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Gallbladder diseases in pregnancy: Sonographic findings in an indigenous African population

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gallstones, sludge. pregnancy, ultrasonography

Abstract

Aim of the study: This study aimed to evaluate the prevalence of gallbladder disease in gravid Nigerian women and to elucidate any association with gravidity and ABO blood group. **Materials and Methods:** This was a descriptive cross-sectional study of six hundred and fifty-six (656) pregnant women recruited from March 2015 to March 2016. Hemoglobin genotype and blood group were recorded and a sonographic examination was performed using Siemens ultrasound scanner. Statistical analysis was done using STATA software for Windows. **Results:** Age had a significant association with the occurrence of gallbladder diseases (Likelihood ratio = 7.116, $P = 0.03$). Two (0.3%) pregnant women had biliary sludge, 11 (1.7%) had gallstones while 643 (98%) had normal gallbladders. Also, only one (9.1%) primigravida woman with gallstone was found in this study while 10 (90.9%) of the women with gallstones were multigravida. All the pregnant women who had gallstone(s) had blood group O. Of the two women with biliary sludge; one had blood group A while the other had blood group O. **Conclusions:** The incidence of gallbladder disease increased with age in this study. There was a higher prevalence of gallstones than sludge in pregnancy. Also, the incidence of gallstones increased with the number of pregnancies among the women with gallstones. Attention should be paid to the gallbladder during abdominal sonography in pregnancy.

Introduction

During pregnancy, gallbladder disease is often due to gallstones and biliary sludge[1]. Although gallbladder disease also occurs in men, a higher prevalence has been reported in women[2,3]. Hossain *et al.*[4] reported that gall bladder diseases are four times more common in women than men. Likewise, Eze *et al.* reported a male-to-female ratio of 2.8:1 in the prevalence of these diseases[2]. This gender predilection constitutes a risk during pregnancy, and it has been found that gall bladder disease is the second most common indication for non-obstetric surgical intervention in pregnancy[1]. Gallbladder disease in pregnancy is reportedly higher among multigravid women[5].

The prevalence of gallbladder disease also varies with geographical location. For example, in the United States, 10%–15% of the adult population has gallstones. In other populations, such as those of Latin-American countries, the prevalence of gallstones is higher, up to 50% in adult women[1]. The prevalence of gallstones in Africa is low, even though this varies from one part of the continent to another[2,6–8]. With respect to race, 70% of Native American women older than 30 years of age develop cholelithiasis. Mexican American women have an intermediate prevalence of about 14%, with Caucasians and Black women at 4% and 5%, respectively. Chilean women are also reported to be at high risk for developing gallstones[9].

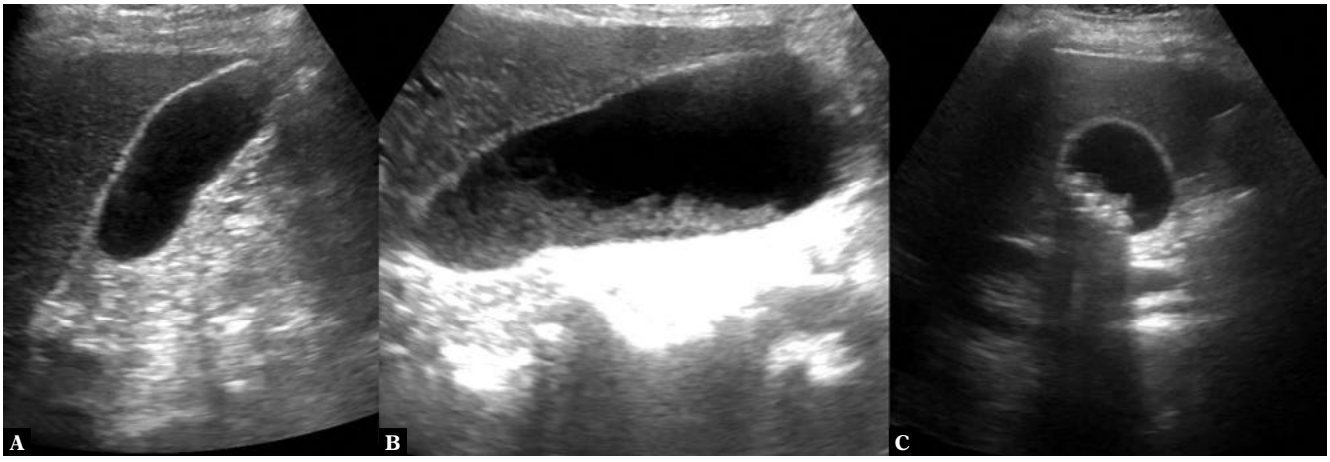

Fig. 1. *Sonograms of the gallbladder showing a normal gallbladder with anechoic lumen* **(A)**, *layering sludge* **(B)**, *and gallstones casting posterior acoustic shadows* **(C)**

A number of risk factors for gallbladder disease have been identified; the most important ones being obesity (and its consequence, the metabolic syndrome), diet and hormones[1]. The risk factors for gallbladder disease during pregnancy include history of gallbladder disease, high body mass index, and prenatal physical activity[1]. Gallbladder disease in pregnancy may be due to an increased level of estrogen during pregnancy that causes an indirect increase in cholesterol saturation of bile[5]. It could also be as a result of the inhibition of gallbladder contractility which may be caused by a higher level of progesterone[10].

The purpose of this study was to evaluate the prevalence, pattern, and characteristics of gallbladder disease in gravid Nigerian women and to elucidate any association of gallbladder disease in pregnancy with gravidity and ABO blood group.

Materials and methods

This was a descriptive cross-sectional study of six hundred and fifty six gravid women at Union Diagnostics and Clinical Services Plc, Yaba, Lagos state, Nigeria from March 2015 to March 2016. The institutional board approved the study. All the participants were recruited consecutively after informed consent had been obtained. Only asymptomatic and clinically stable women were enrolled. Biodata was obtained by oral interviews. Hemoglobin genotype and blood group were retrieved from the subjects' antenatal clinic cards.

Siemens ultrasound scanner model GM-6800A2E00 (Siemens AG, Erlangen, Germany) with a convex transducer (frequency range = 3.5–6.0 MHz) was used for the sonographic examinations. Hepatobiliary sonography was performed with the patient lying supine, augmented with left posterior oblique positioning as necessary. The third and fourth authors who have 10 and 8 years' experience with abdominopelvic and obstetrics sonography, respectively, performed the sonographic evaluations.

The normal gallbladder (Fig. 1 A) is seen on ultrasound as a pear-shaped, hollow organ with anechoic lumen[11]. Biliary sludge (Fig. 1 B) is low-level echoes without acoustic shadowing that layer in the dependent portion of the gallbladder or may fill its entire lumen[12]. Ultrasonographic features of gallstones include a highly reflective echo from the anterior surface of the gallstone (Fig. 1 C), mobility of the gallstone with change in subjects' position, and marked posterior acoustic shadowing[13]. Gallbladder wall thickening >3 mm with sonographic Murphy's sign with/without pericholecystic fluid was regarded as acute calculous cholecystitis[11]. Subjects with previous cholecystectomy, ascites, diabetes mellitus, metabolic syndrome, and pre-existing hepatobiliary diseases were excluded.

Gravidity was defined as the sum of all pregnancies (including all live births and pregnancies that terminated at <6 months or did not result in a live birth)[14]. The subdivisions of gravidity were: primigravida (first pregnancy), multigravida (2–5 pregnancies), and grandmultigravida (>5 pregnancies)[15].

The study data were analyzed using STATA (StataCorp LLC Texas, USA) software version 16 for Windows. Normality was determined using the Kolmogorov-Smirnov's test. Categorical variables like gallbladder status and blood group were presented using frequency tables. The mean values of age, gestational age, and gravidity were compared Mann Whitney U. Gallbladder status was compared to age group, gravidity, trimester, genotype, and blood group using the likelihood-ratio Chi-squared test. Statistical significance was set at $P \leq 0.05$.

Results

Table 1 shows the demographic data of subjects. The mean age of the subjects was 30.95 ± 4.56 years (range, 18–44 years) (Tab. 2). Table 3 shows the comparison of means of pregnant women with and without cholelithiasis; women with cholelithiasis had a higher mean age, gestational age and gravidity.

Tab. 1. *Descriptive statistics of subjects*

Parameter		Frequency	Percent
Gallbladder status	Normal	643	98.0
	Stone(s)	11	1.7
	Sludge	2	0.3
	Total	656	100.0
Gravidity group	Primigravida	232	35.4
	Multigravida	281	42.8
	Grandmultigravida	143	21.8
	Total	656	100.0
Gallbladder status	Normal	643	98.0
	Stone(s)	11	1.7
	Sludge	2	0.3
	Total	656	100.0
Blood group	A	97	14.8
	B	70	10.7
	O	467	71.2
	AB	22	3.3
	Total	656	100.0
Trimester	1st	76	11.6
	2nd	256	39.0
	3rd	324	49.4
	Total	656	100.0
Genotype	AA	533	81.2
	AS	114	17.4
	AC	8	1.2
	SS	1	0.2
	Total	656	100.0
Age group	11–20	5	0.8
	21–30	312	47.6
	31–40	325	49.5
	41–50	14	2.1
	Total	656	100.0

Tab. 2. *Mean and standard deviation of patient demographics*

	N	Mean	Standard deviation
Age	656	30.95	4.562
Gestational age	656	25.18	8.786
Gravidity	656	2.21	1.240

Tab. 3. *Comparison of pregnant women with and without cholelithiasis*

	Cholelithiasis (*n* = 11)		No Cholelithiasis (*n* = 645)		U	*P*
	Mean	SD	Mean	SD		
Age (years)	32.73	3.85	30.92	4.57	2563.5	0.11
GA (weeks)	26.45	9.81	25.16	8.78	3168.5	0.54
Gravidity	2.73	1.35	2.20	1.24	2.653	0.13

Of all the parameters studied, age group had a significant association with the occurrence of gallbladder disease (Likelihood ratio = 7.116, $P = 0.029$). Two (18.2%) of subjects with gallstone(s) were <31 years old while 9 (81.8%) were ≥31 years old. All (100%) of the pregnant women studied who had biliary sludge were ≥ 31 years old (Tab. 4).

Out of the 656 pregnant women enrolled, 643 (96%) had normal gallbladder, 11 (1.7%) had gallstones (cholelithiasis) and 2 (0.3%) had sludge. There were no cases of cholecystitis. Two hundred and thirty-two (35.4%) were primigravida while 424 (64.6%) had two or more pregnancies. There was one (9.1%) primigravid woman with gallstone, while 10 (90.9%) of the women with gallstones had two or more pregnancies (Tab. 4). The number of pregnant women with biliary sludge was one each in the gravid groups (Tab. 4).

Most of the subjects [467 (71.2%)] had blood group O, followed by blood group B in 70 (10.7%) subjects. Ninety-seven (14.8%) subjects had blood group A while 22 (3.4%) had blood group AB (Tab. 1). All the pregnant women with gallstones had blood group O. Of the two women with biliary sludge, one had blood group A while the other had blood group O (Tab. 4).

In total, 76 (11.6%) of the subjects were in the first trimester, 256 (39%) in the second trimester, while 317 (48.3%) were in the third trimester. Seven (63.6%) of the 11 women with gallstones were in the third trimester while two (18.2%) were in the second and third trimesters, respectively. Also, the two subjects with biliary sludge were in the third trimester (Tab. 4).

The pregnant women with hemoglobin genotype AA were 533 (81.2%) while 123 (18.8%) had hemoglobinopathies (both trait and clinical disease). Seven (63.6%) of the 11 subjects with gallstones had hemoglobin AA while 4 (36.4%) had hemoglobinopathies. The two women (100%) who had biliary sludge had hemoglobin AA (Tab. 4).

Table 5 is a succinct comparison of this study to previous studies.

Discussion

A spectrum of gallbladder diseases in pregnancy has been reported[16]. Even though many imaging modalities

Tab. 4. *Cross-tabulation of subjects' demographics and gallbladder status*

	Gallbladder status, N (row %, column %)					
	Normal	**Stone(s)**	**Sludge**	**Total**	**χ^2**	***P value***
Age group						
<31 years	315 (49.0)	2 (18.2)	0 (0.0)	317 (48.3)	*7.116*	*0.029*
≥31 years	328 (51.0)	9 (81.8)	2 (100.0)	339 (51.7)		
Gravidity						
Primigravida	230 (35.8)	1 (9.1)	1 (50.0)	232 (35.4)		
Multigravida	275 (42.8)	6 (54.5)	0 (0)	281 (42.8)	6.694	0.153
Grandmultigravida	138 (21.5)	4 (36.4)	1 (50.0)	143 (21.8)		
Trimester						
1	74 (11.5)	2 (18.2)	0 (0.0)	76 (11.6)		
2	254 (39.5)	2 (18.2)	0 (0.0)	256 (39.0)	5.179	0.269
3	315 (49.0)	7 (63.6)	2 (100.0)	324 (49.4)		
Genotype						
AA	524 (81.5)	7 (63.6)	2 (100.0)	533 (81.2)		
AS	111 (17.3)	3(27.3)	0 (0.0)	114 (17.4)	10.263	0.114
AC	8 (1.2)	0 (0.0)	0 (0.0)	8 (1.2)		
SS	0 (0.0)	1 (9.1)	0 (0.0)	1 (0.2)		
Blood group						
A	96 (14.9)	0 (0.0)	1 (50.0)	97 (14.8)		
B	70 (10.9)	0 (0.0)	0 (0.0)	70 (10.7)	9.268	0.159
0	455 (70.8)	11 (100.0)	1 (50.0)	467 (71.2)		
AB	22 (3.4)	0 (0.0)	0 (0.0)	22 (3.4)		

(CT, MRI, radionuclide imaging, magnetic resonance cholangiopancreatography – MRCP, endoscopic retrograde cholangiopancreatography – ERCP, etc.) could be used to evaluate the gallbladder and/or biliary tree, ultrasonography is the preferred imaging method in gravid women because it is fast, cheap, sensitive, and does not use ionizing radiation[9]. Cholelithiasis and biliary sludge were the gallbladder pathologies seen in this study.

Age had a significant association with the occurrence of gallbladder disease (Likelihood ratio = 7.116; P = 0.03). This is similar to findings in a study by Ferguson *et al*. where a significant correlation was found between patients' age and an increased prevalence of gallstones: the incidence of calculi was 2.9% in patients younger than 22 years of age and 5.8% in patients ≥22 years old (P = 0.031)[17]. Similarly, Gangwar *et al*.[5] found a statistically significant correlation between gallbladder diseases and advanced age, while Saha *et al*. reported that adults (both male and female) of age below 40 years were more affected[18]. Tica *et al*. also reported that the prevalence of biliary disorders is higher in older multiparous pregnant women who are in the third trimester[19]. Two (18.2%) of the subjects with gallstones in the study were <31 years old while 9 (81.8%) were ≥31 years old. All (100%) of the pregnant women with biliary sludge were ≥31 years old.

There was one (9.1%) primigravida woman with gallstone in this study while 10 (90.9%) of the women with gallstones had two or more pregnancies. This is in line with a number of studies which show that the incidence of gallstone increases with the number of pregnancies[4,20]. However, the review by Watemberg *et al*. stated that while some studies show a relationship between gravidity and gallstone occurrence, others have failed to show this relationship[10].

In contrast to eleven women with stones, two women had biliary sludge. A number of clinical events and conditions have been associated with the formation of biliary sludge[21]. Biliary sludge is a mixture of bile precipitate and bile, which is believed to be transient and a precursor to the formation of bile stones[21].

In this study, all the pregnant women who had gallstone(s) [11 (100%)] had blood group O. Of the two women with biliary sludge, one had blood group A while the other had blood group O. According to our results, blood group O was the commonest blood group seen followed by group A. This is at variance with other studies in our locality where blood group B was the second commonest. The population was also found to be in Hardy-Weinberg equilibrium[22].

In total, 76 (11.6%) of the pregnant women in this study were in the 1st trimester, 256 (39%) were in the 2nd

Tab. 5. *Gallbladder sonographic findings in pregnant women around the world*

Study	Country	Year	Design	Sample Size	Age group (years)	Stone (%)	Sludge (%)	Other findings
Stauffer[25]	USA	1982	P	338	24–40	3.5%	NS	Nil
Bartoli[26]	Italy	1984	P	36	20–34	5.6%	36%	Nil
Williamson[27]	USA	1984	P	142	19–40	11.3%	NS	NS
Mintz[28]	USA	1985	P	103	NP	3.9%	2%	Nil
Christenson[29]	USA	1986	P	175	NP	6.3%	NS	NS
Maringhini[30]	Italy	1987	P	298	26.8 ± 5.7	5.2%	26.2%	Nil
Sali[31]	Australia	1989	P	121	16–42	4.1%	Nil	Nil
Basso[32]	Ireland	1992	P	512	15–43	4.5%	Nil	Nil
Valdivieso[33]	Chile	1993	P	980	16–30	12.2%	NS	NS
Maringhini[34]	Italy	1993	P	272	27.0 ± 5.0	2%	31%	Nil
Giangrande[23]	Italy	1993	P	56	N	2.9%	10.7%	NS
Tsimoyiannis[20]	Greece	1994	P	669	25.0 ± 3.0	2%	NS	NS
Deutchman[35]	USA	1994	P	228	13–40	5.3%	NS	PLP
Hansen[36]	USA	1994	P	585	15–42	5.3%	NS	Nil
Ferguson[17]	USA	1994	P	572	NP	4.2%	NS	NS
De Alba[37]	Mexico	1997	P	292	N	14.04%	0.68%	PLP, CHL
Bodegraven[38]	NTHLD	1998	P	111	29.1 ± 4.1	5.4%	42.3%	Nil
Akute[39]	Nigeria	1999	P	3832	15–54	2.1%	NS	Nil
Rambal[40]	India	2001	P	200	16–40	6%	18%	Nil
Hossain[4]	Banglad	2003	P	1336	20–45	8.08%	U	U
Lindseth[41]	USA	2004	P	128	18–40	12.5%	NS	NS
Ko[42]	USA	2005	P	3254	NP	1.8%	4.5%	NS
Bolukbas[43]	Turkey	2006	P	97	19–35	6.3%	10.9%	NS
Tica[19]	Romania	2010	P	130	Md: 25.11	9.23%	33.85%	NS
Moghaddam[44]	Iran	2013	P	380	26.3 ± 5.0	0.7%	3.7%	Nil
Ibitoye[24]	Nigeria	2014	P	1283	14–43	2.9%	2%	PLP
Ilhan[45]	Turkey	2016	R	96 567	28.0 ± 5.0	0.06%†	NS	AC, GSP, CHG, CHDL
Kolbeinsson[46]	Iceland	2016	R	77 000	Mn: 29	0.09%	NS	AC, GSP, CHG, CHDL
Ramirez[47]	Mexico	2016	P	348	15–35	16%	NS	PLP
Idowu	Nigeria	2019	P	656	18–44	1.7%	0.3%	Nil

**AC – acute cholecystitis; Banglad – Bangladesh; CHDL – choledocholithiasis; CHG – cholangitis; CHL – cholesterolosis; GSP – gallstone pancreatitis; Md – median; Mn – mean; NTHLD – Netherlands; NS – not stated; P – prospective; PLP – polyp; R – retrospective; U – unavailable; USA – United States of America; †evaluated symptomatic cases only (excluded asymptomatic cholelithiasis)*

trimester and 317 (48.3%) were in the 3rd trimester. Most [7 (63.6%)] of the pregnant women with gallstones were in the 3rd trimester. There were two (18.2%) in the first and second trimesters, respectively. This correlates with literature, as most gallstones have been reported during the second and third trimester[23]. Also, the two pregnant women who had biliary sludge were both in the third trimester. This finding is similar to those of a study by Mendez-Sanchez *et al*.[1] who documented that new sludge or stones were found in 30% and 2% of the women, respectively, at the end of their pregnancies. Contrarily, Giangrande *et al*. observed that gallstones were found at ultrasound examination in 5 out of 56 women in the first trimester (one woman with gallstones, 4 with sludge) and 9 out of 49 women examined in the third trimester (2 women with gallstones, 7 with sludge)[20]. This present study shows a higher incidence of gallstones compared to sludge in pregnant women.

Five hundred and thirty three (81.2%) of the pregnant women studied had hemoglobin genotype AA, 114 (17.4%) were AS, 12 (1.4%) were AC, and 1 (0.2%) was SS. Gallstones were identified on ultrasound in 7 of 533 (1.3%) AA patients, 3 of 114 (27.3 %) AS patients, and in the only SS patient (100%). The trend of an increasing prevalence with the presence of haemoglobin S, is similar to findings obtained by Ibitoye *et al*.[24]. Ibitoye *et al*. studied 633 women and identified gallstones on ultrasound in 17 of 633 (2.7%) AA patients, 6 of 168 (3.6%) AS patients, and 2 of 6 (33.3%) SS patients[24].

Conclusions

In conclusion, age had a significant association with the occurrence of gallbladder disease in this study. There was a higher prevalence of gallstones than sludge. The incidence

of gallstones increased with the number of pregnancies. A similar statement cannot be made for those with sludge as only two were detected. The majority of the gallstone and biliary sludge cases were in women in the third trimester.

Being cross-sectional, this study was unable to ascertain the exact period of onset of biliary stones and sludge. However, its findings suggest the need for including abdominopelvic scan in routine obstetric examination. This is important in women at higher risk of biliary stone and sludge such as those who are in their thirties and are multigravida.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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