ORIGINAL ARTICLE

Ultrasound prevalence of gallstone disease in diabetic patients at Ibadan, Nigeria

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Abstract

Background: Gallstones (GS) in the gallbladder (GB) can be responsible for a whole spectrum of disease entities which may lead to a surgical emergency with high mortality. Diabetes mellitus (DM) is a debilitating disease that affects all systems in the body, and literature documents a higher incidence of gallstone disease (GSD) and its complications in diabetics than in the non-diabetic population. Most local studies on the association between GS formation and DM have focused on type 2 diabetics. This study was therefore designed to determine the prevalence of GS in both type 1 and type 2 DM and elucidate the demographic and social factors associated with formation of GS in diabetic patients.
Materials and Methods: Four hundred diabetic patients aged between 15 and 82 years had abdominal ultrasound to diagnose or exclude the presence of GS.
Results: GS was found in 70 (17.5%) of the 400 patients. Positive cases had a male to female ratio of 3:4 and 59 (51.92%) were above the age of 40 years with type 2 DM. Body mass index (BMI) greater than 25 kg/m^2 was seen in 56 (48.3%) patients; smoking and alcohol intake were insignificantly implicated. Jaundice was recorded in 8 (11.4%) while abdominal pain was in 24 (34.3%) patients, and 52 (74.3%) patients of those with GSD had had diabetes for more than 4 years.
Conclusion: GSD in DM is influenced significantly by age, BMI, and duration of the disease, while gender, social factors, and parity do not influence as strong associated factors.

Key words: Diabetes mellitus, gallstones, ultrasound

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Introduction

Diabetes mellitus (DM) has been frequently associated with cholelithiasis and inflammation of the biliary tract,[1-3] but the exact cause of gallstones (GS) in diabetics has not been completely clarified. It is known that the contraction of gallbladder (GB) is poor in diabetic patients, especially with autonomic neuropathy often referred to as diabetic neurogenic gall bladder.[4] On the other hand, obesit y, frequently associated with DM, may also affect cholesterol saturation in bile, which is a significant factor in GS formation.

The choice of ultrasound scanning (USS) in GB evaluation is ideal as it is cheap, non-invasive, safe, and repeatable without known adverse effect to the patient in clinical scenarios. Plain X-ray may fail to identify non-calcified GS, but USS is highly discriminatory as all stones appear echogenic. USS can detect GS as small as 3 mm in diameter.[1,2]

Most local studies on the association between GS formation and DM have focused on type 2 diabetics. The aim of this study is to determine the prevalence of gallstone disease (GSD) in both type 1 and 2 diabetic patients.

Materials and Methods

This is a prospective study and ethical approval was obtained from the institutional ethics review board. A total of 400 diagnosed diabetic patients attending the diabetic clinic over

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a 6-month period had ultrasound of the abdomen to assess the GB, cystic and common bile ducts for the presence of GS.

All consenting diabetic patients within the study period were recruited. Written or oral consent was obtained from all patients. Non-consenting patients, subjects with previous cholecystectomy, and those with known risk factors for GS, like sickle cell disease and hemolytic anemias, were excluded from the study.

Clinical and social parameters obtained included age, duration of DM, height, body weight, parity (in women), smoking history, and alcohol consumption. Subjects were classified as non-smokers, light smokers (3–5 sticks per day), and heavy smokers (more than 10 sticks per day). For alcohol consumption, subjects are classified as nominal drinkers and heavy drinkers (>2500 ml per day). Symptoms like jaundice, and abdominal pain, if present, were also recorded. Body mass index (BMI) was calculated using the formula:

$$BMI\ (kg/m^2) = weight/height^2$$

Normal BMI for adult is 20–24 kg/m^2; BMI <20 kg/m^2 is regarded as underweight; BMI 25–30 kg/m^2 is overweight; and BMI >30 kg/m^2 is obesity.

Ultrasound was performed in the morning following a 12-h overnight fast to allow for adequate distension of the GB, most appropriately on the day scheduled for a fasting blood sugar by the managing physician.

USS technique

All the patients were scanned using an ALOKA SSD-1700 ultrasound machine with a variable frequency transducer. Scanning was done in both transverse, longitudinal, and any other plane deemed necessary to adequately visualize the GB and biliary ducts. On USS, GS is seen as a reproducible echogenic mass in the GB or biliary ducts with posterior acoustic shadowing [Figure 1].

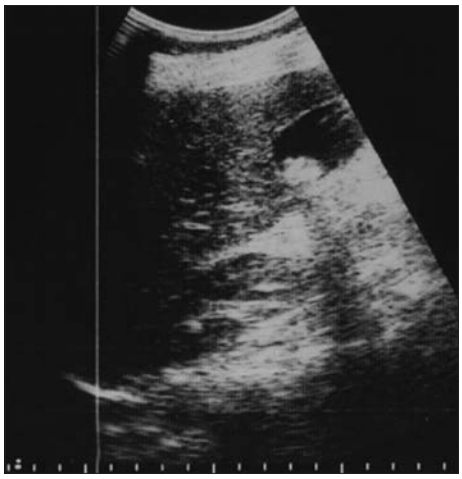

Figure 1: Ultrasound of the gall bladder showing a calculus in the gall bladder with posterior acoustic shadowing

Statistical analysis of the data was done using SPSS software version 10.0 for Windows using percentages for categorical variables, and associations between categorical variables were explored with the Chi-square test. Associations were deemed significant if *P* values were <0.05.

Results

There were a total of 400 subjects with age ranging from 15 to 82 years; mean age was 53.27 years ± 13.4 years [Table 1]. There were 185 (46.3%) males and 215 (53.7%) females. The mean weight and height were 74.83 kg and 1.67 m, respectively, with mean BMI of 26.75 kg/m^2. There were 327 (81.75%) non-smokers, 68 (17%) light smokers (3-5 sticks per day), and 5 (1.25%) heavy smokers (more than 10 sticks per day). Of the 400 subjects, 142 (35.5%) were nominal drinkers and just 10 (2.5%) were heavy drinkers who consumed more than 2500 ml on the average per day.

Of the 400 diabetic patients, 30 (7.5%) had type 1 insulin-dependent diabetes mellitus (IDDM) and the remaining 370 (92.5%) had type 2 non–insulin-dependent diabetes mellitus (NIDDM). Majority of the patients [270 (67.5%)] had been diagnosed for over 4 years; while 109 (27.25%) had their diagnosis between 1 and 4 years and 21 (5.25%) were diagnosed less than a year before this study.

The prevalence of GS was 17.5% amongst diabetics as 70 of the 400 patients had USS diagnosed GS. Of these, 3 (4.3%) were in patients with IDDM and 67 (95.7%) were in those with NIDDM. The overall prevalence of USS diagnosed GS was 10% and 18.11% in IDDM and NIDDM, respectively [Figure 2].

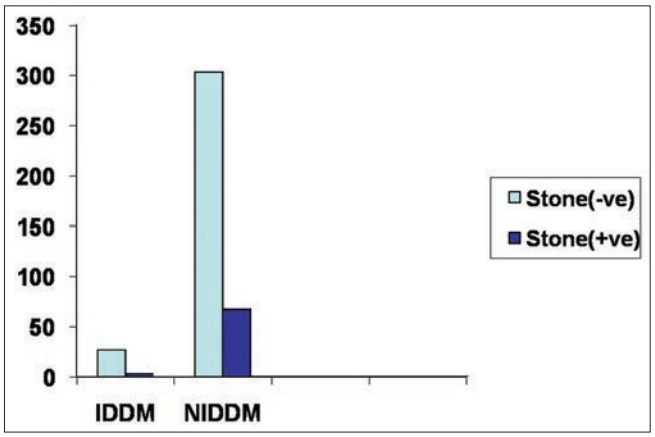

Figure 2: Bar chart representation of prevalence of gallstones in diabetic types

There was no significant association between age and GS formation; however, GSD increased with age of the diabetic patients. No GS was found in subjects less than 20 years old while the highest prevalence was in those between 51 and 70 years old. Women showed higher incidence of GS than men, but this was not significant [Tables 2 and 3].

Of the 70 diabetic patients who had USS diagnosed GSD, 8 (11.4%) gave a history of jaundice, while 24 (34.3%) complained of recurrent abdominal pain. However, all jaundiced patients with GSD had associated abdominal pain.

There was a significant association ($P = 0.03$) between heavy cigarette smoking and GS formation in diabetics [Table 4]. Of the 5 heavy smokers, 3 (60%) had GS while only 58 of 269 (17.7%) non-smokers had GS. However, the association between alcohol consumption and GS formation was not significant [Table 5].

Table 1: Age and BMI of participants

Characteristics	Frequency	Percentage
Age group (years)		
11–20	6	1.50
20–30	21	5.25
31–40	40	10.00
41–50	92	23.00
51–60	103	25.75
61–70	114	28.50
71–80	22	5.50
81–90	2	0.50
Total	400	100.00
BMI (kg/m2)		
<20	12	3.0
20–24	89	22.25
25–30	244	61.00
>30	55	13.75
Total	400	100.00

Table 3: Sex and prevalence of gallstone formation

Gender	GS absent *n* (%)	GS present *n* (%)	Total *n* (%)
Male	156 (84.3)	29 (15.7)	185 (100)
Female	174 (80.9)	41 (19.1)	215 (100)
Total	330 (82.5)	70 (17.5)	400 (100)

χ^2=0.79, P=0.37

Table 5: Association between alcohol consumption and GS formation

Alcohol consumption	GS absent *n* (%)	GS present *n* (%)
None	201 (81.00)	47 (19.00)
Mild	123 (86.60)	19 (13.40)
Heavy	6 (60.00)	4 (40.00)
Total	330 (82.50)	70 (17.50)

χ^2=5.54, P=0.06

There was a significant association ($P = 0.01$) between GSD and the BMI of diabetics [Table 6]. The highest prevalence of GS (32.7%) was in the obese category with BMI >30 kg/m^2.

Incidence of GS increased with the duration of DM as 52 (74.3%) of 70 diabetics with GSD had diabetes of greater than 4years, while only one 1.4% of patients with diabetes of less than a year had GS ($P = 0.01$).

Discussion

GS form in the GB and are responsible for a whole spectrum of disease entities ranging from simple biliary colic, acute emphysematous cholangitis (AEC) to fulminant cholangitis, necrotizing pancreatitis, and bowel perforation.[4] Mechanisms involved in GS formation include: (i) supersaturation of bile with cholesterol, consequent sedimentation, crystallization, and stone formation[5] and (ii) abnormal GB motor function with resultant delayed emptying and stasis of bile.[3,6-9] These mechanisms have been implicated in DM. Symptoms and

Table 2: Prevalence of gallstone formation within age groups

Age group (years)	GS absent *n* (%)	GS present *n* (%)	Total *n* (%)
11–20	6 (100.0)	0 (0.00)	6 (100)
21–30	9 (90.47)	2 (9.53)	21 (100)
31–40	31 (77.50)	9 (22.50)	40 (100)
41–50	81 (88.04)	11 (11.96)	92 (100)
51–60	82 (79.61)	21 (20.39)	103 (100)
61–70	93 (81.58)	21 (18.42)	114 (100)
71–80	17 (77.27)	5 (22.73)	22 (100)
81–90	1 (50.00)	1 (50.00)	2 (100)
Total	330 (87.50)	70 (17.50)	400 (100)

$\chi^2 = 5.85$, $P = 0.32$

Table 4: Association between smoking and GS formation

Cigarette smoking	GS absent *n* (%)	GS present *n* (%)
None	269 (82.26)	58 (17.74)
Mild	59 (86.76)	9 (13.24)
Heavy	2 (40.00)	3 (60.00)
Total	330 (82.5)	70 (17.5)

χ^2=7.13, P=0.03

Table 6: Prevalence of GS within BMI groups

BMI	GS absent *n* (%)	GS present *n* (%)	Total (%)
<20	11 (91.7)	1 (8.3)	12 (100)
20–24	76 (85.4)	13 (14.6)	89 (100)
25–30	206 (84.4)	38 (15.6)	244 (100)
>30	37 (67.3)	18 (32.7)	55 (100)
Total	330 (82.5)	70 (17.5)	400 (100)

χ^2=10.68, P=0.01

signs attributable to GSD include jaundice, abdominal pain, right hypochondrial tenderness, fever, and Murphy sign.[3-5,10]

De Santis *et al.*[11] concluded in an epidemiological study in Rome that an altered glucose metabolism increases the risk of developing GS. Many workers in Japan also found GSD to be prevalent in diabetic patients with an incidence as high as 48%.[8,12-14] In this study, 17.5% of the diabetic patients had GS on ultrasound. This falls within the range of previous studies of 10-32% in DM[3,7,12,13,15-17] and is higher than that in non-diabetic subjects, put at 7% by Olokoba *et al.*[15] The incidence of GS formation increases with duration of DM,[18] and in this study, 74.3% of patients with GSD had been diagnosed for over 4 years.

Diabetics are particularly prone to biliary complications from GS like acute cholecystitis and gangrene, and this has made some workers advocate prophylactic cholecystectomy in asymptomatic diabetic patients.[17,19,20] This option remains controversial.[21-23] However, some other workers showed no significant association of GS with DM.[8,9]

Previous studies from Nigeria have shown that the incidence of GSD generally increases with age,[6,16,18,24-26] with peaks above 40 years, but no significant association was recorded in this study. This study shows that GSD is more commonly seen in NIDDM (type 2) diabetes in agreement with earlier studies.[2,7,27]

As in previous studies,[6,7,10,18,25-27] there were more female (53.7%) than male diabetics in the cohort studied. The reason for this difference could not easily be deduced within the scope of this study. The incidence of GS was also higher in female diabetics (19.1%) compared to male diabetics (15.6%), but this difference was not statistically significant. This is partly based on the increased incidence of obesity in females.[16,24] The gender difference is said to be less pronounced in developed countries, where the female to male ratio is less than 1.5:1, compared to sub-Saharan Africa where the same ratio is in the range of 1.8:1-3:1.[24] A higher parity in African women compared to their counterparts in developed countries is a possible explanation for this.[11,16] Increased parity has been shown to be remotely associated with GSD.[6,12,13]

Other contributing factors to GS formation include high BMI, age, cigarette smoking, and alcohol consumption.[13,26] There is a strong association between obesity and DM, especially NIDDM, as about 80% of such patients are obese or have past history of obesity.[2,6,24,27] GS formation is up to six times more frequent in obese than in lean subjects.[6,18] High BMI in the study population is seen to predispose to GSD as 80% of those with GSD had BMI greater than 25 kg/m^2.

There was a statistically significant association between heavy cigarette smoking in diabetics and GSD, while alcohol consumption had a positive but non-significant association. These social factors as identified by previous authors may be implicated as promoters rather than being sole cause effects and it is probable that this effect is cumulative if present in an individual diabetic.[13,23,27]

Clinical diagnosis of GS may be difficult in diabetic patients due to variable clinical presentation;[27] hence, it may be beneficial to routinely examine diabetic patients using ultrasonography.[2,7,27] Majority of the study population with GSD were asymptomatic. However, all the jaundiced patients with GSD had associated abdominal pain. This was also the trend in the reports of different workers.[4,9,14] Hence, presence of these two symptoms in a diabetic patient should raise the suspicion of the presence of GS.

Conclusion

GSD often complicates DM, especially type 2 (NIDDM). There is a strong link between GSD and obesity. Increasing age is also a factor in GSD, and in the presence of diabetes the chance almost doubles. Cigarette smoking and alcohol consumption are probably only GS formation promoters rather than arbiters.

Recommendations

1. The incidence of GSD in DM in this study was about 18%; it is therefore recommended that USS of the biliary system should be part of baseline investigative modalities in diabetes, especially in NIDDM (type 2).

2. Diabetic patients who are obese and those who have had the disease for over 1-4 years should have routine US examination.

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