference for the average measurements should be used as correction factor for the error margin associated with the sonographic measurement of the liver dimension in the antero-posterior diameter.

The lower value for intra-class correlation than Pearson's correlation coefficient in the assessment of inter-observer reliability shows that intra-class correlation coefficient is a more conservative measure and should be predominantly adopted in clinical setting. High inter-observer reproducibility observed in this study indicates that proper sonography training is obtainable at the undergraduate radiography program of Nnamdi Azikiwe University, Anambra State, Nigeria.

CONCLUSION

This study showed that intra-observer A's reproducibility and intra-observer B's reproducibility were high. Intra-observer A's reproducibility was seen to be higher than the intra-observer B's reproducibility which implies that the level of agreement between measurements depends on experience. Intra- observer reproducibility was higher than the inter-observer reproducibility which is an indicative of greater consistency of measurements within an observer.

The study showed that the mean of the average measurements made by both examiners for the antero-posterior dimension of liver was 11.73 ± 0.70 cm in apparently healthy female subjects within the age range of 18 years and 59 years. The individual measurements (A_1 , A_2 , B_1 , and B_2) by the observers ranged between 9.80 cm to 13.50 cm. These measurements showed a Gaussian (normal) response which statistically will permit the use of moderate sample size as against large sample size for the establishment of nomograms.

In addition, the mean of the absolute differences between the average measurements for the experienced (A_{av}) and the graduating student (B_{av}) was gotten to be 0.5 cm (S.D=0.45) from the study. The 0.5 cm (S.D=0.45) should be used as correction factor for the error margin associated with the sonographic measurement of liver in the antero-posterior diameter.

The authors recommend that in taking measurement using ultrasound, three measurements should be gotten after which the average of the last two measurements will be used. This is because the first measurements between the observers showed less inter-observer reproducibility than the second measurements between the 2 observers.

Hence, it is thought that second and third measurements could be better than the first measurement.

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