Nigerian Journal of Clinical Practice
June 2008 Vol 11(2):89-93

THE RELATIONSHIP BETWEEN GALLSTONE DISEASE AND GALL BLADDER VOLUME

*** A.B Olokoba, * B.J Bojuwoye, * L.B Olokoba, * K.W Wahab, * A.K Salami, ** K.T, Braimoh **A.K Inikori**

**Departments of Medicine and **Radiology,University of Ilorin Teaching Hospital, Ilorin. Kwara State. Nigeria*

ABSTRACT

Background: The role of a large gallbladder volume with regards to a predisposition to gallstones is unknown. It is likely that an increase in gallbladder volume could result in impaired gallbladder motility and bile stasis which may encourage gallstone formation. This study is therefore to determine the relationship between the presence of gallstone disease and gall bladder volume.

Methodology: One hundred type 2 diabetic patients and 100 age and sex- matched controls underwent real time ultrasonography to determine the relationship between the presence of gallstone disease and gallbladder volume. Their demographic characteristics were recorded and compared. The ultrasound examinations was done in the morning following an overnight fast (to prevent gall bladder contraction) without sedation. Longitudinal and transverse scans of the right upper quadrant was done in both the supine and left lateral positions The gallbladder volume was measured.

Result: The mean gallbladder volume in diabetic patients with gallstone disease 28.4 $\pm$ 18.6ml was higher than in those without gallstone disease 27.4 $\pm$ 14.8ml p = 0.844.The mean gallbladder volume in the controls with gallstone disease 26.5 $\pm$ 14.7ml was also higher than in those without gallstone disease 24.1 $\pm$ 12.7ml p = 0.189.

Conclusion: The fasting gallbladder volume tended to be larger in patients with gallstones (i.e both diabetic patients and controls).

Keywords: Gallstone Disease; Gallbladder Volume; Relationship (*Accepted 3 April 2007*)

INTRODUCTION

Gallstone (GS) disease is one of the most common gastrointestinal diseases seen in clinical practice. Most patients with gallstone (GS) are asymptomatic[1].

The chief constituents of GS are cholesterol, bilirubin and calcium[2]. Other constituents may include fatty acids, triglycerides, protein and polysaccharide. In the great majority of stones encountered in the western world, the principal constituent is cholesterol, which usually comprises from 70% to as much as 98% of the dried substance of the stone[3].Gallstones can be classified (based on analysis of its constituents by infra-red spectroscopy[4]) into: pure GS of cholesterol or of calcium bilirubinate (pigment stones), mixed GS (Cholesterol, calcium bilirubinate, calcium carbonate) composed chiefly of 2 or all 3 of the components, and combination stones with a nucleus of one type and a shell of another substance[4].

The pathogenic mechanism (s) by which GS form is generally agreed to be due to: alteration in the composition of bile, stasis and infection[5,6]

The risk factors for cholesterol GS are; increasing age, female gender, multi-parity, obesity, rapid weight loss, diet (those high in animal fat), drugs (such as contraceptive pills) and ileal disease or resection. Others are liver cirrhosis, haemoglobinopathy and diabetes mellitus[7].

Studies have shown that Gallbladder (GB) volumes tend to be larger in patients with GSD[8,9,10.]

This study will therefore serve as a baseline in Ilorin and indeed the whole Nigeria as similar studies have not been done locally

SUBJECTS, MATERIALS AND METHOD

This study was a case-control one. The setting of the

Correspondence: Dr A.B Olokoba
Email:drabolokoba@yahoo.com

study was the Medical Out-patient Department (MOPD) of the University of Ilorin Teaching Hospital (UITH), Ilorin. The study was carried out between June 2003 and May 2004.

Approval for the study was obtained from the Research and Ethical committee of UITH. Verbal and informed consent was obtained from participants.

100 type 2 diabetic patients and 100 age and sex matched controls underwent real time ultrasonography (USS) to determine Gallbladder volume.

Their demographic characteristics and biochemical parameters were recorded and compared.All consenting patients with confirmed diagnosis of DM [(by the WHO criteria of 1999: fasting plasma glucose concentration equal to or greater than 7.0mmol/L (126mg/dL), 2hr postprandial glucose equal to or greater than 11.1mmol/L (200mg/dL)] attending the DM clinic of the MOPD were recruited into the study. Patients labeled as having type 2 DM were those whose age at onset of disease was equal to or greater than 40 years, those who did not require insulin for survival or those who were not ketosis prone. Controls were recruited from normal hospital health workers, patients with minor ailments such as malaria and upper respiratory tract infection and students without DM.

Only patients with haemoglobin genotype Hb AA were recruited into the study. Both the study group and the controls were matched for age and sex.

The examinations were done in the morning following an overnight fast (to prevent Gall bladder contraction) without sedation.Longitudinal and transverse scans of the right upper quadrant was done in both the supine and left lateral positions.

Ultrasound findings were considered positive for the presence of GSD only in those in whom reproducible echogenic masses with possible acoustic shadows were seen.

The Gallblader volume of the patients (both diabetic patients and controls) were determined.

Blood glucose was determined using 5ml of blood collected in fluoride oxalate bottles. Blood samples were centrifuged and plasma separated.

Trinders' analytical method was used for glucose determination [11].

Equipment:

Real-time ultrasound scanner (Sonoline SL-1, Siemens Incorporated Company) with linear and sector probes of selectable frequency. 3.5 and 5.0 megahertz frequencies was used for this study.

Statistical analysis:

The data obtained were entered into a computer using the Epi- info version 6.1 statistical software for analysis.The statistical significance of means of continuous variables like age, BMI,WHR etc were estimated using the student t-test while those for categorical variables eg presence or absence of risk factors was determined using the chi-square test. Statistical significance was said to have been achieved when the p value was equal to or less than 0.05.

RESULTS

At the conclusion of the study, one hundred patients each for the diabetic group and controls completed the study. They were all native Nigerians and all had Hb AA genotype.

Demographic and anthropometric data of study subjects.

Age

The ages ranged from 25-78 years with a mean of 52.9±10.7 years for the diabetic group and 25-75 years with a mean of 49.0 ±12.5years for the controls. The study and control groups were similar in age as shown in Table 1. P= 0.062 (NS).

Body mass index (BMI)

The BMI ranged from 15.6kg/m^2 to 43.1kg/m^2 with a mean of 26.1±5.7kg/m^2 for the cases and 14.7kg/m^2 to 34.5kg/m^2 with a mean of 23.5±5.4kg/m^2 for the controls. The mean BMI for the subjects was slightly above the normal range (i.e pre-obese) while the mean BMI for the controls was in the normal range (i.e 18.5-24.9kg/m^2). The diabetic patients had a significantly higher mean BMI than the controls, P= 0.00655 (S). See Table 1.

Waist Hip Ratio (WHR)

The WHR ranged from 0.85 to 1.24 with a mean of 0.97±0.08 for the study group and 0.81 to 1.19 with a mean of 0.95±0.07 for the controls. The study and control groups were similar in their WHR, P= 0.208 (NS), as shown in Table 1.

Age distribution of patients with GS

Seventy-nine (79%) of the diabetic patients and controls fell within the age group 40-69 years.

Eleven of the diabetic patients with GS (73.3%) were in the age range 40-69 years, with six (40%) of them in the age range 60-69 years i.e seventh decade of life.

There was a steady increase in the incidence of GS in diabetic patients with age, with a peak incidence in the seventh decade i.e 60-69 years, and a decline in the eighth decade i.e 70-79 years.

Four patients (57.1%) in the control group with GS were in the age group 40-59 years. The peak incidence (57.1%) was also in the age group 40-59 years i.e fifth and sixth decades, with a steady decline towards the eighth decade i.e 70-79 years. See Table

Sex distribution of patients with gallstones

Fifty (50%) were males for the diabetic group and controls, while fifty (50%) were females for the diabetic group and controls.

In the DM group, seven of the patients with GS (46.7%) were males while eight (53.3%) were females giving a male to female ratio of 1:1.14 .

In the control group, three of the patients with gallstones were males (42.9%) while four (57.1%) were females giving a male to female ratio of 1:1.3 . This difference is not statistically significant,

Relationship between gallstones and some parameters

The mean gallbladder volume in diabetics with GS was higher than those without GS 28.4+/-18.6mL and 27.4+/-14.8mL respectively although this was not statistically significant, (p=0.844).

The mean gallbladder volume was higher in controls with GS than those without GS 26.5+/-14.7 mL and 24.1+/-12.7 mL respectively, (p=0.189).This was not significant.

Table **1. Demographic and Anthropometric Data of the Study Subjects**

Variables	Range		Mean±SD		p-value
	DM	Controls	DM	Controls	
Age (years)	25-78	20-75	52.9± 10.7	49.0 ±12.5	0.062 (NS)
BMI (kg/m^2)	15.6-43.1	14.7-34.5	26.1± 5.7	23.5 ± 5.4	0.0065(S)
WHR	0.85-1.24	0.81-1.19	0.97 ± 0.08	0.95± 0.07	0.208(NS)

KEY:
N = Number of patients
NS= Not significant
S= Significant

Table **2. Age Distribution of Patients With Gallstones**

Age group (Years)	DM SUBJECTS N	GS	%GS	N	CONTROLS GS	%GS
20-29	1	0	0	1	0	0
30-39	12	1	6.7	12	1	14.35
40-49	26	2	13.3	26	2	28.6
50-59	28	3	20.0	28	2	28.6
60-69	25	6	40.0	25	1	14.3
70-79	8	3	20.0	8	1	14.3
Total	**100**	**15**	**100**	**100**	**7**	**100**

KEY
N= Number of patients
GS= Number of patients with gallstones
%GS = Percentage of patients with gallstones

Table **3. Relationship between Gallstones and Some Parameters (Diabetic Patients)**

Parameters	Dm patients With gs Mean±SD	Dm patients With ngs Mean±SD	P-value
Age (years)	59.1 ± 9.5	51.8± 10.5	0.014 (S)
BMI (kg/m^2)	26.2 ± 5.5	25.7 ± 6.7	0.755 (NS)
WHR	0.97 ± 0.07	0.95 ± 0.07	0.414 (NS)
Gall bladder volume (mls)	28.4 ± 18.6	27.4 ± 14.	0.844 (NS)

Key:
GS = Gallstone
NGS=No Gallstones

TABLE 4. **Relationship Between Gallstones And Some Parameters (Controls)**

Parameters	CONTROLS With gs Mean±SD	CONTROLS With ngs Mean±SD	P-value
Age (years)	50.8 ±13.2	48.9±12.6	0.776 (NS)
BMI (kg/m^2)	25.5 ± 5.0	23.3 ± 5.4	0.446 (NS)
WHR	0.97 ± 0.06	0.95 ± 0.08	0.981 (NS)
Gall bladder volume (mls)	26.5 ± 14.7	24.1 ± 12.7	0.189 (NS)

Key:
GS = Gallstone
GS=No Gallstones

DISCUSSION

Literature review has shown that the prevalence of cholelithiasis is very low in most parts of Africa compared to the Western nations[7,12,13,14,15].

GS and gallbladder volume.

From this study, it was found that the mean gallbladder volume in diabetics with GS was higher than in those without GS 28.4+/-18.6mls and 27.4+/-14.8mls respectively although this was not statistically significant (p=0.844). It was also found that the mean gallbladder volume was higher in controls with GS than in those without GS 26.5+/-14.7 mls and 24.1+/- 12.7 mls respectively (p=0.189). These findings are in agreement with those of Chapma *et al*[8] and Bucceri *et al*[9] who compared the gallbladder volume in diabetic and non-diabetic controls. They found that the variations in gallbladder volume between diabetics and non-diabetic controls were influenced by the presence of GS. Chapma *et al*[8] also demonstrated that NIDDM is an independent predictor for increased gallbladder volume. Hahms *et al*[10] also found that gallbladder volume in diabetic patients was significantly greater compared with that of controls. Pazzi *et al*[12] in a review of gallbladder motor function in DM proposed that the mechanism of gallbladder emptying abnormalities in diabetes mellitus may represent a manifestation of denervation caused by visceral neuropathy, a decreased sensitivity of the smooth muscle of the gallbladder to plasma cholecystokinin, and/or decreased cholecystokinin receptors on the gallbladder wall. Hahms *et al*[10] suggested that impairment of gallbladder motility complicated by autonomic neuropathy causes stasis and results in cholesterol GS crystal formation and GS growth.

Gourtsoviannis *et al*[16] found that Greek patients with GS had larger fasting gallbladder volumes as compared to subjects without GS. Similarly Portincasa *et al*[17] working in Italy were able to establish that patients with GS exhibit gallbladder motor dysfunction which manifested as increased fasting and postprandial residual gallbladder volume. Nko'o *et al*[18] working in Cameroon concluded that impaired gallbladder emptying and/or increased fasting gallbladder volume probably played a role in lithogenesis. Kishk *et al*[19] also found that patients with larger gallbladder volume tend to form gallstones compared to controls. However Caroli-Bosc *et al*[20] did not establish a significant relationship between the presence or absence of GS and gallbladder volume amongst Frenchmen. There is a paucity of local data on this study with which the authors can compare.

CONCLUSION

The fasting GB volume tended to be larger in patients with GSD (both diabetic patients and controls). The presence of a large fasting GB volume may therefore help to identify patients who are more prone to the development of GSD.

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