SONOGRAPHIC ASSESSMENT OF GALLBLADDER SIZE AND MOTILITY AMONG APPARENTLY NORMAL PREGNANT WOMEN IN ANAMBRA STATE, NIGERIA

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ABSTRACT

Background: Pregnancy had been associated with a number of physiologic changes which affect many organs and systems, for example, the gastrointestinal system. Gallbladder, an accessory organ of digestion could be predisposed to disorders in pregnancy but he nature and to which extent it could be affected remained unclear.

Aim: This study aimed to investigate the gallbladder changes that could occur in pregnancy.

Materials and methods: A prospective cross-sectional survey design was used to sonographically study 201 pregnant and 27 non-pregnant women who met the inclusion criteria, both in the fasting and post prandial states. Both descriptive and inferential statistics were used to analyze data.

Results: Means of age, BMI, fasting gallbadder volume (FGbV), post prandial gallbladder volume (PGbV), ejection fraction (EjF) were respectively, 29.12 ± 7.52years, 26.00 ± 4.23kg/cm^2, 26. 10 ± 13.32cm^3, 13.36 ± 8.59cm^3 and 47.38 ± 17.58%. The means FGbV in pregnant women was 26.12 ± 13.35cm^3, EjF was 47.41 ± 17.61%. The mean FGbV and EjF in the non– pregnant women was 74.15 ± 28.91cm^3 and 77.58 ± 9.74% respectively. Age showed no statistically significant difference with FGbV and EjF. Statistically significant difference existed between BMI and FGbV but not with EjF. No statistically significant difference existed between FGbV and PGbV. The mean fetal gestational age was 25.81 ± 8.41 weeks, and showed no statistically significant relationship with FGbV or EjF.

Conclusion: Fasting gallbladder volume and gallbladder motility among pregnant women in Anambra state were both reduced.

Keywords: *Gallbladder, Pregnancy, Sonography, Fasting gallbladder volume, Ejection fraction*

Introduction

The gallbladder is a hollow elastic organ with an average volume of 30-50 ml in adults that functions as the body's bile storage tank. It serves as the repository for bile produced in the liver[1] Some of the bile components are synthesized by the liver cells (hepatocytes) while the rest are extracted from the blood by the liver[2] Bile is a thick alkaline fluid secreted by the liver and stored temporarily in the gallbladder. It consists of water, electrolytes, bile acids, cholesterol, phospholipids and conjugated bilirubin[2]. Between meals, secreted bile is stored in the gallbladder where 80-90% of the water and electrolytes can be absorbed, leaving the bile acids and cholesterol[3]. During a meal, the smooth muscles in the gallbladder wall contract, leading to the bile being secreted into the duodenum to rid the body of waste stored in the bile. The bile salts also help to emulsify fats in the duodenum, so that they can be more easily digested by pancreatic lipase into fatty acids and glycerol[3].

The gallbladder is roughly pear-shaped and its size and shape varies among individuals, with the volume of bile it contains at any point in time. It is a gastrointestinal organ located within the right hypochondriac region of the abdomen[4] It is intraperitoneal and lies within a fossa formed between the inferior aspects of the right and quadrate hepatic lobes. In adults, the gallbladder measures approximately 7- 10 cm in length and 4 cm in diameter when fully distended[5] During embryological development, the gallbladder and biliary tree develop from outpouchings of the duodenum at the end of the 4th week of gestation[6]. The gallbladder is divided into three sections: the fundus, body and neck. The fundus is the rounded base, angled so that it faces the abdominal wall. The body lies in a depression on the surface of the lower right lobe of the liver. The neck tapers and is continuous with the cystic duct, part of the biliary tree[5]. The cystic duct unites with the common hepatic duct to become the common bile duct. The biliary tract refers to the liver, gallbladder and bile ducts and how they work together to make, store and secrete bile[2].

The gallbladder has tone reflecting inherent compliance of smooth muscle and fibroelastic tissues within its walls. Smooth muscle tone is continually influenced by neural and humoral factors. It also contains neural tissues connecting it to the enteric nervous system. These all contribute in making the gallbladder perform its function[6]. The motility and emptying of the gallbladder are stimulated by food.

Three common types of gallbladder disorders are cholelithiasis (characterized by the formation of gallstones and/or the accumulation of biliary sludge in the gallbladder or cystic duct), cholecystitis (characterized by chronic or acute infection and inflammation of the gallbladder) and functional gallbladder disorder (characterized by an inability of the gallbladder to contract or to release bile)[8] The gallbladder though not a major organ of digestion, can experience changes in functional status during pregnancy which poses great risk for the pregnant woman. In as much as not every woman in cyesis is at risk; body changes associated with pregnancy can have serious impact on the gallbladder, presenting complications that could affect the overall health of the baby and even the pregnant woman[9].

It is a known fact that women are at higher risk of presenting with cholelithiasis than men. Pregnancy is associated with greater risk because in this state, more oestrogen is produced by the body. Estrogen increases biliary cholesterol secretion, causing cholesterol supersaturation of bile resulting in decreased gallbladder contractions[9]. This condition is known as cholestasis of pregnancy and slows the emptying of bile into the duodenum. Besides, the gallbladder varies in size, shape and position between different people[7]. It also varies in shape and size between the fasting and post prandial states[10]. Bile is a yellowish liquid made by the liver. It helps the body break down fat and get rid of waste[8]. If bile is not needed for digestive purposes, it is stored for future use in the gallbladder[11]. Under normal conditions, eating is the main stimulus to gallbladder emptying.

Meals containing fat, especially polyunsaturated fat, are the most powerful stimuli but protein and carbohydrate meals also result in some emptying[12-14]. The gallbladder normally contracts when foods such as fats or fatty acids are in the duodenum. These foods stimulate the duodenal mucosa to secrete the hormone cholecystokinin (CCK). Cholecystokinin is a peptide hormone synthesized by the small intestine. It is secreted when fatty food enters the digestive tract. Gallbladder motility is controlled by a complex interplay of hormonal and neural factors. It is being recognized increasingly that the key mediators of gallbladder motility – the gastrointestinal peptides – act through both neural and hormonal pathways to influence gallbladder motility[15]. When triggered by the appropriate hormonal responses, the gallbladder goes ahead to release bile into the duodenum for the digestion of fatty foods. The gallbladder can store up to a volume of 50 ml of bile under normal conditions. Being a distensible sac, it can store more quantity when the cystic duct is obstructed.

During the fasting period the gallbladder maintains a moderate tonic contraction that is superimposed with nonpropulsive and propulsive contractions[16]. The non-propulsive contractions are probably to ensure the insoluble bile contents are kept in solution, to avoid precipitation of contents like cholesterol, avoiding the development of gallstones. The propulsive contractions result in small fractions of bile being emptied into the duodenum during the interdigestive period[17]. In the digestive period strong gallbladder contractions and sphincter of Oddi relaxation lead to the high rates of bile discharge flowing into the common bile duct and duodenum[17]. During this period, the gallbladder motor activity like the rest of the gastrointestinal tract is influenced by the three phases of digestive process: cephalic, antral, and duodenal[18]. The cephalic phase is initiated by stimuli that activate the central nervous system, as individuals are exposed to olfactory, visual and the taste of food.

This phase is mediated by preganglionic vagal fibres that synapse with postganglionic cholinergic neurons[18]. It is estimated that as much as 30-40 % of the gallbladder bile may be emptied during this phase[18] Once food reaches the stomach it triggers an antral- gallbladder reflex also mediated by vagal fibers. The gallbladder empties most of its remaining contents during the intestinal phase induced by the release of CCK from the duodenum and proximal jejunum[19]. Duodenal CCK contracts the gallbladder mostly by acting directly on cholinergic neurons and like with the pancreas, and it may also activate long reflexes through the vagus nerve[17] .

Imaging modalities employed in evaluating diseases of the gallbladder include ultrasonography, oral cholescystography, endoscopic retrograde cholangiopancreatography (ERCP), computed tomography (CT), magnetic resonance imaging (MRI) and cholescintigraphy (nuclear medicine HIDA scan)[20]. Ultrasonography is the modality of choice in examining the gallbladder of pregnant women because it is cheap, non-invasive, safe and repeatable without known adverse effects on the pregnant women or the foetus[21]. Furthermore, ultrasonography is usually readily available and does not utilize ionizing radiation. This presents it as a safe imaging examination in pregnancy.

As real-time ultrasonography is a cheap, noninvasive, relatively easy, validated and reproducible technique, it can be repeated over time to document time-related changes of gallbladder motor function. Ultimately, functional ultrasonography estimates gallbladder shape and volume in the fasting state and in response to a test meal (liquid or mixed solid-liquid, provided there is sufficient fat content) or exogenous stimulus (e.g., i.v. cholecystokinin)[17]. Patients are scanned in the supine, right anterior oblique position. Longitudinal and axial cross-sectional images of the gallbladder in its largest dimensions are obtained in triplicate. Average measurements are used for calculation of the gallbladder volume. The volume of the gallbladder (V) is subsequently calculated using the ellipsoid method described as: $V = 0.52 \times L \times W \times H$, where L is the length, W is the width, and H is the height or depth of the gallbladder[22].

All subjects are studied in the morning after an overnight fast. Fasting volume of the gallbladder (ml) represents the mean of three volume measurements taken 5 min apart.

After taking the fasting volume, gallbladder contraction is stimulated by a fatty meal. Gallbladder contraction and refilling are monitored with ultrasonography and images are taken over time to document time related changes of gallbladder volume. The difference between the basal volume and the corresponding residual Volume represents the gallbladder ejected volume (ml). The gallbladder ejection fraction (GBEF) (%) is calculated according to the formula[23]: $GBEF(\%) = 1 - (\text{residual volume/fasting volume}) \times 100$.

Although functional ultrasonography of the gallbladder has been mainly used for research purposes in specific referral centers, its simplicity makes such a technique appealing in the clinical setting to assess gallbladder motor function both in healthy and diseased subjects[24]. Indications include the study of healthy subjects and patients during pathophysiologically relevant conditions; in particular when subjects are at risk for gallbladder stasis and gallstone disease or during gallstone disease when a decision concerning medical dissolution therapy is required[25]. A decreased emptying rate of the gallbladder has been demonstrated in patients with gallstones, dyspepsia, diabetes mellitus, obesity[25, 26-28], and in patients operated on with Billroth type II for duodenal ulcer[29]. Any of these conditions during pregnancy is most likely to present a greater problem. Pregnancy is a time when the gallbladder is vulnerable to various conditions[29].

Studies have shown that women are more likely than men to develop gallstones[30] and pregnant women are more at risk because their bodies are secreting more estrogen which can lead to an increased amount of cholesterol in the bile, while also reducing gallbladder contractions[31]. This presents a condition known as cholestasis of pregnancy. In this condition, bile does not empty from the gallbladder easily. Complications that could arise from this include premature birth and still birth[31].

There is paucity of data on gallbladder changes during pregnancy in this locality and so this study is focused on exposing the potential for the gallbladder to malfunction during pregnancy. This will make pregnant women watch out for tell-tale signs of such disorders and report to their physicians on time. In addition, it will buttress the need for obstetricians to make sonographic examination of the gallbladder, a routine in caring for pregnant women.

Materials and methods

A prospective cross-sectional study design was adopted to study the relative gallbladder size and motility among apparently healthy pregnant women in Anambra State, Nigeria. The study was carried out at two radiodiagnostic centres: one at Onitsha and one at Awka, both in Anambra State Nigeria. Power analysis software, G* Power 3.0.10 (University of Dusseldorf, Germany) was used to obtain the studied sample of 201 pregnant women of between 19years and 46years. The age matched control group comprised 27 apparently healthy non-pregnant women volunteers.

For the experimental group, inclusion criteria includes being above 18 years, having clinical evidence of pregnancy, having functioning gallbladder and having no evidence of gastrointestinal and/ hepatobiliary diseases, no history of cardiovascular or cerebrovascular disease and consenting to participate in the study. The same inclusion criteria apply to the control group except that there should be no clinical evidence of pregnancy.

A convenience sampling method was used in selecting the desired sample for the study.

Before commencement of the study institutional ethical approval: ERC/FHST/NAU/2018/048 was obtained. Informed consent was also obtained from each participant. Approval was also obtained from the management of the study centres.

Data collection

Data for this study was collected using DC-N3 Mindray ultrasound Scanner with a 3.5MHz convex transducer at each of the centres. For anthropometric measurements, a balanced beam scale was used for measurement of weight while a flexible but non-stretchable insertion tape was used for height measurement.

For anthropometric measurements of body weight and height, subjects were asked to remove their heavy outer garments (jacket, coat, trousers, skirts and hair ornaments) and shoes. In measuring the body weight, a balanced beam scale was placed on a hard- floor surface. The scale was balanced with both sliding weights at zero and the balance bar aligned. The subject was asked to stand on the centre of the beam balance platform, weight evenly distributed on both feet. The weight was moved until the beam balanced.

The body weight (in kg) was read and recorded. For the height measurement, a flexible but non-stretchable insertion tape was attached to the erect wall, close to a horizontal hard-floor surface, with the base of the tape at the floor level. The subject with bare feet, stood next to the wall with her back to the measurement tape inserted to the wall. The subject placed her feet together and the back of the head, back, buttocks, calves of the leg and the heels were touching the wall. The subject was then asked to look straight ahead. The researcher gently grasping the back of the subject's head placed the subject's head into the Frankfort Plane. The Frankfort plane (an imaginary line running from the bottom of the subject's eye orbit to the subject's ear hole) was positioned horizontal - parallel with the floor according to Songra et al[32]. The subject was then asked to maintain the position. The head piece was placed firmly on top of the subject's head, with sufficient pressure to compress the hair and make contact with the skull. Whilst the subject breathed out, a linear height measurement was made from the floor to the top of the subject's head. The height measurement was recorded in centimeters, to the nearest millimeters and later converted to meters. Body mass index (BMI) was calculated by dividing the subject's body weight (in kg) by the square of the subject's height (in metre).

For the measurement of the gallbladder dimensions, the subjects, certified normal by their referral clinicians were provided with adequate information about all the research involves (including the overnight fasting requirement and scanning procedures. The overnight fasting was to ensure maximum distension of the gallbladder making it possible for reliable and reproducible measurements to be obtained.

The subject on coming into the scan room was made to lie supine on the examination couch. The subject bared her abdomen and placed her hands under her head to widen the intercostal spaces. A clear, warm coupling gel was applied over the right upper quadrant of the abdomen, in order to ensure good ultrasound wave coupling and transmission through the abdomen.

The stomach was first scanned to confirm compliance, to the nil per oral instruction. The gallbladder was then scanned both longitudinally and transversely. The neck, fundus and body of the gallbladder were assessed. The cystic duct also, was assessed for stones. Measurements (in cm) of the maximum longitudinal and transverse axes of the gallbladder were taken thrice on a frozen gallbladder image on the oscilloscope screen and the average value for each of the set of measurements was recorded according to Adeyekun et a[33].

The obliquity of the transducer was varied while obtaining the longitudinal view, until the maximum length of the gallbladder was seen. An additional view of the gallbladder was obtained with the subject in the left lateral decubitus position. In this position, the liver was used as an acoustic window for proper visualization of the gallbladder. Measurements of the gallbladder length, width and antero-posterior diameter (height) measurements were obtained on a frozen gallbladder image on the oscilloscope screen (fig.1).

Dimensional measurements of the gallbladder were recorded. Similar scanning procedure and measurement of gallbladder dimensions were repeated after administering fatty meal (liquid tinned milk and boiled egg). Gallbladder motility was determined by assessing the gallbladder ejection fraction after the subject ingested a fatty meal.

The scans were performed by the researcher under the guidance of certified Sonographers (of over 15years of experience). Intra-observer and Inter-observer variability were tested for, before commencement of data collection. Each set of dimensions obtained by the researcher were confirmed by the sonographers and measurements were obtained thrice and the average of each set of measurements were recorded.

Data Analysis

Statistical analysis of the data obtained, was done using the MedCalc Statistical Software for Biomedical Research, version 18.5 (MedCalc Software, Acacialaan 22, b-8400 Ostend, Belgium). The volume of the gallbladder was calculated using the prolate ellipsoid formula[22] given thus: length× height ×width ×0.523. The ejection fraction, which is equivalent to the percentage of gallbladder contraction, was calculated using the formula[34]:

EF = Fasting gallbladder volume – Postprandal gallbladder volume / Fasting gallbladder volume x 100%

The effect of age, BMI and GA on gallbladder size and ejection fraction was assessed using the Analysis of Variance (ANOVA) test. Quantitative variables were assessed using mean values ± standard deviation. Statistical significance was tested for, using the Students *t*-test, with the level of significance (p- value) set at $p \leq 0.05$. Measurement data obtained was presented in tables using descriptive statistics of mean and standard deviation. Test of normality of the data distribution was done using D'Agostino-Pearson test.(table 1). The result revealed that none of the parameters was normally distributed. The age, BMI, parity, fasting gallbladder volume, post-prandial gallbladder volume and ejection fraction of the pregnant subjects were skewed to the right, as opposed to the gestational age which was skewed to the left.

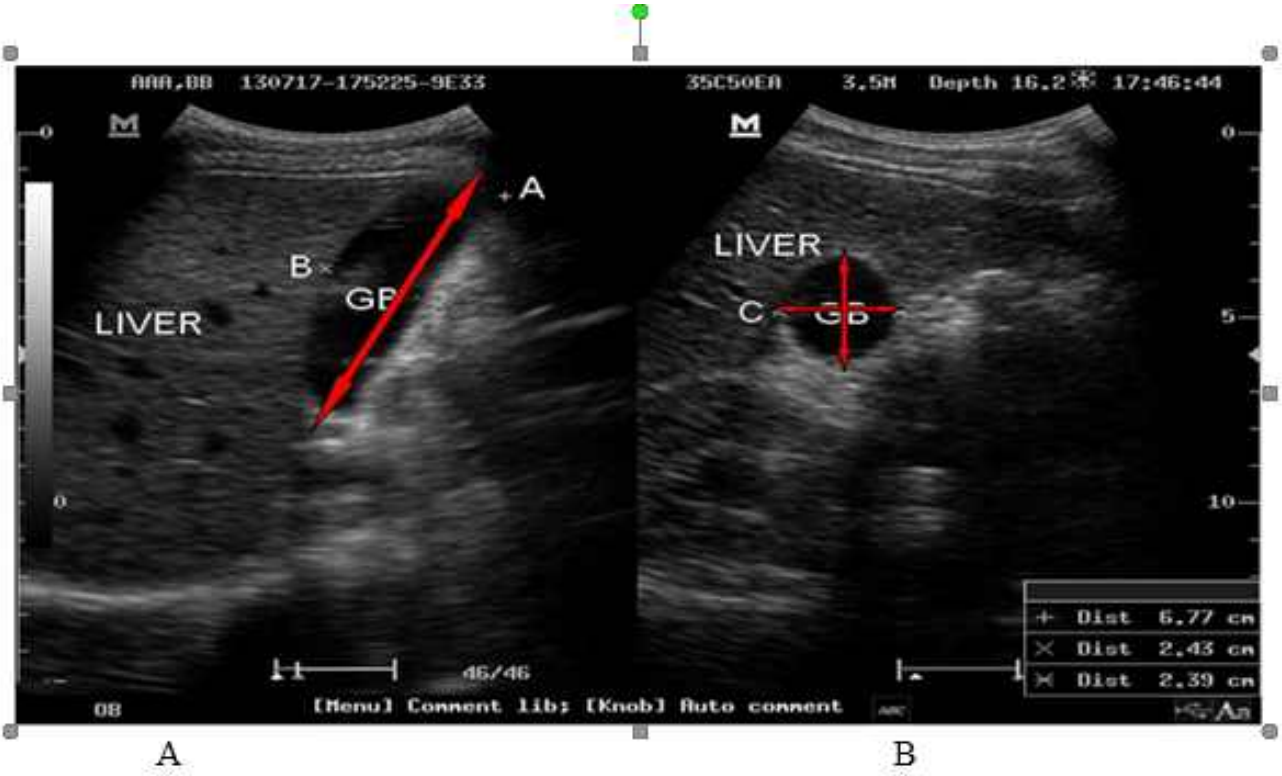

Fig. 1: Measurement axes of the gallbladder (A) sagittal and (B) transverse

Table 1: D'Agostino-Pearson test for normality

Parameters	Skewness	Kurtosis	Standard error of the mean	p-value	Remarks
Age(years)	0.31	- 0.91	0.53	< 0.0001	Non-normal
BMI(kg/m^2)	1.26	2.87	0.29	< 0.0001	Non-normal
GA(weeks)	- 0.38	- 0.45	0.59	0.0232	Non-normal
Parity	0.77	0.48	0.11	0.0001	Non-normal
FGbV(cm^3)	1.67	6.00	0.93	< 0.0001	Non-normal
PGbV(cm^3)	2.96	15.75	0.60	< 0.0001	Non-normal
EjF(%)	0.13	- 0.78	1.24	0.0009	Non-normal

Key: BMI = Body mass index; GA= Gestational age; FGbV = Fasting gallbladder volume; PGbV = Postprandal gallbladder volume; EjF = Ejection fraction.

Results

As shown in table 1, the mean age was 29.12± 7.52 years, mean BMI was 25.99± 4.23 kg/m^2. mean GA and Parity were 25.81± 8.46 weeks and 2.74 ± 1.69 respectively. The mean Fasting Gallbladder Volume, Post-prandial gallbladder Volume and Ejection Fraction were 26.10 ± 13.32 cm^3, 13.36 ± 8.59 cm^3 and 47.41 ± 17.61% respectively. The test revealed the data as an unsymmetrical distribution. bese and further analyzed(table 3b)..

The ages, BMI, parity, Fasting Gallbladder Volume, Post-prandial gallbladder Volume and Ejection Fraction of the participants were positively skewed to the right as opposed to the gestational age which was skewed negatively to the left (table 1) As a result, the data was divided into four (4) Age groups; A,B,C and D and three (3) BMI groups of Normal weight, Overweight and O

Table 3a: D'Agostino-Pearson test for effect of maternal age on Gallbladder motility

Fasting gallbladder volume(cm^3)	**Group A (Ages 19-25 years)**	**Group B (Ages 26-32 years)**	**Group C (Ages 33-39 years)**	**Group D (Ages 40-46 years)**
No of subjects	72	63	43	23
Lowest value	8.15	4.41	8.03	9.17
Highest value	106.83	65.40	56.43	54.86
Mean± S.D	24.13±14.25	26.81±12.47	28.46±12.36	25.92±14.27
Median	20.22	26.54	27.19	22.55
p-value	**(p<0.0001)reject normality**	**(p=0.0224)reject normality**	**(p=0.1685)accept normality**	**(p=0.1596)accept normality**
Ejection Fraction (%)				
No of subjects	72	63	43	23
Lowest value	11.53	17.17	14.78	13.45
Highest value	84.63	86.37	84.49	76.59
Mean± S.D	48.68±18.41	48.66±17.16	44.91±15.91	44.40±19.31
Median	50.48	48.07	40.53	41.72
p-value	**(p=0.0760)accept normality**	**(p=0.3205)accept normality**		**(p=0.1582)accept normality**

The data was divided into four (4) age groups namely- group A (ages 19-25), group B (ages 26-32), group C (ages 33-39) and group D (ages 40-46). Further analysis revealed a mean Fasting gallbladder volume of 24.13± 14.25 cm^3, 26.81± 12.47 cm^3, 28.46± 12.36 cm^3 and 25.92± 14.27 cm^3 for Age group A, B, C and D respectively. Their Ejection Fraction also presented a mean value of 48.68± 18.41%, 48.66± 17.16%, 44.91± 15.91% and 44.40± 19.31% for age group A, B, C and D respectively. D'Agostino-Pearson test for normal distribution presented the Fasting gallbladder volume of Age groups A and B as not normal while it presented the Fasting gallbladder volume of groups C and D and the Ejection fraction of the four (4) groups as a normal distribution as seen in table 3a.

Table 3b: D'Agostino-Pearson test for effect of Body-mass Index on gallbladder motility

Fasting Gallbladder Volume(cm^3/ml)	Normal weight	Overweight	Obese
Sample size	87	87	27
Lowest value	4.41	7.49	9.17
Highest value	58.19	106.83	53.64
Mean± S.D	25.19±11.46	27.55±15.66	24.75±10.39
Median	23.17	23.91	23.21
p-value	**(p=0.0157)reject normality**	**(p<0.0001)reject normality**	**(p=0.0319)reject normality**
Ejection Fraction (%)	51.06±1739%,	45.27±17.90%	42.61±15.66%

Table 4: ANOVA test between Age, BMI, GA and Fasting Gallbladder Volume

ANOVA between Age and Fasting Gallbladder Volume	**Sum of squares**	**DF**	**Mean Square**
Between groups (influence factor)	6552.5638	28	234.0201
Within groups (other fluctuations)	28945.2363	172	168.2863
Total	35497.8001	200	
F-ratio			1.391
Significance level			P=0.105
ANOVA between BMI and Fasting Gallbladder Volume			
Between groups (influence factor)	32364.2481	171	189.2646
Within groups (other fluctuations)	3133.5520	29	108.0535
Total	35497.8001	200	
F-ratio			1.752
Significance level			P=0.038
ANOVA between GA and Fasting Gallbladder Volume			
Between groups (influence factor)	7343.0034	33	222.5153
Within groups (other fluctuations)	28154.7967	167	168.5916
Total	35497.8001	200	
F-ratio			1.320
Significance level			P=0.132

Given that Ejection Fraction is a measure of gallbladder motility, variation between the Ejection Fraction and the independent factors of Age, Body Mass Index (BMI) and Gestational Age (GA) was analyzed to ascertain if the factors had any effect on gallbladder motility. The analysis revealed a no statistically significant relationship between FGbV/EjF and maternal age (p = 0.595), FGbV/EjF and BMI (p = 0.489), and FGbV/EjF and foetal GA (p = 0.600)(table 5).

Table 5 comparison among Age, BMI, GA and Ejection Fraction using the One-way Analysis of Variance (ANOVA)ANOVA between Age and Ejection FractionSum of squaresDFMean Square

Between groups (influence factor) 8003.2090 28285.8289 Within groups (other fluctuations) 53832.8966172312.9820 Total61836.1056200 F-ratio 0.913

Significance level P=0.595

ANOVA between BMI and Ejection Fraction

Table 5 comparison among Age, BMI, GA and Ejection Fraction using the One-way Analysis of Variance (ANOVA)ANOVA between Age and Ejection FractionSum of squaresDFMean Square

Between groups (influence factor) 8003.2090 28285.8289 Within groups (other fluctuations) 53832.89661723 12.9820Total61836.1056200

F-ratio

0.913Significance level P=0.595

ANOVA between BMI and Ejection Fraction

Between groups (influence factor)53075. 3414171310.

821Within groups

(other fluctuations) 8760.764229302. 0953 Total 61836.1056200 F-ratio 1.027 Significance level P=0.489

ANOVA between GA and Ejection Fraction

Between groups (influence factor) 9496.2294 33287.7645Within groups (other fluctuations) 52339.8763167313.4124Total61836.1056200

F-ratio

0.918Significance

level P=0.600

ANOVA between Age and Ejection Fraction	Sum of squares	DF	Mean Square
Between groups (influence factor)	8003.2090	28	285.8289
Within groups (other fluctuations)	53832.8966	172	312.9820
Total	61836.1056	200	
F-ratio			0.913
Significance level			P=0.595
ANOVA between BMI and Ejection Fraction			
Between groups (influence factor)	53075.3414	171	310.3821
Within groups (other fluctuations)	8760.7642	29	302.0953
Total	61836.1056	200	
F-ratio			1.027
Significance level			P=0.489
ANOVA between GA and Ejection Fraction			
Between groups (influence factor)	9496.2294	33	287.7645
Within groups (other fluctuations)	52339.8763	167	313.4124
Total	61836.1056	200	
F-ratio			0.918
Significance level			P=0.600

Independent sample t- test showed no statistically significant difference between the pregnant and non-pregnant subjects in terms of the mean age, mean BMI, mean FGbV, mean PGbV, and mean EjF(table 6).

Table 6: Sample t-test for difference in the measured variables between the subject groups

Subject groups	Parameters	Mean ± SD	Calculate t-values
Pregnant (n= 200)	FGbV (cm^3)	26.12 ± 13.35	-0.127
Non-pregnant (n=27)		74.15 ± 28.91	
Pregnant (n= 200)	PGbV (cm^3)	13.35 ± 8.61	
Non-pregnant (n=27)		15.17 ± 7.13	-0.009
Pregnant (n= 200)	EjF (%)	47.41 ± 17.61	
Non-pregnant (n=27)		77.58 ± 9.74	-0.104
Pregnant (n= 200)	Age (years)	29.17 ± 7.62	
Non-pregnant (n=27)		30.51 ± 7.25	-0.007
Pregnant (n= 200)		25.75 ± 4.47	
Non-pregnant (n=27)	BMI(kg/m^2)	24.50 ± 4.93	0.012

Key: FGbV= Fasting Gallbladder volume; PGbV = Postprandial gallbladder volume;

EjF = Ejection fraction. BMI = Body mass index.

Discussion

A total of 201 pregnant subjects and 27 non-pregnant subjects were studied. The age ranged from 19-46years with a mean of 29.17 ± 7.62years. The BMI ranged from 18.21 – 45.97kg/m^2 with a mean of 25.99 ± 4.23kg/m^2 . The mean fasting gallbladder volume in pregnant women was 26.12 ± 13.35cm^3 , mean postprandial gallbladder volume, 13.35 ± 8.61cm^3 and the mean ejection fraction was 47.41 ± 17.61cm3. No statistically significant difference existed in the fasting gallbladder volume, the postprandial gallbladder volume and the ejection fraction between the pregnant subjects and the non-pregnant control group.

Fasting gallbladder volume was used as a measure of gallbladder size in this study. Our study showed average fasting gallbladder volume (FGbV) of 26.12cm^3 in the pregnant subjects. This is similar to the results obtained independently by[30, 35-36]. However, contrary to the higher value of FGbV in the non-pregnant subjects than the pregnant group in our result, the result obtained by each of the authors was higher in the pregnant group than the non-pregnant group. This may be due to some physiological processes or even due to differences among individuals[7]. Other possible cause of the observed lower FGbV in the pregnant group in our study could be non-proper observation of the fasting period especially as pregnant women often feel hungry and might not withstand the temptation of taking small quantities of food before coming for the scan. Statistically, the difference in FGbV between the two groups was non-significant (t = -0.127).

In our study, both the postprandal gallbladder volume (PGbV) and the ejection fraction/motility (EjF) were higher in the non-pregnant(control group) than in the pregnant group. These findings agree with findings by Kapicioglu et al[36]. The lower EjF in the pregnant subjects could be due to secretion of estrogen during pregnancy. The estrogen reduces the contractility and predisposes to bile stasis and cholecystitis[9] and gallbladder stone formation and the condition can cause complications of pregnancy such as premature birth or stillbirth[31] .

Our study also revealed that maternal age and BMI affects gallbladder contractility/ejection fraction. The FGbV and the EjF were higher in the younger age group. The higher EjF in the younger pregnant subjects may be due high contractility due to lower estrogen secretion in the age group in accordance with the report by Panagiotopoulou et al[37] which said that estrogen secretion during pregnancy is lowest in young people. The implication is that the younger pregnant women have lower probability of having bile stasis and the pregnancy complications with it. The gallbladder motility/EjF from our result decreases with increase in BMI. This agrees with the findings by researchers[38-39] . The implication is that obese pregnant women have greater probability of pregnancy complications related to gallbladder diseases.

Conclusion

A total of 201 pregnant subjects and 27 non-pregnant subjects were studied. The age ranged from 19-46years with a mean of 29.17 ± 7.62years. The BMI ranged from 18.21 – 45.97kg/m^2 with a mean of 25.99 ± 4.23kg/m^2 . The mean fasting gallbladder volume in pregnant women was 26.12 ± 13.35cm^3 , mean postprandial gallbladder volume, 13.35 ± 8.61cm^3 and the mean ejection fraction was 47.41 ± 17.61cm3. No statistically significant difference existed in the fasting gallbladder volume, the postprandial gallbladder volume and the ejection fraction between the pregnant subjects and the non-pregnant control group. The age and BMI affected the fasting gallbladder volume and the ejection fraction. Both the FGbV and EjF decreased as both the age and BMI decreased. Foetal gestational age (GA) did not significantly affect any of the parameters apart from BMI.

Limitations of the study

A major limitation of this study is the likelihood that some of the pregnant subjects did not properly observe the fasting requirements. Hence the group had lower FGbV compared to the non-pregnant control group.

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Conflict of interest

Authors declare no conflict of interest.

References

1. Schneider G., Grazioli L., Saini S. Imaging of the Biliary Tree and Gallbladder Diseases. In: Schneider G., Grazioli, L., Saini, S. MRI of the liver. Heidelderg, Germany: Springer, 2005; 2: 237-266.
2. Boyer J.L. Bile formation and secretion. Compr.Physiol.2013; 3(3): 1035-1078. Doi:10.1002cphy.c120027.
3. Lindenmeyer C.C. Overview of the biliary function. Reviewed/Revised Sep 2021/ Modified Sep 2022. Merk &Co. Inc. Rahway NJ. USA 2023.
4. Baguley M. The Gallbladder. Teachme Anatomy series 2023. Available: https://teachmeanatomy.info./abdomin/viscera/gallbladder/ 2018. Accessed 4th August, 2023.
5. Drake R., Vogl W., Mitchell A., Gray H. Gray's Anatomy for students. Philadelphia, Elsevier/Churchill Livingstone, 2005.
6. Nagendram S., Lynes K., Hamade A. A case report on a left sided gallbladder: A rare finding during cholecystectomy. Int J Surg Case Reports, 2017; 41: 398-400.
7. Standring, S., Borley, N., Gray H. Gray's anatomy: the anatomical basis of clinical practice (40th ed.).Anniversary edition, London: Churchill Livingstone/Elsevier, 2008; . ISBN – 0 – 8089 – 2371 – 8. https://adams.marmot.org
8. Strachan, G. Gallbladder disease: What you need to know. Medical News Today. 2019. Retrived from https://www.medicalnewstoday.com/articles/312460.php. Accessed 28th June, 2023
9. Eze, C., Ezugwu E., Ohagwu, C. Prevalence of Cholelithiasis Among Adult Igbo Subjects in Nnewi, Southeast Nigeria: A Community – Based Sonographic Study. Journal of Diagnostic Medical Sonography; 2016;, 33(2): 1-8.
10. Ewunonu E. Sonographic evaluation of gallbladder dimension in healthy adults of a South-Eastern Nigerian population. Journal of Scientific and Innovative Research; 2016; 5(3): 96-99.
11. Bontrager K., Lampignano J. Textbook of Radiographic Positioning and Related Anatomy. 7th ed. St. Louis, Mo, Elsevier/Mosby, 2010; ISBN: 978- 0-323- 05410- 2.
12. Ryan J. Motility of the gallbladder and biliary tree. In: Johnson L, ed. Physiology of the gastrointestinal tract. New York: Raven Press, 1981; 473-476.
13. Everson G., Lawson M., McKinley C., Showalter R., Kern F. Gallbladder and small intestine regulation of biliary lipid secretion during intraduodenal infusion of standard stimuli. J Clin Investig; 1983; 71: 596-603.
14. Fried M., Jansen J., Harpole T., Taylor IL, Lamers CB, Reedy T.,Elashoff J., Meyer JH. Pancreatobiliary response to an intragastric amino acid meal; comparison to albumin, dextrose and a maximal cholecystokinin stimulus. Gastroenterology, 1989; 97: 1544-9.
15. Tierney S, Pitt H, Lilemoe K. Physiology and pathophysiology of gallbladder motility. Surg Clin North America, 1993; 73(6): 1267 – 1290.
16. Abiru H., Sarna S., Condon R. Contractile mechanisms of gallbladder filling and emptying in dogs. Gastroenterology, 1994; 106(6): 1652- 1661.
17. Behar J. Physiology and Pathophysiology of the Biliary Tract: The Gallbladder and Sphincter of Oddi – A Review. ISRN Physiology,2013 ; Article ID 837630. https://dx.doi.org/10.1155/2013/837630
18. Takahashi I., Kern MK, Dodds WJ, Hogan WJ, Sarna SK, Soergel KH, Itoh Z. (1986). Contraction pattern of opossum gallbladder during fasting and after feeding. Am J PhysioL, 1986; ; 250(2Pt 1): G227-G235. PMID: **3953802** DOI: 10.1152/ajpgi.1986.250.2.G227
19. Burhol P, Rayford P, Jorde R, Waldum H, Schulz T, Thompson J. Radioimmunoassay of plasma cholecystokinin (CCK), duodenal release of CCK, diurnal variation of plasma CCK, and immunoreactive plasma CCK components in man. Hepato-Gastroenterology, 1980; 27(4): 300-309

20. Eisenberg, R.L, Johnson, NM. (2007). Comprehensive radiographic pathology, ed 4, St. Louis, Mosby, 2007; p. 213.
21. Bricker L., Garcia J., Henderson J., Mugford M., Neilson J., Robert T., Martin M.A. Ultrasound screening in pregnancy: a systematic review of clinical effectiveness, cost effectiveness and women's view. Health Technology Assessment, 2000; 4(16): 1-193. Available: https://doi.org/10.3310/hta4160
22. Dodds W., Groh W, Darweesh R. Sonographic measurement of gallbladder volume. Am J Roentg., 1985; 145(5): 1009-1011.
23. Baert A, Knauth M., Sartor K. Ultrasound of the Gastrointestinal Tract. In: MEDICAL RADIOLOGY, Diagnostic Imaging. Maconi G., Bianchi, porro (Eds). . Springer Berlin Heidelberg New York, , Springer, 2006 ; 3-540-25826-4.
24. Palasciano G, Serio G, Portincasa P, Palmieri V, Fanelli M, Velardi A, Calo'Gabrieli B, Vinciguerra V. Gallbladder volume in adults, and relationship to age, sex, body mass index, and gallstones: a sonographic population study. Am J Gastroenterol, 1992; 87: 493–497
25. Fischer R, Seltzer F, Rock E, Malmud L. Abnormal gallbladder emptying in patients with gallstones. Digest Disease and Sci, 1982; 27:1019–1024
26. Marzio L, Di Felice F, Laico M, Imbimbo B , Lapenna B, Cuccurullo F. Gallbladder hypokinesia and normal gastric emptying of liquids in patients with dyspeptic symptoms. A double-blind placebo-controlled clinical trial with cisapride. Digest Diseases and Sci, 1992; 37:262–267.
27. Stone BG, Gavaler JS, Belle SH, Shreiner DP, Peleman RR, Sarva RP, Yingvorepant N VanThiel DH. Impairment of gallbladder emptying in diabetes mellitus. Gastroenterol, 1988; 95:170–176.
28. Marzio L, Capone F , Neri M, Mezzetti A, DeAngelis C, Cuccurullo F. Gallbladder kinetics in obese patients: Effect of a regular meal and a low caloric meal. Digest Diseases and Sci; 1988a 33:4–9.
29. Marzio L, Di Felice F, Celiberti V , DiGioacchino M, Mezzetti A, Cuccurullo F. Gallbladder emptying in duodenal ulcer patients having undergone Billroth II gastrectomy. Digestion, 1988; 41:223–228
30. Van Bodegraven A A, Bohmer CJ, Manoliu RA, Paalman E, Van de Klis AH, Roex AJ, Kruishoop AM, Deville WL, Lourens J. (1998). Gallbladder contents and fasting gallbladder volumes during and after pregnancy. Scand J Gastroenterol,1998; 33(9): 993-997. PMID: **9759958** DOI: 10.1080/003655298750027047
31. Nall, R. (2016). Pregnancy and gallbladder: Is it affected? Healthline. Available at https://www.healthline.com/health/pregnancy/gallbladder Accessed 28th June, 2023.
32. Songra G, Mittal TK, Williams JC, Puryer J, Sandy JR, Ireland A. Assessment of Growth in Orthodontics. Ortho Update, 2017; 10(1): 16-23.
33. Adeyekun A A, Ukadike IO. Sonographic evaluation of gall bladder dimensions in healthy adults in Benin City Nigeria. WAJR, 2013; 20(1): 4-8.
34. Festi D., Frabboni R, Bazzoli F, Sangermano A, Ronchi M, Rossi L, Parini P, Orsini M, Primerano AM, Mazzella G, Aldini R, Roda. Gallbladder motility in cholesterol gallstone disease. Effect of ursodeoxycholic acid administration and gallstone dissolution. Gastroenterol, 1990; 99(6): 1779-1785.
35. Hahm J, Park J, Song S, Cho Y, Moon K, Song Y, Lee O, Choi H, Yoon B, Lee M, Kee C, Park K. (1997). Gallbladder Motility Change in Late Pregnancy and after Delivery. Korean J Intern Med; 12(1):16-20. doi: 10.3904/kjim.1997.12.1.16
36. Kapicioglu S, Guburz S, Danalioglu A, Senturk O, Uslu M. (2000). Measurement of gallbladder volume with ultrasonography in pregnant women. Can J Gastroenterol, 2000; 14(5):403-405 PMID: **10851280** DOI: 10.1155/2000/561739
37. Panagiotopoulou K, Katsouyanni K, Petriodou E, Garas Y, Tzonou A, Trichopoulos D. Maternal age, Parity and PregnancyEstrogens. Cancer Contrl, 1990; 1(2): 119-124 PMID 2102281 doi: 10.1007/BF00053162
38. Sari R, Balci MK, Cban E, Kerayalcin U. Sonographic evaluation of gallbladder volume and ejection fraction in obese women without gallstones. J Clin Ultrasound, 2003; 31:352-357
39. Wedmann B, Schmidt G,Wegener M, Coenen C, Ricken D, Altoff J: Effects of age and gender on fat-induced gallbladder contraction and gastric emptying of a caloric liquid meal. Am J Gastroenterol 1991; 86:1765–1770.