African Scientist Vol. 7, No. 4, December 31, 2006
Printed in Nigeria

1595-6881/2006 $12.00 + 0.00

http://www.klobex.org

AFS 2006036/7403

The relationship between gallstone disease and gallbladder wall thickness

A. B. Olokoba†*, B. J. Bojuwoye*, L. B. Olokoba*, K. W. Wahab*, K. T. Braimoh**, A. K. Inikori** and S. A. Kuranga***

*Department of Medicine, University of Ilorin Teaching Hospital, P. M. B. 1459, Ilorin, Kwara State, Nigeria
**Department of Radiology, University of Ilorin Teaching Hospital, P. M. B. 1459, Ilorin, Kwara State, Nigeria
***Department of Surgery, University of Ilorin Teaching Hospital, P. M. B. 1459, Ilorin, Kwara State, Nigeria

(Received September 11, 2006)

ABSTRACT: **Background:** The presence of Gallstones in the gallbladder is known to cause irritation of the gallbladder wall thereby resulting in the thickening of the gallbladder wall. On the other hand, an inflamed gallbladder, with its thickened wall, has been postulated to encourage super-saturation of gallbladder bile and subsequent gallstone formation. This study was therefore designed to determine the relationship between the presence of Gallstones and Gallbladder wall thickness.

Methodology: 100 type 2 diabetic patients and 100 age and sex matched controls under-went real time ultra-sonography to determine the influence of the presence of Gallstone on Gallbladder wall thickness. Their demographic characteristics and biochemical parameters were recorded and compared. Patients with confirmed diagnosis of type 2 diabetes mellitus (DM) (by WHO criteria) had right upper quadrant abdominal scan. 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 Gallstones only in those in whom reproducible echogenic masses with possible acoustic shadows were seen. The Gallbladder wall thickness was determined.

Result: The mean Gallbladder wall thickness in diabetic patients with Gallstone was 2.8 ± 1.4mm compared with 1.9 ± 0.9mm in those without Gallstones p=0.161. The mean GB wall thickness in the control patients with GSD was 4.6 ± 3.7mm compared with 2.1 ± 1.2mm in those without GSD p=0.513.

Conclusions: The presence of Gallstones appears to increase the thickness of the Gallbladder wall (i.e in both diabetic patients and controls) .

Key Words: Gallstone disease; Gallbladder wall thickness.

†To whom correspondence should be addressed: Email: drabolokoba@yahoo.com
Tel: 08038050480, 08053357173

Introduction

Gallstone (GS) disease is one of the most common gastrointestinal diseases seen in clinical practice. Most patients with 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].GS 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 (such as those high in animal fat), drugs (eg contraceptive pills), and ileal disease or resection. Others are liver cirrhosis, haemoglobinopathy and diabetes mellitus[7].

Materials and Methods

The study was a prospective one. The setting of the study was the Medical Out-patient Department (MOPD) of the University of Ilorin Teaching Hospital (UITH), Ilorin.

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

One hundred type 2 diabetic patients and 100 age and sex matched controls underwent real time ultrasonography (USS) using real-time ultrasound scanner from Siemens Incorporated, to determine the presence of GS disease and Gallbladder wall thickness. 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 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 RUQ 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 Gallbladder wall thickness of the patients (i.e diabetic patients and controls) was 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 [8].

Equipment:

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

Statistical analysis:

The data obtained were entered into a computer and analysed using Epi- info version 6.1 statistical software.

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).

Table 1: Demographic and anthropometric data of the study subjects.

Variable	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)

DM = Type 2 diabetes mellitus; BMI = Body Mass Index; WHR = Waist Hip Ratio; NS = Not statistically significant; S = Statistically significant.

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 2.

Table 2: Age distribution of patients with gallstones.

Age Group (Years)	DM Subjects			Controls		
	N	GS	% GS	N	GS	% GS
20 – 29	1	0	0	1	0	0
30 – 39	12	1	6.7	12	1	14.3
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

N = Number of patients; GS = number of patients with gallstones; % GS = Percentage of patients with gallstones.

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, p=0.198.

Prevalence of cholelithiasis in the study population

Fifteen diabetic patients had GS while seven control subjects had GS. This gives a prevalence rate of 15% in the diabetic patients and 7% in the controls.

Relationship between gallstones and some parameters

The mean gallbladder wall thickness in diabetic patients with GS was higher than that of those without GS 2.8+/-1.4mm and 1.9+/-0.9mm respectively although this was not statistically significant, (p=0.161). The mean gallbladder wall thickness was also higher in controls with GS than those without GS 4.6+/-3.7mm and 2.1+/-1.2mm respectively, (p=0.513).This was also not significant (Tables 3 & 4).

Table 3: Relationship between gallstones and some parameters in diabetic patients.

Parameters	DM Patients with gallstone (Mean ± SD)	DM Patients without gallstone (Mean ± SD)	P-value
Age (Years)	59.1 ± 9.5	51.8 ± 10.5	0.014 (S)
BMI (kg/m2)	26.2 ± 5.5	25.7 ± 6.7	0.755 (NS)
WHR	0.97 ± 0.07	0.95 ± 0.07	0.414 (NS)
Gallbladder volume (ml)	28.4 ± 18.6	27.4 ± 14.8	0.844 (NS)
Gallbladder wall thickness (mm)	2.8 ± 1.4	1.9 ± 0.9	0.161 (NS)

S = Significant; NS = Not significant

Table 4: Relationship between gallstones and some parameters in controls.

Parameters	Controls with gallstone (Mean ± SD)	Controls without gallstone (Mean ± SD)	P-value
Age (Years)	50.8 ± 13.2	48.9 ± 12.6	0.776 (NS)
BMI (kg/m2)	25.5 ± 5.0	23.3 ± 5.4	0.446 (NS)
WHR	0.97 ± 0.06	0.95 ± 0.08	0.981 (NS)
Gallbladder volume (ml)	26.5 ± 14.7	24.1 ± 12.7	0.189 (NS)
Gallbladder wall thickness (mm)	4.6 ± 3.7	2.1 ± 1.2	0.513 (NS)

S = Significant; NS = Not significant

Discussion

Literature review has shown that the prevalence of cholelithiasis is very low in most parts of Africa compared to the Western nations[7,9,10,11]. From this study, the mean gallbladder wall thickness in diabetic patients with GS was higher than in those without GS 2.8 ± 1.4 mm and 1.9 ± 0.9mm respectively (p= 0.16). This difference is however of no statistical significance. Similarly, the mean gallbladder wall thickness in controls with GS was higher than in those without GS 4.6 ± 3.7mm and 2.1 ± 1.2mm respectively (p= 0.513). This value is also of no statistical significance. These observed differences might be due to the fact that the presence of GS in the gallbladder causes irritation of the gallbladder wall thereby resulting in thickening of the gallbladder wall. The healthy gallbladder absorbs cholesterol and desaturates bile. This protective function is lost in chronic cholecystitis resulting from inflammation of the gallbladder wall. The inflamed gallbladder, with its thickened wall, encourages super-saturation of gallbladder bile and subsequent gallstone formation[12].

Hofmann[12] postulated that chronic inflammation of the gallbladder wall (i.e. in cholecystitis) is a risk factor for cholesterol GS disease. LaMorte *et al*[13] also postulated that infection within the gallbladder appears to contribute to the formation of macroscopic stones. Portincasa *et al*[14] working in Italy found a significant increase in gallbladder wall thickness amongst Italians with GS compared to those without GS. There is a paucity of local data on this study with which the authors can compare . This study will therefore serve as a baseline in Ilorin and indeed the whole of Nigeria as similar studies have not been done locally.

Conclusion

The presence of Gallstones appear to increase the thickness of the Gallbladder wall (ie in diabetic patients and controls) even though the difference is of no statistical significance.

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