PEER REVIEWED **ORIGINAL ARTICLE**

Ultrasound quantification of gallbladder volume to establish baseline contraction indices in healthy adults: A pilot study.

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Abstract

Introduction

Gallbladder contractility helps clinicians assess morbidity and the presence of some hepatobiliary diseases. No such study to the best of knowledge has been conducted in Africa bearing in mind possible racial variations.

Aims

To evaluate the gallbladder contraction indices in adult Nigerians and derive prediction formulas for gallbladder contraction index in healthy adults in order to help the assessment of gallbladder diseases .

Methods

The length, width and height of the gallbladder of 50 normal subjects (29 males and 21 females) in Ebonyi State, Nigeria were measured by real time ultrasonography between January and November 2005. The gallbladder volume was calculated using the ellipsoid formula. Gallbladder contraction index (GBCI) taken at the 10th and 20th minute following the ingestion of a standardized fatty meal (SFM) was obtained from the 50 subjects and the mean of the two values adopted as the actual GBCI. Pearson's correlation established relationship between GBCI and anthropometric variables and a t-test was carried out between the GBCI of males and females. Regression equations were established. Tests were two tailed with $P<0.05$ indicating statistical significance.

Results

The mean GBCI (± SD) was 42.8% (± 19.33%) in males and 37.66% (± 16.29%) in females. No statistically significant difference exists between GBCI in males and females ($P>0.05$). Equations comparing GBCI with subject anthropometric variables based on simple linear regressions gave GBCI (%) = - 110.94 (subject height) m + 236.38 for males and GBCI (%) = - 0.7646 (weight) kg + 82.7798 for females. Height correlates better with GBCI in males and weight in females

Conclusion

This study has established prediction equations for GBCI in this locality and could be useful in the assessment of gallbladder diseases. This will impact on patient management and diagnosis as cut off values established or predicted should help in assessing prognosis in patients with gallbladder diseases.

Keywords

Gallbladder contraction index, ultrasonography, standardized fatty meal

Introduction

Ultrasonography is an accurate method for studying gallbladder volume variations and thus indirectly gallbladder emptying and refilling in humans. The gallbladder contraction index is an indication of gallbladder motor function [1] which is affected in some gallbladder diseases, such as cholecystitis or diabetes induced cholestasis

A study has shown that gallbladder contraction is not decreased in obese subjects, compared to controls, suggesting that gallbladder hypocontractility is not a lithogenic risk factor in obesity [2]. The acetyl choline (ACH) released from these intrinsic nerves acts on smooth muscle muscarinic receptors, causing gallbladder contractions [3]. Cholecystokinin (CCK), the gastrointestinal hormone that mediates meal-stimulated gallbladder emptying has been shown to facilitate ACH release from gallbladder neurons [4]. Recently, immunohistochemical studies have verified the presence of intrinsic cholinergic neurons in the gallbladder [5]. Furthermore, it has been reported that the fat content of meals affects the motility of gallbladder emptying [1].

Increased gallbladder volume and reduced gallbladder motility have been reported in patients with non-insulin- diabetes mellitus [6]. Impairment of gallbladder emptying is increasingly suspected to be a potential patho-physiological factor in the development of gallstones [7,8]. The inflammatory response of the gallbladder wall could precede cholecystitis and could also lead to decrease in gallbladder motility before obvious wall thickening appears on sonography. Large gallbladder volume and gallbladder hypomotility are predictors of biliary stasis and the formation of biliary sludge [9]. Ho *et al* [10] opined that the presence of hepatobiliary disease might be detected by evaluating serial changes of gallbladder volume and contractility under ultrasonography in the neonatal state.

From available literature and to the best of our knowledge, there has not been any documentation of normal values of gallbladder contraction index in this locality and no prediction formula for gallbladder contraction index has been established. The only study in this locality established motility using gallbladder emptying rate [11]. This study was therefore designed to consider a relationship between contraction index and

anthropometric variables in order to establish a body weight or height specific contraction index.

Materials and methods

Fifty (n=50) participants (subjects), comprising 29 males and 21 females, were recruited as volunteers for this study in Ebonyi State, Nigeria between January and November 2005. The participants had no history of hepatobiliary disease or family history of diabetes. Their ages ranged from 18 to 63 years. Obese participants were excluded from the study because lower ejection fractions have been noted in non-obese females compared to obese women [12]. Pregnant women were excluded as hormonal changes in pregnancy predispose to cholestasis [13].

The subjects had to be aware of the nature of the study and had to willingly provide informed consent before entering the study. Ethics committee approval for the protocol was obtained from the Federal Medical Centre, Abakaliki, Ebonyi State according to the Declaration of Tokyo (1975) and Declaration of Helsinki (1996).

Ultrasound examinations of the gallbladder were performed using a Siemens SL–1 ultrasound unit with a 3.5MH_z linear transducer as this was available in the centre used in this study.

Subjects were scanned in the morning following overnight fasting. Ages, weights and heights of subjects were recorded and the corresponding BMI (body mass index) calculated. BMI could influence the study as obese subjects have reduced gallbladder motility [2]. For the purpose of this study the supine position was selected instead of, for example, a lateral position, because patients tend to be more relaxed in the former one. Three serial ultrasound scans and measurements of the gallbladder in the supine position were carried out for each subject as follows:

1. Before ingesting a tin (165mls) of evaporated skimmed milk. Skimmed milk was used in the study because it is preferable among adults as it contains less fat compared to the cream milk and also it was cheaper and no sponsorship was given. The use of a standardized fatty meal (SFM) was based on the fact that the fat content of meals in healthy volunteers affects the motility of gallbladder emptying and refilling [1].
2. Ten (10) minutes after ingesting 165mls of milk.
3. Twenty (20) minutes after ingesting 165mls of milk.

This protocol enabled the variations of gallbladder volumes with bile emptying to be obtained.

Upper abdominal ultrasonography was performed for gallbladder assessment. Subjects lay supine during the procedure. After visualization of the maximal gallbladder longitudinal outline, the length and maximal antero-posterior diameter (height) measurements were taken on arrested respiration, with calipers crossing each other at 90º [14]. Subsequently, the probe was rotated through 90º to obtain the maximal transverse dimension [14]. The width was measured on arrested respiration. These made three orthogonal plane (perpendicular) measurements as shown in Figures 1a and 1b. Subjects' weights were measured on a bathroom weighing scale: model H 89 LT Blue, and the heights measured on a calibrated vertical wall. Ages of subjects were ascertained The body mass index (BMI) was obtained as weight /height [2,15].

Ten and twenty minutes post prandial measurements were adopted in this study because there was no dedicated ultrasound machine available for this research to enable unlimited time for each subject to be studied. A hospital machine used for routine investigation of patients was employed for this research and required time-sharing between the two demands.

The use of a small sample size is also a limitation and hence its notation as a pilot study. More rigorous study in this area in this Nigerian locality and beyond are necessary for wider clinical application.

In the determination of GBCI, the measurements of length, width and height of gallbladder were performed at 10 and 20 minutes following milk ingestion. These time frames are in keeping with gallbladder emptying rates following a fatty meal. However scans later than 20 minutes were not done since the unit used in this study was also required to scan patients. Thus departmental workflow and service delivery had to be taken into consideration. Gallbladder volumes were obtained using volume calculation (0.523 x length x width x height) for a prolate ellipsoid [10]. Gallbladder contraction index is defined as the percentage decrement of post prandial size from initial size [10]. In this study, the contraction index was obtained at 10 and 20 minutes using fasting gallbladder volumes as the initial volumes in the two calculations. The mean of the two values of GBCI was adopted as the actual GBCI.

Data analysis

Subjects were categorized into sex and age. Cross tabulation tables

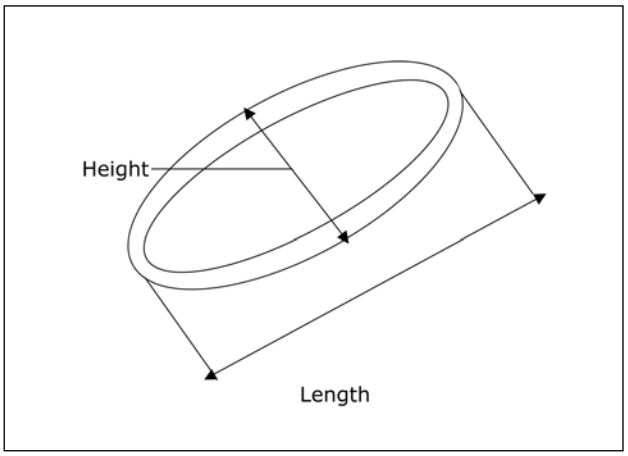

Figure 1a: A line drawing showing a longitudinal section of the gallbladder.

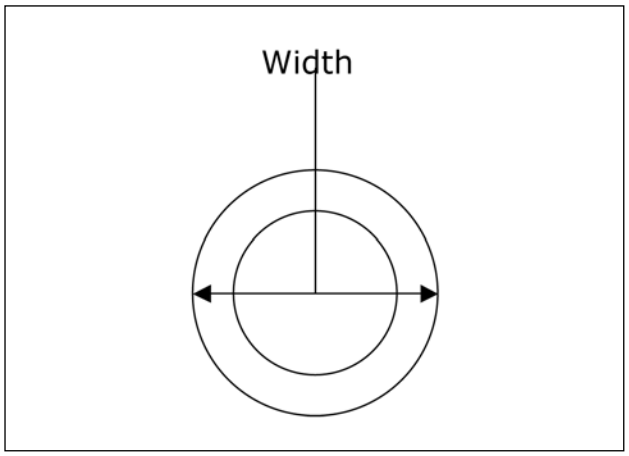

Figure 1b: A line drawing showing a transverse section of the gallbladder.

Table 1: Variation of GBCI with age subjects

	Males		Females	
Age range	No of subjects (% of total)	Mean GBCI ± SD	No of subjects (% age of total)	Mean GBCI ± SD
18-28	15 (51.72)	39.73 ± 20.11	13 (61.90)	36.63 ± 16.45
29-39	8 (27.59)	49.67 ± 15.75	7 (33.33)	39.60 ± 18.34
40-70	6 (20.69)	41.34 ± 22.49	1 (4.76)	37.62
Total	29 (100)	42.80 ± 19.33	21 (100)	37.66 ± 16.29

and frequency tables of GBCI were created. Mean, range and standard deviation of measured variables were computed.

All statistical analysis was performed using Microsoft Excel Office 2000 software. The degree of linear relationships between gallbladder contraction index (GBCI) and anthropometric variables were investigated using Pearson's correlation coefficient. Parametric tests were performed to determine whether there were significant difference between GBCI in males and females and also to show if there were significant correlations between GBCI and anthropometric variables. Regression equations were also established to relate GBCI with height in males and GBCI with weight in females.

A significant difference in GBCI of males and females was calculated by paired (2 tailed) t-tests with $P<0.05$ regarded as significant.

Results

Table 1 shows variation of GBCI based on the age of subjects. The subjects' height ranged from 1.41m to 1.53 for females and 1.49 to 1.61m for males. The weight in males ranged from 57 to 88kg while it ranged from 39 to 75kg in females. The range of BMI (body mass index) in males was 19.02 - 27kg/m^2 while it was 14.51 - 29kg/m^2 in females. GBCI ranged from 5.25 - 76.71% in males and 15.47 - 69.65% in females.

The mean GBCI ± standard deviation (SD) in males was 42.8% ± 19.33% and 37.66% ± 16.29% in females.

In males the correlation coefficient r between GBCI and age was low (0.0151); GBCI and subject height was fair (-0.3948) as was GBCI and weight (-0.3224); GBCI and BMI was low (-0.1186).

In females the correlation coefficient r between GBCI and age was fair (0.2508); GBCI and subject height was fair (-0.3300); GBCI and weight was moderate (-0.5059); GBCI and BMI was fair (-0.4364). Significant correlations, namely the relationships that are statistically significant ($p<0.05$) existed only between height and GBCI in males and in females between weight and GBCI. Regression analysis gave GBCI (%) = - 110.94 (subject height) m + 236.38 and GBCI (%) = - 0.7646 (weight) kg + 82.778 for males and females respectively. There was no statistically significant difference ($p>0.05$) between the GBCI of males and females.

Discussion

Radiological investigation of the gallbladder and biliary tract has evolved from cholecystography to other imaging modalities such as dynamic ultrasonography (DUS), dynamic cholescintigraphy (DCS), magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP).

The result of this study has given a mean GBCI of 42.8% and 37.66% for males and females respectively in this locality. These results could not be compared directly with any other established value as different timing and cholecystokinetic agents were used by various researchers. There was no significant difference between the GBCI of males and females.

No significant correlation was also established between age and GBCI. These findings have similarities with a previous study by Wedmann *et al* [16] which showed that age and gender do not significantly influence fat induced gallbladder contraction in man. Hence, higher incidence of stone formation in females cannot be sex related on the basis of contractility. This could be as a result of other factors present in females but absent in males such as oestrogen. Pregnant women, or women who have used birth control pills or oestrogen replacement therapy, have been reported to be more likely to develop gallstones [17]. Obesity has been shown to be a major risk factor for gallstones [17].

The lack of significant correlations between GBCI and BMI suggests that gallbladder contractility is not a high lithogenic risk factor in obesity, which is determined by BMI. This finding is contrary to that reported by Sari *et al* [12] but in agreement with other reports in the literature [3,18] which excluded gallbladder contractility as a lithogenic risk factor in obesity. The increased lithogenesis in obesity could be attributed to excess cholesterol in bile and low bile salts in obese subjects, which predispose to gallstone formation [18].

Men and women over 60 years have been reported to be more predisposed to gallstone formation [18]. The GBCI in this study was noted to be highest in the 29 to 39 years age group and it decreased thereafter in both males and females. Hence, increased lithogenesis at higher age brackets could be attributed to hypocontractility of the gallbladder. The decrease in GBCI at higher age brackets could be attributed to ageing, differences in feeding habits or differences in hormonal and neurological profiles between the young and the elderly. As age increases, the number of people in each group begins to fall. This could be due to the fact that in this locality, it is more difficult to persuade older people to participate in such surveys. In addition, it reflects the nature of our demographic structures.

A study by Pons *et al* [19] shows that dynamic ultrasonography (DUS) performed using simple technique, as described in this study, lacks diagnostic value in gallbladder dysfunction when dynamic cholescintigraphy (DCS) is taken as a reference test. When gallbladders that were ellipsoidal were sub-selected, correlation between DUS and DCS was noted to have improved [20]. Another research study by Cay *et al* [21] showed that ultrasonographic evaluation of fatty meal stimulated gallbladder contraction provides relatively reliable and reproducible results. These differences could be as a result of using the same formula to evaluate volumes for different gallbladder shapes and contour. Further studies adopting the supposed formula for different gallbladder shapes is advised. When the shape resembles the ellipsoid or sphere, the ellipsoid formula is recommended [14]. When the gallbladder is less distended; the use of method of cone is suggested. When the gallbladder is more distended and exhibits atypical shape, the method of cylinder [22] can provide more accurate results. Three dimensional (3D) ultrasonography is becoming highly utilized in the ultrasound laboratory and may well prove to be the appropriate technology in future studies [23]. The use of 2D ultrasound and one volumetric formula in this study could have obvious limitations. Future studies using DUS and DCS in a larger population in this locality is advised so that research results could be applied widely in clinical environments. Moreover, standardized milk ingestion technique

used in this research, provided an alternative to the use of cholecystokinin [CCK] and the invasive nature of its infusion. An additional limitation of this study was the use of skimmed milk as a fatty meal.

Conclusion

Despite the observed limitations, this study has established a relationship between GBCI and some anthropometric variables. The sample size needs to be increased before obtaining a nomogram. The regression equations should be applied to subjects within the same age, weight, height and BMI ranges with the subjects evaluated in this study. It is an added advantage that these prediction formulae were derived with anthropometric variables that significantly correlated with GBCI.

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