Original Article

The prevalence of diabetes and metabolic syndrome and associated risk factors in Sudanese individuals with gallstones: a cross sectional survey

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Background: The gallstones are common health problem across the world with huge financial burden on health authorities. Obesity and insulin resistance are associated with risk of gallstones disease (GSD). The aim of this study was to assess the prevalence of metabolic syndrome (MetS) and diabetes and associated risk factors in Sudanese patients with gallstones.

Methods: A prospective cross-sectional study, enrolled patients with gallstones attending Ibn Sina Specialized Teaching Hospital for gastrointestinal and hepatobiliary diseases. A structured questionnaire was applied, anthropometric measures were taken, and blood tested for HbA1c, fasting glucose and lipid profile. Data was analysed using SPSS version 23.

Results: A total number of 151 participants were recruited in the study, 71 of them were ultrasound confirmed GSD patients, and the other 80 were controls without GSD over a period of six months. The prevalence of the MetS and diabetes was 30% and 23.9% respectively. Borderline diabetes was 16.9% and overweight and obesity constituted more than half of the sample 59.6%. Using Chi-Square test, a statistically significant association was found between MetS and HDL, TG, LDL level, waist circumference and blood pressure (BP). Absolute predictors and the risk factors for gallstone disease were waist circumference, age, HbA1c and LDL.

Conclusions: The prevalence of MetS and diabetes among gallstone patients was 30% and 23.9% respectively. Absolute predictors and the risk factors for gallstone disease were waist circumference, age, HbA1c and LDL.

Keywords: Gallstones; obesity; diabetes; metabolic syndrome (MetS); Sudan

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Introduction

Gallstones disease (GSD), metabolic syndrome (MetS) and Obesity are major health challenges for health authorities in both developed and developing countries (1). The overall prevalence of MetS was in range of 20–25%, though it varies among different populations (2,3). The underlying causes of MetS include overweight and obesity, insulin resistance, an unhealthy dietary pattern, physical inactivity, genetic factors and advanced age (4-6). Adults with MetS carry two to three times the risk of cardiovascular disease such as heart attack, stroke and death and five times risk of developing type 2 diabetes and a near double risk of developing gallstones (7). On the other hand, gallstones, also known as cholelithiasis, are common benign gastrointestinal disease affecting 10–15% of people around the world (8). Generally speaking, risk factors for the formation of gallstones were ethnic background, increasing age, female gender, family history, obesity, diabetes mellitus, hyperinsulinism, dyslipidemia, MetS, lack of exercise and with high-calorie diets, rapid weight loss and non-alcoholic Fatty liver (9,10). The rates of gallstone complications are higher in older people and in some ethnic groups, and are also influenced by socio-economic factors (11,12).

The prevalence of GSD in USA is estimated 15% (13), and 9–21% in Europe (8,14), 5% in Ethiopia and 5.2 in Sudan in 1994 (15). Interestingly, in Sudanese population pigment stones were most prevalent and that gall stones were more frequent in women aged between 40–49 years (16). GSD are common presentation in the Sudanese surgical departments, usually diagnosed and surgically treated, but little is known about cholelithiasis in Sudan, its prevalence, risk factors and metabolic associations. Therefore, the aim of the current study was to assess the prevalence of MetS and diabetes among patients with gallstone and associated risk factors.

Methods

Study design

A prospective, cross-sectional, hospital-based study. The study was conducted at Ibn Sina Specialized Teaching Hospital for gastrointestinal, hepatobiliary diseases and urology in capital city of Sudan, Khartoum. It serves patients from almost all parts of the country. The study population was patients attending the Hospital between May and December 2018.

Inclusion criteria

The cases group were participants attending the outpatient department (OPD)/Referred Clinic in Ibn Sina Hospital scheduled for cholecystectomy from the period of May till December 2018 and those with Ultrasound confirmed cholelithiasis/gallstone and the control group were cross-matched patients without gallstone disease. Patients aged 18 years and above and those who agreed to participate in the study. Patients with hematological disorders (sickle cell disease, thalassemia), patients with chronic liver disease (cirrhosis, hemochromatosis), pregnant women and patients who were on statins were excluded from the study.

Sample size and sampling technique

A purposive convenient sampling technique was used. sample size was calculated based on an expected prevalence between (5.2%) to guide the sample saturation stage to reach a 95% confidence interval. Therefore, 76 patients with gallstone were sequentially enrolled in accordance to their informed consent.

The equation used for the sample size calculation is:

$$n=Z^2P(1-P)/d^2 \quad [1]$$

Whereas:

n is the sample size, Z is the statistic corresponding to level of confidence assumed 95% confidence interval, P is expected prevalence estimated at (5.2%) reference, d is precision (corresponding to effect size).

$$n=\frac{(1.96)^2\times 0.052(1-0.052)}{(0.05)^2}=75.75 \quad [2]$$

i.e., 76 patients with gallstone

Besides that, we selected other 80 participants and considered them as a control group which had the same characteristics of the cases group (cross-matching) except for gallstone disease, so the total sample size in this study was 156 participants.

Data collection methods

About 151 Sudanese patients participated in the study, the response rate was 96.7%. Interview guided structured questionnaire was administered containing personal information, medical history, laboratory finding on basic metabolic profile and ultrasonography findings. Information on basic metabolic profile are requested pre-operatively by the surgeon [liver function test, renal function test (including electrolytes) and fasting blood glucose (FBG),

Table 1 Socio-demographic characteristics among studied participants (n=151)

Variable		N	%
Gender	Male	25	16.6
	Female	126	83.4
Residence	Urban	97	64.2
	Rural	54	35.8
Marital status	Married	76	50.3
	Single	65	43.0
	Divorced	2	1.3
	Widowed	8	5.3
BMI	Under weight	8	5.3
	Normal weight	53	35.1
	Overweight	53	35.1
	Obese	37	24.5

BMI, body mass index.

lipid profile, and HbA1c]. In addition, all participants were offered abdominal ultrasonography in order to meet the criteria for 'Ultrasound confirmed cholelithiasis' by a senior expert specialist in Ibn Sina Hospital. Structured questionnaire was used to collect data for sociodemographic data. Stethoscope and sphygmomanometer, measurement tape, weighing scale, height scale, and calculator, were used for measurement of blood pressure (BP), body mass index (BMI) and waist circumference. The reference values used to determine the diabetic status was obtained from the standard NICE guidelines; HbA1c below 5.7% was considered non diabetic range, 5.7–6.4% was pre-diabetic and 6.5% or higher was diagnostic for diabetes.

MetS was defined if three out of five criteria of the standard adult treatment panel (ATP) III were met, namely (I) Waist >102 cm in males and >88 cm in females; (II) serum TG >150 mg/dL, OR being treated for hypertriglyceridemia; (III) serum HDL <40 mg/dL in males and <50 mg/dL in females, OR being treated for low HDL level; (IV) BP >130/85 mmHg, OR being treated for high BP; (V) FPG ≥110 mg/dL, OR being treated for high blood sugar.

Data analysis

Data was analysed using SPSS version 23, Descriptive statistics (frequency tables, means and standard deviations) and inferential statistics (Chi-square test and logistic regression analysis) were used.

Ethical consideration

It was sought from SUMASRI Institutional Review Board (SIRB) as well as the Ibn Sina Institution Research committee.

Results

Socio-demographic characteristics

The study enrolled 151 patients, 71 (47.0%) of them had gallstone disease, and 80 control without gallstones. Majority (83.4%) were females. The mean age was 51.5±14.7. Married patients made up 50.3% of the study population, followed by single 43.0%, widowed 5.3% and divorced 1.3%.

In this study, the number of patients with normal weight were equal to those with overweight (35.1%), while obese patients were 24.5%. The two categories of overweight and obese constituted above half of the sample 59.6%. while only 5.3% of them were categorized as underweight (n=8) (*Table 1*).

The prevalence of diabetes among participants with GSD

The fasting blood glucose (FBG) was reported high in 49.7% of the total participants and in 39.4% (n=28) among the participants with GSD. HbA1c was used to classify the patients with GSD into diabetic, pre-diabetic and non-diabetic. Diabetes was found in 23.9% (n=17) among participants with GSD (*Table 2*). When performed Chi-square test, the only significant result was found between diabetes and LDL level (P=0.002).

Lipid profile among GSD patients

High cholesterol was reported in 23.9%, while high TG was also seen in 21.1%. Low HDL-cholesterol was reported in 33.8% of the female and only in 2.8% of male (*Table 2*).

BP among patients with GSD

About 27% (n=19) of the GSD participants were found to have high BP. A total of 25% (n=18) of the respondents with GSD reported that they were formerly diagnosed with hypertension and being treated for high BP at the time of the gall stone operation.

Table 2 Distribution of FBG, HbA1c, and lipid profile among participants with GSD (n=71)

Variables		N	%
FBG	Normal (<110 mg/dL)	43	60.6
	High (≥110 mg/dL)	28	39.4
HbA1c	High (>6.5%)	17	23.9
	Normal (<6.5%)	54	76.1
Cholesterol	Normal (<200)	54	76.1
	High (≥200)	17	23.9
TG	Normal (<150)	56	78.9
	High (≥150)	15	21.1
HDL	Normal		
	M (≥40)	9	12.7
	F (≥50)	36	50.7
	Low		
	F (<50)	24	33.8
	M (<40)	2	2.8
LDL	Normal (<100 mg/dL)	30	42.3
	High (≥100 mg/dL)	41	57.7

FBG, fasting blood glucose; GSD, gallstones disease.

The prevalence of MetS among participants with GSD

In this study, MetS was diagnosed in 30% (n=21) of patients with GSD. The number of metabolic abnormalities was variable from five to none among all GSD patients included in this study. Diagnosis of MetS was made if three out of five metabolic parameters were abnormal according to the ATP III criteria.

Test of associations

Chi-square test

(I) MetS was significantly associated with HbA1c (P=0.027), BP (P=0.001), HDL (P=0.008), TG (P=0.004), LDL (P=0.013) and waist circumference (P=0.000) but the association between BMI and MetS was statistically insignificant (P=0.323);

(II) The association between GSD with waist circumference, BP, HbA1c and LDL was statistically significant (P=0.000, 0.002, 0.001, 0.000) respectively.

Logistic regression

(I). MetS was associated with higher odd ratio in relation to gender, HbA1c and BMI (*Table 3*). For instance, females with GSD are more exposed to develop MetS by about 5 times more than their counterparts' males (odd ratio =4.848), similarly, uncontrolled HbA1c contribute in the development of MetS by approximately 3 times than the controlled HbA1c. Also being an overweight or obese patient, this may increase the probability of getting MetS by approximately 2 times than those who have normal weight or underweight (odd ratio 1.950) (*Table 3*);

(II). When logistic regression was performed to determine the predictors and the risk factors for gallstone disease, we found that, waist circumference, age, HbA1c and LDL had a significant association with the presence of GSD (P=0.013, 0.022, 0.000, 0.000) respectively. Furthermore, LDL was a strong predictor for the GSD, in other words, uncontrolled LDL level may predict the presence of GSD by approximately 17.5 times more than the controlled. Similarly, increased waist circumference is more likely to contribute to GSD by approximately 3.7 times than the normal level. although there are insignificant associations, between GSD and BP and MetS, but the presence of MetS, as well as the increased BP level are more likely to contribute to the presence of GSD by approximately 1.6 times than those hadn't Met and had normal BP (*Table 4*).

Discussion

Obesity is an important risk factor for diabetes, MetS and gallstones. In this study, patients who were in the overweight zone constituted 35%, while obese patients were 24%, and the two categories constituted more than on half of the sample 59% .Several studies showed that overweight and obesity are main risk factors for MetS (4-6). The prevalence of MetS in this study was found to be 30% of patients with gallstones. MetS and insulin resistance are an important factors that lead to the formation of gallstones (17). Therefore, it is not surprising that the global prevalence of MetS was estimated to be in the range of 23–25% (18,19). Sasazuki *et al.* also showed that glucose intolerance is associated with a modest increase in the risk

Table 3 the predictors of MetS among GSD patients by using logistic regression test (n=71)

Variable	B	S.E.	χ^2	P value	Odd ratio
Age in Years	–0.047	0.027	3.11	0.078	0.954
Gender	1.579	0.979	2.599	0.107	4.848
HbA1c	1.111	0.875	1.614	0.204	3.038
BMI	0.668	1.111	0.361	0.548	1.950
Constant	3.866	1.875	4.251	0.039	47.754

MetS, metabolic syndrome; GSD, gallstones disease; BMI, body mass index.

Table 4 the predictors of GSD by using logistic regression test (n=151)

Variable	B	S.E.	χ^2	P value	Odd ratio
Waist circumference	1.308	0.529	6.107	0.013	3.698
Age in Years	–0.034	0.015	5.219	0.022	0.967
MetS	0.490	0.702	0.488	0.485	1.633
HbA1c	–2.764	0.669	17.081	0.000	0.063
LDL	2.862	0.669	18.310	0.000	17.492
BP	0.481	0.514	0.876	0.349	1.618
Constant	0.996	0.761	1.715	0.190	2.707

GSD, gallstones disease; MetS, metabolic syndrome; BP, blood pressure.

of gallstone disease (20). Pacchioni *et al.* showed that obesity is a stronger risk factor for gallstones than type 2 DM (21). However, the prevalence of gallstone among diabetic patients in Nigeria was found to be 17.5% (22). Importantly, in China the risk of cholelithiasis increases with the number of components of MetS for males but not for females (23). Nahum Méndez-Sánchez *et al.* showed that MetS was associated with more than three-fold risk of gallstone disease (24). In Iran, it was shown that individuals with MetS had 2.2 times more occurrence of gallstones in both gallbladder and biliary tract than patients without MetS (25). Furthermore, Tsai *et al.* found that the risk of cholelithiasis is directly affected by the number of metabolic abnormalities in a non-diabetic population (26). In this study MetS was associated with 1.6 times more occurrence of gallstones.

Importantly, MetS has been observed to place people at increased risk for developing diabetes mellitus and cardiovascular disease as well as increased mortality from cardiovascular disease (27). In this study, the prevalence of diabetes mellitus among GSD patients was 23.9% while in the study done by Hazari *et al.*, the prevalence was slightly higher 35.5% (28). Several studies showed the association between GSD and diabetes and these were listed in the review by Ahmed *et al.* (10).

Risk factors for the formation of gallstones were ethnic background, increasing age, female gender, family history, obesity, diabetes mellitus, hyperinsulinism, dyslipidemia, MetS, lack of exercise and with high-calorie diets, rapid weight loss and non-alcoholic Fatty liver (9,10).

In this study, we showed that waist circumference, age, HbA1c and LDL were important risk factors for gallstone formation.

This study is not without limitations. The patients were recruited from single center and this may not represent all population living in Sudan. Furthermore, different tribes are living in Sudan and have different dietary habits. Therefore, future studies should address all these concerns. Despite these limitations our study is novel and showed high prevalence of both MetS and diabetes among cohort population with gallstones.

Conclusions

The prevalence of MetS and diabetes among gallstone

patients was 30% and 23.9% respectively. Absolute predictors and the risk factors for gallstone disease were waist circumference, age, HbA1c and LDL.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the SUMASRI Institutional Review Board and Ibn Sina Institution Research committee (00008867).

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