Comparative study of gallbladder volumes in pregnancy and puerperium in a Tertiary Hospital in Nigeria

Nicholas Kogha [1], Kikelomo T Adesina [2], Joyce E Ikubor [1], Kolawole T Braimoh [3], Adewale E Oguntoyinbo[3]

Abstract

Background: While gallbladder disease often mimic other conditions, pregnant women are more at risk probably because of physiological changes in gallbladder functions in pregnancy. This study aimed to determine gallbladder volume and ejection fraction in third trimester pregnancy and compare with postpartum values.

Methods: This was a cross sectional study involving 65 pregnant women who were evaluated within 32 and 40 weeks of gestation. They were re-evaluated 40days postpartum. Patients were scanned with a commercially available Siemens Ultrasound scanner using a curvilinear probe with a transducer frequency of 3.5MHz. The fasting and 30mins postprandial gallbladder volumes were calculated using the prolate ellipsoid method. Gallbladder ejection fraction was determined using the fasting and postprandial gallbladder volumes.

Results: A total of 65 participants were included in the study, the fasting gallbladder volume (FGBV) was higher significantly in third trimester of pregnancy (50.72±21.55ml) than postpartum (25.11±11.29ml) ($p<0.001$). Postprandial gallbladder volume (PGBV) showed more increment in pregnancy (22.18±13.17ml) than after delivery (12.12±8.25ml) ($p<0.001$). A slightly higher gallbladder ejection fraction (EF) at 30minutes was found in pregnancy (56.99±15.74%) compared with after delivery (53.22±15.92%) with a significant p-value ($p<0.001$).

Conclusion: Gallbladder volumes (fasting and postprandial) are significantly higher in pregnancy than postpartum period, probably due to gallbladder hypomotility with likely risk of gallstone formation in pregnancy.

Key words: gallbladder volumes, pregnancy, pueperium, ultrasound

Date received: 3 November 2021; accepted: 6 January 2022

Highland Med Res J 2021;21(2):12-17

Introduction

Gallbladder disease is commoner in women and pregnancy has been implicated as one of the factors contributing to the development of gallstones in females.[1-3]A study carried out in Obafemi Awolowo University Teaching Hospital, Ile-Ife showed a prevalence of 2.9% of gallstone disease in pregnant women.[3] A much higher prevalence of up to 12% is shown among Caucasians.[4] The risk of developing gallstone disease is directly related to the number of pregnancies.[2] Other factors such as maternal age, high body mass index (BMI), previous oral contraceptive (OCP) use and family history of gallbladder disease may contribute to gallbladder disease in pregnancy[2,5] Approximately one-third of pregnant women with gallstones are asymptomatic.[6] The most common clinical presentations in symptomatic cases are biliary colic, acute cholecystitis, gallstone pancreatitis and jaundice.[7] Surgical studies showed that 50% of patients with asymptomatic gallstones eventually develop symptoms and 20% develop major complications.[8] The operative mortality is 0.7% in asymptomatic patients and 5% in patients with acute cholecystitis.[8]

Although the mechanism of gallbladder disease in pregnancy is not well defined, alteration in biliary lipid metabolism and gallbladder function occur during pregnancy and may contribute to the increased risk.[9]The pregnant woman experiences physiological changes to support fetal growth and development.[10] The hormonal changes that occur during pregnancy puts a woman at higher risk for gallstone formation.[9]It has been noted that hormonal changes of pregnancy decrease the contractility of the gallbladder leading to stasis, increased volume and tendency to promote precipitation of cholesterol into stones.[11] Serum concentration of progesterone, a smooth muscle relaxant, increases during pregnancy causing decreased tone or receptive relaxation of the gallbladder. This may contribute to gallbladder enlargement.[9]It has been noted that the serum progesterone concentration is highest in third trimester.[9]Other factors that may contribute to alteration in gallbladder functions during pregnancy are high oestrogen levels and impaired contractility due to cholecystokinin (CCK) secretion.[12,13]

Studies on gallbladder motility revealed increased gallbladder volume and decreased ejection fraction during pregnancy.[14,15] The gallbladder has the largest volume during the third trimester of pregnancy.[5,6] In addition, it has also been shown that fasting and

[1]Department of Radiology, Delta State Teaching Hospital, Oghara, Nigeria [2]Department of Obstetrics and Gynaecology, University of Ilorin Teaching Hospital, Ilorin, Nigeria [3]Department of Radiology, University Of Ilorin Teaching Hospital, Ilorin, Nigeria

All correspondences to:
Nicholas Kogha,
Email:nicholaskogha6@gmail.com

postprandial gallbladder volumes in pregnancy were larger than during postpartum period.[14,15] In the postpartum period after gallbladder motility is restored, sludge and stones may pass from the gallbladder to the small intestine causing biliary colic or other complication. [2]

The risk of radiation to the growing fetus has limited the use of radiological procedures such as cholecystography or radioisotopic scan in evaluating gallbladder motility in pregnant women.[16,17] Ultrasonography (US), however, can provide the measurement of gallbladder volume and ejection fraction easily and safely. [18]

Gallbladder hypomotility (reduced ejection fraction) and large gallbladder volume in pregnancy are predictors of biliary stasis and formation of biliary sludge and gallstone.[2]This study was carried out to measure gallbladder volume and ejection fraction in the third trimester and postpartum period in the same subjects in Ilorin, Nigeria, so as to compare gallbladder parameters in pregnancy and immediate postpartum period. This becomes useful for evaluation and prediction of possible risks of gallbladder in pregnancy and post delivery.

Patients and methods

This cross sectional study was carried out in the Fetal Assessment Unit (FAU) of the Department of Radiology, University of Ilorin Teaching Hospital (UITH). UITH is a tertiary health institution located along Old Jebba Road, Ilorin. Apart from directly serving the Ilorin city and Kwara State population, it also serves as referral centre for health facilities in surrounding five states namely- Kogi, Niger, Ekiti, Oyo and Osun.

A total of 65 pregnant women referred for routine obstetric scan from the Department of Obstetrics and Gynaecology, UITH, Ilorin were recruited between 32-40weeks of gestation. Gestational age was determined by last menstrual period (LMP) and early trimester Ultrasound scan

Convenience sampling was employed to select the subjects from study population. This was done by recruiting consenting patients consecutively until the desired sample size was achieved. Subjects were recruited during antenatal visit and booked for ultrasound scan in the third trimester. Subjects were counseled after which informed and written consent was obtained. Participants had at least 12 hours overnight fast before the morning of study. This was to ensure satisfactory gallbladder distension and to reduce the amount of gastric and intestinal gas.

Healthy pregnant women at 32-40 weeks gestation with singleton fetus were included in the study. However, subjects with the following criteria were excluded from the study : multiple gestation, diabetes mellitus, sickle cell anaemia, hypertension and pre-eclampsia, patients with other systemic illness such as gastrointestinal, gallbladder, liver or other endocrine diseases, patients taking medications known to affect gallbladder emptying such as calcium channel blockers, opoids, anticholinergics, progestrogens and oestrogens, post-cholecystectomy patients, patients who have allergy to liquid evaporated milk.

All booking investigations which include haemoglobin genotype (to rule out sickle cell anaemia), urinalysis (to rule out pre-eclampsia), blood glucose level assessment (in patient at risk for example obese patients and patients with positive family history of diabetes) were reviewed.

A Siemens Sonoline SI-400 ultrasound scanner with a 3.5MHz curvilinear probe and acoustic coupling gel was used for the study. A self-designed proforma was used to record fasting and postprandial gallbladder volumes as well as ejection fraction.

The patients were positioned supine on the examination couch and the abdomen exposed down to the pubic line. After applying coupling gel to the skin, a brief obstetric scan was carried out to ascertain the gestational age. This was determined using a combination of multiple biometric parameters {biparietal diameter (BPD), femur length (FL) and abdominal circumference (AC)} and was compared with published Western Normogram (Hadlock's) for each parameter.[19]

To assess the maternal gallbladder, two serial right upper quadrant scans was carried out on each patient : before drinking 120mls (2 sachets) of Three Crowns Filled Evaporated Milk (Produced by Friesland Campina WAMCO Nigeria PLC ®) containing 10.2g of fat, 8.9g of protein and 14.3g of carbohydrate) and thirty (30) minutes postprandial (after milk ingestion).

The probe was angled cephalad in both longitudinal and transverse planes. Compliance with fasting was assessed by scanning the stomach and duodenal regions for food residue or fluid. After visualization of the maximal gallbladder longitudinal outline, the length was measured on breathholding either in supine or right anterior oblique position (Fig 1a). Subsequently, the probe was rotated through 90º to obtain the maximal transverse dimensions i.e., the width and height, with the calipers crossing each other at 90º (Fig1b). Inner to outer wall dimensions were used for all measurements. Measurements were taken thrice and the average for each recorded. Measurements of gallbladder dimensions were repeated 30minutes postprandial.

Gallbladder volumes [fasting gallbladder volume (FGBV) and postprandial gallbladder volume(PGBV)] were obtained using the volume calculation for prolate ellipsoid (length x width x height x 0.523).[20]Ejection at 30

minutes was obtained using fasting and postprandial gallbladder volumes.

Ejection fraction (EF) [21] = (FGBV-PGBV)/FGBV X 100. Where FGBV is the fasting gallbladder volume and PGBV is the 30minutes postprandial gallbladder volume. Forty (40) days postpartum when patient presented to the Obstetrics and Gynaecology clinic for postnatal visit, fasting and 30minutes postprandial gallbladder volumes as well as ejection fraction as described above were obtained again on same patients and compared with third trimester values.

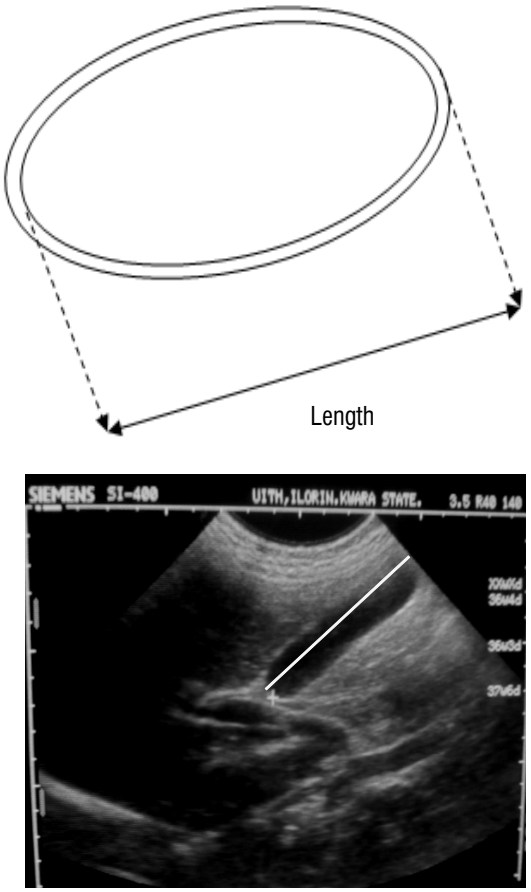

Figure 1a: Line diagram and US image of Longitudinal view of Gallbladder showing length measurements

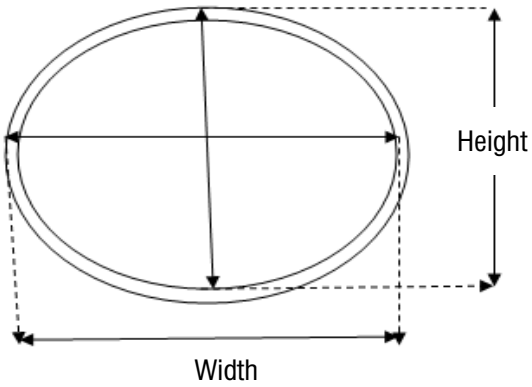

Figure 1b: Line diagram and US image of transverse view of Gallbladder showing width and height measurements

Statistical remarks

The data was entered and analyzed using the Statistical Package for Social Sciences version 21. (SPSS Inc. Chicago, IL, USA). Continuous variables like the gallbladder volume and ejection fraction were presented as means with standard deviation and compared using Paired samples t-test and Independent samples t-test as appropriate. Also, relationship between fasting gallbladder volume; and postprandial gallbladder volume and ejection fraction was also compared using Pearson's correlation coefficient. Probability (p) values < 0.05 was considered statistically significant.

Results

A total of sixty five pregnant women were evaluated within 32 and 40 weeks of gestation. They were re-evaluated 40days postpartum.

The mean FGBV in third trimester was 50.72±21.55ml while mean FGBV in postpartum was 25.11±11.29ml. The mean FGBV in third trimester was observed to be much higher than postpartum and the difference was statistically significant (t=11.58, p<0.001)..

The mean PGBV was also higher in third trimester than postpartum. The difference was also statistically significant (t=6.90, p<0.001). The mean PGBV in third trimester was 22.18±13.17ml while mean PGBV in postpartum was 12.12±8.25ml.

However, the EF in third trimester was slightly higher than postpartum, though the difference was not statistically significant (t=1.58, p=0.118). The mean EF in third trimester was 56.99±15.74% while mean EF in postpartum was 53.22±15.92% (Table 1)

Pearson's correlation coefficient was used to show relationship between mean fasting gallbladder volume and mean postprandial gallbladder volume as well as mean fasting gallbladder volume and mean ejection fraction. (Table 2)

Table 1: Comparing the gallbladder volume and ejection fraction in the third trimester of pregnancy and postpartum period

Variable	Pregnancy Mean ± SD	Postpartum Mean ± SD	T	p value
Gall bladder volume (ml)				
Fasting	50.72 ± 21.55	25.11 ± 11.29	11.581	<0.001*
30 minutes	22.18 ± 13.17	12.12 ± 8.25	6.896	<0.001*
Ejection fraction (%)	56.99 ± 15.74	53.22 ± 15.92	1.584	0.118

T: Paired samples t test; *: *p* value <0.05 is significant.

Table 2: Correlation of FGBV with PGBV and EF in third trimester of pregnancy and postpartum period

Variable	Fasting gallbladder volume R	p value
Pregnancy		
30 minutes postprandial gallbladder volume	0.766	<0.001*
Ejection fraction	-0.108	0.391
Postpartum period		
30 minutes postprandial gallbladder volume	0.811	<0.001*
Ejection fraction	-0.210	0.092

R: Pearson's correlation coefficient; *: *p* value <0.05 is significant.
*FGBV-fasting gallbladder volume
*PGBV- postprandial gallbladder volume
*EF- ejection fraction

In pregnancy, mean FGBV showed statistically significant positive correlation with mean PGBV (r=0.766, p<0.001). However, there was negative correlation between mean FGBV and mean EF, and the correlation was not statistically significant (r= -0.108, p=0.391), (Table2)

In postpartum period, mean FGBV showed similar relationship with mean PGBV and mean EF (r=0.811, p<0.001 and r=-0.210, p=0.092 respectively) (Table 2).

Discussion

The study documents the fasting and postprandial gallbladder volumes as well as ejection fractions in 32-40weeks of pregnancy and postpartum.

The mean fasting gallbladder volume was shown to be higher in third trimester than postpartum, this is in consonance with previous studies. Halm *and colleagues*[15] in Korea recorded mean fasting gallbladder volume of 25.28±14.26ml in third trimester compared to 17.44± 82ml in postpartum. Another similar study in Turkey[14] recorded 37.8±10.5ml in third trimester compared to 27.4±6.5ml in postpartum. The reason for the increase in fasting gallbladder volume in pregnancy has been attributed to oestrogen induced biliary hypersecretion during pregnancy. The higher gallbladder volume in pregnancy may result in prolong retention of bile in the gallbladder, thus predisposing to gallstone formation in pregnancy as reported by previous authors. [11,22]

Similarly, postprandial gallbladder volume was shown to be higher in third trimester than postpartum, as also demonstrated in previous studies.[14,15] This is attributed to increased levels of progesterone in pregnancy which blocks the G-protein formation in the gallbladder smooth muscle cells and this is responsible for signal transduction decoupling and impaired contractility to cholesterol after fatty meal ingestion resulting in higher postprandial gallbladder volume in pregnancy.[9]

High serum levels of oestrogen and progesterone in pregnancy have been shown by previous authors[9,11,12,13] to cause reduced gallbladder contractility or ejection fraction in pregnancy compared to postpartum period. However, mean ejection fraction in pregnancy was slightly higher than postpartum period in this study, even though fasting and postprandial gallbladder volumes in pregnancy were higher than postpartum. On the contrary, studies done in Asia and Europe showed lower EF in pregnancy than postpartum, with mean ejection fractions of 60.56±18.80% and 77.48±13.37% in third pregnancy and postpartum respectively, in Asia[15] and

10.2-39.8% and 14.9-43.2% in pregnancy and post-partum respectively, in Europe. [14] The contrary finding observed in this study may be due to the methodology. This study evaluated ejection fraction at a specified time (30min), whereas, in studies done in developed countries[14,15,23] ejection fraction was determined using serial time intervals of 15mins within an hour. Higher parity in the study area or racial differences may also be possible reasons for the different observation in this study.

Fasting gallbladder volume was shown by this study to have positive relationship with postprandial gallbladder volume and negative relationship with ejection fraction (though not statistically significant) in pregnancy and postpartum. This means that participants who showed higher fasting gallbladder volume may also record higher postprandial gallbladder volume and low ejection fraction. This, therefore, may confirm the suggestion by previous studies that fasting gallbladder volume is an indicator of gallbladder contractility.[14,15]

Conclusion

Gallbladder volumes (fasting and postprandial) are significantly higher in pregnancy than postpartum period. This may be due to gallbladder hypomotility which plays an important role in gallstone formation in pregnancy. Early detection of large gallbladder volume and poor contractility in pregnant women is important to identify pregnant women at risk of gallbladder disease.

However, there is paucity of data on comparative study of gallbladder volumes in pregnancy and puerperium in this environment. There is therefore need for further multidisciplinary and multicentre research on the subject matter in order to obtain local values to compare with results of this present study and thus generate a more generally acceptable reference values in this environment.

.

References

1 Khan MK, Jalil MA, Khan SU. Pregnancy causing gallstone disease. Mymensingh Med J. 2008; 17(2 Suppl): S91-96.

2 Richa G, Meena D, Manisha D, Ghosh U.K. Gallbladder disease in pregnancy. J Obstet Gyneaecol India. 2011; 61(1): 57-61

3 Ibitoye BO, Adisa AO, Makinde ON, Ijarotimi AO. Gallstone disease among pregnant women in a Nigerian hospital: prevalence and complications. Int J Gynaecol Obstet. 2014; 125(1):41-43

4 Ko CW, Beresford SA, Schulte SJ, Matsumoto AM, Lee SP. Incidence, natural history and risk factor for biliary sludge and stone during pregnancy. Hepatology. 2005; 41:359-365.

5 Galyan MT, Fakheri H, Abdi R, Khosh BR, Bari Z. Pregnancy related biliary sludge/stones: incidence, outcome and potential risk factors. Arch Iran Med. 2013; 16 (1): 12-16

6 Bolukbas FF, Bolukbas C, Horz M, Ince AT, Uzonkoy A, Ozturk A, Aka N, *et al*. Risk factors associated with gallstone and biliary sludge formation during pregnancy. J Gastrenterol Hepatol 2006; 21: 1150-1153.

7 Hay JE Liver disease in pregnancy hepatology. 2008; 47: 1067-1076.

8 Deutchman ME, Connar P, Hahn RG, Rodney WM. Maternal gallbladder assessment during obstetric ultrasound; results, significance and technique. J FamPract. 1994; 39: 33-37.

9 Ornella B, Tony YW, Min L, Change-Nyol P, Piero P, David QW. Cholesterol cholelithiasis in pregnant women: pathogenesis, prevention and treatment. Ann Hepatol. 2014; 13(6): 728-745.

10 Maged MC. Physiology and pharmacokinetic changes in pregnancy. Front Pharmacol 2014; 5:65.

11 Cynthia WK, Shirley AA. Incidence, natural history and risk factures for biliary sludge and stones during pregnancy. Hepatology. 2005; 41:359-365.

12 Wang HH, Liu M, Clegg DJ, Portinacasa P, Wang DQ. New insights into the molecular mechanisms underlying effects of oestrogen on cholesterol gallstone formation. Biochim Biophys Acta. 2009; 1791: 1037-1047.

13 Pazzi P, Gamberini S, Buldrini P, Gullini S. Biliary sludge: the sluggish gallbladder. Dig Liver Dis 2003; 35(3):539-545.

14 Sait K, Sevgi G, Ahmed D, Omer S, Ercument O, Mehmet U . Measurement of gallbladder volume by ultrasonography in pregnant women. Turk J Gastroenterol. 1997; 8: 429-433.

15 Hahm JS, Park JY, Song SC, Cho YJ, Moon KH, Song YH *et al*. Gallbladder motility change in late pregnancy and after delivery. Korean J Intern Med. 1997; 12(1): 16-20

16 Ziessman HA, Tulchinsky M, Lavely WC, Ganghan JP, Allen TW, Maru A. Sinclaclide-stimulated cholescintigraphy: A multicentre investigation to determine optimal infusion methodology and gallbladder ejection fraction normal values. J Nucl Med. 2010; 51(2): 277-281.

17 Kim AH, Choi BI, Lee JY, Kim KW, Han JK. Functional analysis of gallbladder using 3-D Ultrasound. Preliminary result. Ultrasound Med Biol 2002; 28(5):581-588.

18 Portinasa P, Moschetta Colecchia A, Festi D, Palasciano G. Measurement of gallbladder function by ultrasonography: towards standardization. Dig Liver Dis. 2003; 35(Suppl 3): S56-6

19 Hadlock FP, Harris RB, Snah YP. Estimation of fetal age using multiple parameter: a prospective evaluation in racially mixed population. Am J

Obstet Gynaecol. 1987; 150: 955-957.
20 Serra C, Palloti F, Bortolotti M, Caputo C, Felicani C, De Giorgio R *et al*. A new reliable method for evaluating gallbladder 3-D Sonographic examination. J Ultrasound Med. 2016; 35(2): 297-304.
21 Portincasa P, Moschelta A, Colecchia A, Festi D, Palasciano G. Measurement of gallbladder function by ultrasonography: towards standardization. Dig Liver Dis. 2003; 35(Suppl 3):S56-61.
22 Laura MS, Eldon AS. Epidermiology of gallbladder disease: cholelithiasis and cancer. Gut-liver. 2012; 6(2): 172-178.
23 Sari R, Mustafa KB, Erkan C, Umit K. Sonographic evaluation of gallbladder volume and ejection fraction in obese women. J Clin Ultrasound. 2003; 31(7): 352-357.