



Prevalence of Gallstones among Pregnant Women Using Ultrasound in Port Harcourt

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ABSTRACT

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Background: Gallstones disease constitute a common health problem that may require surgical intervention. Pregnancy is a very important pathogenetic factor favoring gallstone development and symptomatic gallstone disease is the second most common surgical abdominal emergency in gravid women. Ultrasonography is a non-invasive, reproducible and affordable procedure that can be used to evaluate the gallbladder for gallstones.

Aims and Objectives: To sonographically determine the prevalence of gallstone in pregnant women in Port Harcourt, to assess characteristics of gallbladder disease among pregnant women, and to illustrate any association with gallbladder wall thickness.

Methodology: This was a descriptive cross-sectional study, involving 316 apparently healthy pregnant subjects in Port Harcourt. Subjects underwent ultrasonographic examination of the gallbladder over a 12-month period.

Data Analysis: Data were analyzed using statistical package for social sciences (SPSS), version 21 for windows. Result was presented using frequency tables and pie chart. Categorical variables were summarized using frequency and percent while continuous variables summarized using mean and standard deviation. The chi-squared statistics was used to test for association. Binary logistic regression model was used to test the strength of association. The level of statistical significance was set at $p < 0.05$.

Results: A total of 316 pregnant women constituted the study group. The age of the study group was between 19 to 46 years with a mean age of 31.9 ± 4.8 years. Majority of the age group was 30-39 years ($n=203$, 64.2%). Of the 316 subjects, 9 (2.8%) had gallstones while 307 (97.2%) had no sonographic evidence of gallstones. Also, of the 9 subjects with gallstones, 2 (22.2%) were nulliparous, 3 (33.3%) were primiparous and 4 (44.4%) were multiparous, however no significant association between the presence of gallstone and parity. Also, no significant association between pregnancy and gallbladder wall thickness was found.

Conclusion: Prevalence of gallstone among pregnant women in Port Harcourt is 2.8%. The presence of gallstones increased with increase in parity and no significant association between pregnancy and gallbladder wall thickness was demonstrated.

KEYWORDS:

Ultrasound, prevalence, gallstones, gallbladder disease, pregnancy

INTRODUCTION

Gallstones are made in the biliary tract, mainly in the gallbladder. About 10-15% of gallstone patients have simultaneous gallbladder and common bile duct stones,

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whereas intrahepatic stones occur less frequently.¹ According to the chemical composition, there are three main types of stones: cholesterol, pigment (bilirubin), and mixed stones.¹ These stones can be asymptomatic or symptomatic; gallstones with symptoms or complications are defined as gallstone disease.² Overall, up to 20% of adults develop gallstones and >20% of those develop symptoms or complications.² Risk factors for gallstone formation are female sex, increasing age, pregnancy, physical inactivity, obesity and nutrition. Common mutations in the hepatic

Gbenga Jacob Aderibigbe et al, Prevalence of Gallstones among Pregnant Women Using Ultrasound in Port Harcourt

cholesterol transporter ABCG8 confer most of the genetic risk of developing gallstones, which accounts for ~25% of the total risk.² Diagnosis is mainly based on clinical symptoms, abdominal ultrasonography and liver biochemistry tests.²

There is striking geographic variation in gallstone prevalence, in Europe, ultrasound studies revealed a prevalence of 9 - 21% and an incidence of 0.63/100 persons/year.³ In Nigeria, a prevalence of 3.3% has been reported from Calabar in the Niger Delta region of the country of which Port Harcourt is also located.⁴ Also, a prevalence of 2.1% has been reported from the South-west region of Nigeria among pregnant women.⁵

Pregnancy induces physiological changes in many body systems. The changes in the gastrointestinal tract, biliary tree and bile are marked, and contribute to the formation of biliary sludge and gall stones.⁶ These changes are due to impaired gallbladder motility, impaired motility of the gastrointestinal tract and the lithogenic changes in the composition of bile, all of which are believed to be mediated by the hormones progesterone and estrogen.⁶⁻⁸ Idowu et al⁹ reported an increased incidence of gallstones with increase in parity among pregnant women.

Ultrasonography is a non-invasive, relatively low cost, non-ionizing and readily available imaging technique for imaging gallstones in the gallbladder.¹⁰ A report by McIntosh et al¹¹ showed an accuracy rate of 98.8% when the gallbladder was evaluated for gallstones using ultrasound. Other imaging modalities that can be used to evaluate gallstones in the gallbladder include conventional radiography, oral cholecystography, computerized tomography and magnetic resonance imaging cholangiopancreatography.¹² Conventional radiography has a limited role in diagnosing gallstones as only 15-20% is seen on an abdominal radiograph.¹² Oral cholecystography is now an obsolete method of evaluating gallstones. Magnetic resonance imaging (MRI) provides good soft tissue detail but it is expensive, not readily available and has an increased scan time. In spite of all these options, ultrasonography is widely preferred, as it is quite dynamic, reproducible and accurate.¹¹ This is in addition to its other advantages of lower cost, lack of ionizing radiation, availability, and lack of need for contrast material.

Symptomatic gallstone disease is the second most common abdominal emergency in pregnant women. The burden of disease is enormous both for the individual and healthcare resources as a result of possible complications and high cost of treatment.¹³ Symptoms often precede the onset of the three common and potentially life-threatening complications of gallstones (acute cholecystitis, acute cholangitis and biliary pancreatitis).²

Unfortunately, gallstone disease has an increased morbidity rate; this has health and economic bearing on a nation.¹⁴ In

Nigeria, its incidence is increasing probably due to modernization and increased admittance to hospitals.^{15,16} In most cases, gallstones do not cause symptoms, however about 10% becomes symptomatic within 5 years, while 20% will eventually become symptomatic within 20 years of diagnosis.^{17,18}

This study is targeted at providing more local data that will be useful in the management of gallstone disease and its complications, as well as to provide vital statistics for planning clinical services in the hospital. There is a need for local ultrasonographic reference value in this regard as there are few documented reports on the ultrasonographic prevalence of gallstones in pregnant women in Nigeria. This study seeks to determine the prevalence of gallstones among pregnant women in a typical Niger delta environment.

AIMS AND OBJECTIVES

To evaluate, by ultrasound, the prevalence of gallstone in pregnant women, to assess the characteristics of gallbladder disease among gravid women, and to illustrate any association between pregnancy and gallbladder wall thickness.

MATERIALS AND METHODS

Study design:

This was a hospital-based descriptive cross-sectional study. It involved participants between the ages of 18 years and 48 years who are pregnant. Using random sampling method, data was collected prospectively from the study group.

This study was carried out at the Ultrasound unit in the Radiology department of University of Port Harcourt Teaching Hospital (UPTH). The study group was recruited from the antenatal clinic of the hospital. UPTH is a 510-bed multi-specialist teaching hospital in the south-south geopolitical region of Nigeria. The catchment area includes much of the Niger delta region with a population of about ten million people.

This study was carried out over twelve months from November 2021 to November 2022.

Eligibility criteria:

Inclusion criteria for subjects:

- 1) Pregnant women in the first, second or third trimester.
- 2) Age between 18 to 48 years of age.

Exclusion criteria for subjects:

- 1) Age below 18 or above 48 years of age.
- 2) Chronic liver disease for example chronic hepatitis virus infection or cirrhosis.
- 3) Subjects on drugs known to favour formation of gallstones such as thiazide diuretics, octreotide, and ceftriazone.
- 4) Systemic hypertension.
- 5) Diabetes mellitus.

Gbenga Jacob Aderibigbe et al, Prevalence of Gallstones among Pregnant Women Using Ultrasound in Port Harcourt

- 6) Hypercholesterolemia.
- 7) Non-consenting subjects.

Sample size determination:

Using the formula for a comparative cross sectional study, with a known prevalence; the Leslie Fisher's formula:

$$N = \frac{Z^2P(1-P)}{(d)^2}$$

Where,

N = Minimum sample size

Z = Standardized normal deviation=1.96

P = Prevalence rate = 0.021 (prevalence of gallstones in a group of pregnant women in Ibadan)⁵

d = Tolerable error margin = 0.05

$$N = \frac{(1.96)^2 \times 0.021 \times 0.979}{(0.05)^2} = 316$$

A sample size of 316 was drawn.

Sampling technique:

Systematic probability sampling was employed in the selection of subjects in the study. A sampling frame drawn from patients referred from the antenatal clinic of UPTH was employed to randomly select the subjects.

Having obtained consent from the institutional ethical committee, the study was explained to the patients that have met the inclusion criteria. The contents of the consent form were read out and explained, the forms were duly signed by participants and a witness. Questionnaires was then administered where the research participants' biodata and demographic data such as age, gestational age, parity, blood group, body weight and height was recorded and subsequently transferred to a data sheet. All personal information was kept anonymous.

Technique of Abdominal scan:

Ultrasound scan was performed following an overnight fast or at least a minimum of 4 hours fast¹⁰ so as to allow adequate distension of the gallbladder. All patients were advised to abstain from fatty or gas forming meals like beans products and fizzy drinks from the night before the examination to the time of investigation. The patients were scanned using real-time ultrasound Canon medical system Xario 200 ultrasound scan machine with a 3-5MHz multivariable curvilinear transducer. Patient were examined in the supine, left oblique and erect positions to optimize visualization of the gallbladder and to determine where the intraluminal opacities moved with gravity where present. Coupling agent (gel) was applied on the abdomen to decrease vacuum and to ensure adequate contact between the transducer and the skin. The transducer was placed in the region of the right anterior axillary line in a subcostal or low intercostal position. The entire gallbladder was scanned in longitudinal axis (as in figure.1) and transverse axis. The ultrasound machine settings were optimized to enable greater depth penetration at a lower transducer frequency.

Criteria for defining gallstones were;

1. Structures with linear or curvilinear echoes within it.
2. Move with change in position.
3. Casting posterior acoustic shadows.

Other parameters that were assessed for include gall bladder wall thickness, presence of biliary sludge and any incidental findings.

Subjects biodata were obtained by oral interviews and documented in the data sheet.



Figure.1. Longitudinal B-mode image of the normal gallbladder showing its parts. 1-Fundus, 2-Body and 3- Neck.

ANALYSIS OF RESULTS

Data were entered into a computer spreadsheet, after recording in a patients’ datasheet. Data were analyzed using statistical package for social sciences (SPSS), version 21 for windows. Result was presented using frequency tables and pie chart. Categorical variables were summarized using frequency and percent while continuous variables summarized using mean and standard deviation. The chi-squared statistics was used to test for association. Binary logistic regression model was use test the strength of association. The level of statistical significance was set at $P < 0.05$.

ETHICAL CONSIDERATIONS

Approval was granted by the Ethical Committee of the UPTH, before commencement of the study. Participation was voluntary. Study was performed after the benefit and safety of the study had been explained to the patient, and an informed consent was obtained.

RESULTS

A total of 316 persons were scanned during the study period. The subjects were aged 19-46 years with a mean age of 31.9 ± 4.8 years [Table 1]. Majority of the subjects are in the 30-39 age group (n=203, 64.2%). One hundred and eighty-three (57.9%) of these were in the third trimester, 113 (35.8%) were in the second trimester, and 20 (6.3%) were in the first trimester. Also, 139 (44.0%) were Multiparous, 110 (34.8%) were Primiparous, while 67 (21.2%) were Nulliparous [Table 2].

Of the 316 subjects, 9 (2.8%) had gallstones while 307 (97.2%) had no sonographic evidence of gallstones. Thus, the prevalence of gallstones among the pregnant women studied is 2.8% [Figure 2]. All 9 subjects with gallstones had no symptoms. Also, 289 subjects representing 91.5% had gallbladder wall thickness within the normal limits while 27 subjects representing 8.5% had gallbladder wall thickness above the normal limit of normal (i.e. above 3mm), and 8 (2.5%) subjects had gallbladder sludge while 308 (97.5%) had no sonographic evidence of gallbladder sludge [Table 3]. Average gallbladder wall thickness of the study group was $0.23\text{mm} \pm 0.06\text{mm}$ with a range of 0.11- 0.50mm. The mean value of the normal wall thickness was $0.22\text{mm} \pm 0.04\text{mm}$ with a range of 0.11- 0.30mm, while the mean value of the abnormal wall thickness was $0.35\text{mm} \pm 0.05\text{mm}$ with a range of 0.31- 0.50mm [Table 4].

Of the 9 subjects with gallstones, 2 (22.2%) were Nulliparous, 3 (33.3%) were Primiparous and 4 (44.4%) were Multiparous, there was no significant association between the presence of gallstone and parity among study participants, P value = 0.995 [Table 5].

Also, of the 9 subjects who had gallstones in this study, 5 were in the third trimester, 4 were in the third trimester, and none was found in the first trimester however there was no significant association between the presence of gallstone and the trimester among study participants (P value = 0.854) [Table 6].

Though the gall bladder wall thickness slightly increased as the pregnancy developed from first to third trimester, there was no significant relationship between Gall Bladder wall thickness and Trimester, P value = 0.447 [Table 7].

Table 1: Age characteristics of the study participants

Variable	Frequency (n=316)	Percent (%)
AGE GROUP (years)		
<20	2	0.6
20-29	96	30.4
30-39	203	64.2
≥40	15	4.7
Mean±SD, range	31.9 ± 4.8 , 19- 46	

Table 2: Obstetric history of the study participants

Variable	Frequency (n=316)	Percent (%)
Trimester		
First	20	6.3
Second	113	35.8
Third	183	57.9

Parity		
Nullipara	67	21.2
Primipara	110	34.8
Multipara	139	44.0

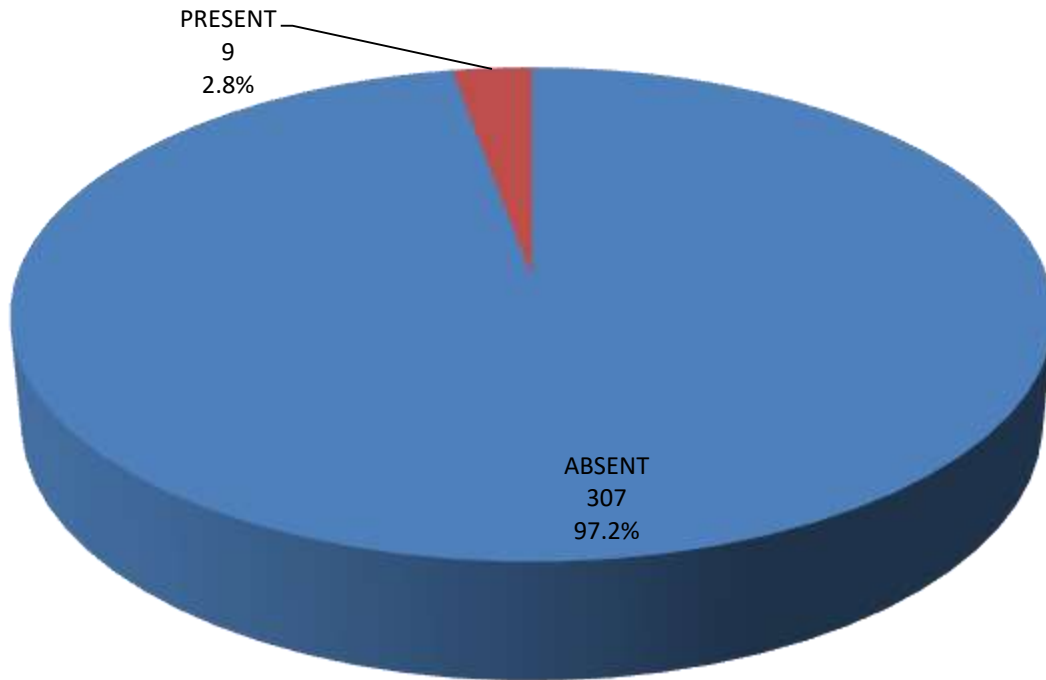


Figure 2: Prevalence of gall stone among study participants

Table 3: Sonographic characteristics of the study participants

Variable	Frequency (n=316)	Percent (%)
Sludge		
Absent	308	97.5
Present	8	2.5
Gall bladder wall thickness		
Normal	289	91.5
Abnormal	27	8.5

Table 4: Gall Bladder wall thickness characteristics among study participants

Gall Bladder wall thickness	Mean	N	Std. Deviation	Minimum	Maximum
Normal	0.22	289	0.04	0.11	0.30
Abnormal	0.35	27	0.05	0.31	0.50
Total	0.23	316	0.06	0.11	0.50

Table 5: Association between gall stone and parity among study participants

Variable	Gall Stone		Fisher's exact	P value
	Present, n = 9	Absent, n = 307		
Parity				
Nullipara	2(22.2)	65(21.2)	0.011	0.995
Primipara	3(33.3)	110(34.8)		
Multipara	4(44.4)	139(44.0)		

Table 6: Association between gall stone and pregnancy trimester among study participants

Variable	Gall Stone		Fisher's exact	P value
	Present, n = 9	Absent, n = 307		
Trimester				
First	0	20	0.327	0.854
Second	4	109		
Third	5	178		

Table 7: Relationship between Gall Bladder wall thickness and Trimester

Variable	Gall Bladder Wall thickness	ANOVA	P value
	Mean±SD		
Trimester			
First	0.227±0.061	0.807	0.447
Second	0.228±0.060		
Third	0.233±0.058		

DISCUSSION

Gallstones are more prevalent in Europe and America than in Asia and Africa.¹⁵ Pregnancy has been identified as a very important pathogenetic factor favoring gallstone formation.⁸ The prevalence of gallstones among the pregnant women studied in our Port Harcourt based study is 2.8%. Similar prevalence values have been reported among pregnant women across Nigeria: Akute et al⁵ reported a gallstone prevalence of 2.1%, Ibitoye et al¹⁹ documented a gallstone prevalence of 2.9%, while Idowu et al⁹ reported a lower gallstone prevalence of 1.7% among pregnant women. These values are lower than the prevalence of 3.3% reported from the general population in Calabar, a city located about 146 km east of Port Harcourt.⁴ Larger studies to determine the prevalence of gallstones in the general population in Nigeria is required. Also, a similar prevalence value of 2% among pregnant women studied by Tsimoyiannisi et al²⁰ in Greece is worthy of mention.

Valdivieso et al⁸ in Chile showed the prevalence of gallstones in pregnant women to be 12.2% when compared to 1.3% in the control population indicating that the risk of gallstone formation in pregnant women is about 9 times more, compared to the general population. Bolukbas et al²¹ also found a prevalence of 6.3% which is higher than the prevalence of gallstones in nulliparous healthy controls. According to Hossain et al²², prevalence of gallstones in

pregnant woman studied was 8.08%, this was also higher compared to the generalized prevalence in the same community. Furthermore, a study done in India by Gangwar et al²³ also buttress the fact that gallstones are common during pregnancy, with a prevalence of 13.12% among pregnant women. Also, Mousa et al²⁴ in a study done in Baghdad, recorded an overall prevalence of gallbladder disease of 10.8% out of 500 pregnant women studied. The wide variations in prevalence values might be due to the fact that gallstone formation is multifactorial with interplay of various risk factors which include geographical factors, dietary habits, physical activity, socioeconomic status, BMI and family history.² Our finding in regards to the prevalence of gallstones among pregnant women seem to suggest that pregnancy is not as important as other risk factors in Nigeria. The high prevalence of gallstones during pregnancy have been explained by the following: impaired gallbladder motility, impaired motility of the gastrointestinal tract and the lithogenic changes in the composition of bile that occur during pregnancy. Also, there is inhibition of gallbladder contraction as a result of increased smooth muscle relaxation mediated by progesterone, and reduced biliary transportation of bile mediated by estrogen, all of which results in cholestasis of pregnancy.⁶⁻⁸

In this study, of the 9 subjects with gallstones, the highest percentage of 44.4% was found among multiparous subjects

and more gallstones were found among primiparous subjects compared to gravid nulliparous subjects, however there was no significant association between the presence of gallstone and parity among study participants (P value = 0.995). In other studies, parity have been shown to have a significant association with the occurrence of gallbladder diseases.^{8-9, 19-24} Notable among the aforementioned studies, is the study by Idowu et al⁹ in which the incidence of gallbladder disease increased with increase in parity, with 90.9% of the women with gallstones having had 2 or more pregnancy carried to term. These findings could be explained by the fact that with each confinement, there is recurrent exposure to high estrogen levels, resulting in a cumulative increase in the chance of developing gallstones subsequently in life.²⁵ the lack of association in this study compared to other studies mentioned above may be due to differences in the sample size.

It is important to note that the pregnant women in the index study with gallstones were asymptomatic, this finding is corroborated by other previous studies.^{8, 20, 23, 24} Gallstones formed during pregnancy is said to be mostly asymptomatic and usually dissolve within months following delivery.^{8, 26}

In the current study, 289 subjects representing 91.5% had gallbladder wall thickness within the normal limits (mean value of $2.2\text{mm} \pm 0.4\text{mm}$ with a range of 1.1mm to 3mm). No significant association between pregnancy and gallbladder wall thickness was demonstrated. In a study by Mohammed et al to determine the ultrasonic gallbladder wall thickness in normal adult Nigerians so as to create standards for defining gallbladder abnormalities in Nigerians, normal gallbladder wall thickness in non-pregnant healthy female adults was found to range from 1.7mm to 2.7mm with a mean of $2.196 \pm 0.504\text{mm}$.²⁷ This similarity shows that gallbladder wall thickness is unaffected by pregnancy in healthy pregnant women. Also, 27 subjects representing 8.5% had gallbladder wall thickness above the normal limit of 3mm (mean value of $3.5\text{mm} \pm 0.5\text{mm}$ with a range of 3.1mm to 5mm.). It is a known fact that gallbladder wall thickness greater than 3mm may be a non-specific finding, and increase in thickness may result from a large spectrum of pathological conditions, nevertheless in a few cases no pathological abnormality can be identified.²⁸ We cannot be certain if the few subjects with thickened gallbladder walls have undiagnosed asymptomatic pathologies, are hale and hearty, or simply falsely claim to be fasting (postprandial gallbladder).

Gallbladder sludge is considered transitory and a precursor to the formation of gallbladder stones.²⁹ In the current study, 8 (2.5%) subjects had gallbladder sludge while 308 (97.5%) had no sonographic evidence of gallbladder sludge. This shows that there was a higher prevalence of gallstones than gallbladder sludge in pregnancy. This is in agreement with the findings reported by Idowu et al⁹ and Mousa et al²⁴, but in variance with the findings reported by Gangwar et al²³ in which they reported higher prevalence of gallbladder sludge

than gallstones in pregnancy. The presence of both gallbladder sludge and gallbladder stones or either are commonly referred to as gallbladder disease.

Of the 9 subjects who had gallstones in this study, 5 were in the third trimester while 4 were in the second trimester, and none was found in the first trimester. However, there was no significant association between the presence of gallstone and the trimester among study participants (P value = 0.854). The findings of gallstones in the 2nd and 3rd trimester with higher frequency in the latter is in agreement with other studies.^{9, 23, 24} In the study done in Baghdad, the rate of gallstones and biliary sludge increased with increase in gestational age, in women followed up from the first to the third trimester, as 5.2% found in the first trimester rose to reach 16.6% at the third trimester with a significant association ($P= 0.003$).²⁴ Again, Idowu et al⁹, Gangwar et al²³ also stated that prevalence of gallstone disease increased with advancing gestational age. This observations could be explained by the fact that the plasma concentration of female sex hormones increases correspondingly with increase in gestational age, with the risk of gallstone formation significantly higher by the third trimester of pregnancy³⁰, also there is a change in bile composition with a decrease in cholesterol saturation during the last two trimesters of pregnancy in addition to the increment in gallbladder volume with a delayed rate of emptying during the last two trimesters.

CONCLUSION

The prevalence of gallstone among pregnant women in Port Harcourt is 2.8%. There was a higher prevalence of gallstones than sludge in pregnancy. The presence of gallstones increased with increase in parity and no significant association between pregnancy and gallbladder wall thickness was demonstrated. Studies on the prevalence of gallstones in the general population of Port Harcourt is needed.

STUDY LIMITATIONS

Due to the fact that excess fat attenuates sound beam, it was difficult to evaluate very obese patients. To overcome this, optimum scanning settings was employed and adequate pressure was applied to the abdominal wall to decrease the distance from the skin surface to the organ of interest.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

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Gbenga Jacob Aderibigbe et al, Prevalence of Gallstones among Pregnant Women Using Ultrasound in Port Harcourt

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Author`s contribution:

GJ Aderibigbe: Concept, study design, manuscript preparation, managed literature searches data collection and analysis, editing and review. C Agi: study design, manuscript editing and review. I Uwaoma-amuneke: data collection, editing and review. VN Akagbue: editing and review. All authors read and approved the manuscript.
