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Original Research Article

Association of metabolic syndrome with complicated gall stone disease: our experience

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ABSTRACT

Background: Gall stone disease is the most common biliary pathology and frequently encountered in our daily practice. Patients with gall stone that experienced at least one attack of acute cholecystitis is defined as complicated gall stone disease (CGSD). Aim of this study was to find out the association between complicated gall stone disease and the metabolic syndrome.
Methods: This prospective, observational study was done from 1st March 2017 to 30th November 2018 in department of general surgery, SMS hospital Jaipur. All patients with cholelithiasis admitted in general surgery department were included. Metabolic syndrome was defined by adult treatment panel III (ATP III) criteria. All patients were divided in two groups: complicated gall stone disease (CGSD) and uncomplicated gall stone disease (UGSD).
Results: Mean age was 47.2 years in CGSD group and 46.7 year in UGSD group. Female to male ratio was 8.2:1 in CGSD group and 4:1 in UGSD. Metabolic syndrome was presented in 64 patients (58.2%) of CGSD group and 24 patients (21.8%) of UGSD patients, which was statistically significant (OR 4.986, CI 2.763-8.995, p value <0.001). Five components of metabolic syndrome were compared in both CGSD group and UGSD group. Lower serum HDL-C level and hyperglycemias was statistically significant in CGSD group as compared to UGSD group.
Conclusions: Metabolic syndrome can be use to predict complicated gall stone disease. Hyperglycaemia and lower HDL-C associated with CGSD. One should be aware about possible metabolic syndrome background when dealing with gall stone disease patients.

Keywords: Cholelithiasis, Gall stone, Metabolic syndrome

INTRODUCTION

Gall stone disease is the most common biliary pathology and frequently encountered in our daily practice.[1] Gall stones are associated with older age, pregnancy, obesity, insulin resistance, specific dietary habits, genetic background and ethnicity.[2-4] The pathogenesis of gallstones is multifactorial and involves environmental and individual factors resulting in three main consequences: bile cholesterol saturation, cholesterol nucleation and gallbladder dysmotility.[5] Acute cholecystitis is usually a complication of gall stone disease and patients with gall stone that experienced at least one attack of acute cholecystitis is defined as having complicated gall stone disease (CGSD).[6]

The presence of three or more of the following five factors is defined as the metabolic syndrome by adult treatment panel III (ATP III) criteria.[7] (1) Hypertriglyceridemia: triglyceride level (TG) ≥150 mg/dl; (2) abdominal obesities: waist circumference ≥102 cm (in men) and ≥ 88 cm (in women); (3) lower high

density lipoprotein cholesterol level (HDL-C): serum HDL-C ≤30mg/dl in men and ≤35 mg/dl in women; (4) Hyperglycemias: fasting plasma glucose ≥100 mg/dl or previously diagnosed as type 2 diabetes mellitus (DM); (5) Elevated blood pressure (BP): systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg or known case of hypertension.

In the recent literature, the association between gall stone disease and metabolic syndrome has been studied widely, but very few studies showing association of metabolic syndrome with complicated gall stone disease.[8-10]

The purpose of this study was to find out the relationship between complicated gall stone disease and the metabolic syndrome and early diagnosis of metabolic syndrome in gall stone disease patients.

METHODS

This prospective, observational study was done from 1st March 2017 to 30th November 2018 in department of general surgery, SMS hospital Jaipur. All patients with cholelithiasis admitted in general surgery department were included and patients with already diagnosed metabolic syndrome, patients taking statins or fibrates, patients with history of cardiovascular disease and pregnant women were excluded.

After history and clinical examination, patient underwent ultrasound (USG) whole abdomen and diagnosis of gall bladder stone disease was established.

Apart from routine blood investigations, fasting blood sugar, serum lipid profile (TG and HDL-C) and C-reactive protein (CRP) were measured. Blood pressure was measured with sphygmomanometer in supine position. Waist circumference measured at the level of umbilicus with the patient standing position. Metabolic syndrome was defined by adult treatment panel III (ATP III) criteria. All patients underwent laparoscopic cholecystectomy.

All patients were divided in two group Complicated Gall Stone Disease (CGSD) and Uncomplicated Gall Stone Disease (UGSD) group. CGSD was defined as patients with gall stone that experienced at least one attack of acute cholecystitis.

This study was approved with ethical committee of our institute. Informed and written consent was taken from the patient.

Statistical analysis

Descriptive and Inferential statistical analysis has been carried out in the present study using computer software (SPSS Trial version 23 and primer). Continuous variables were presented as mean±SD and categorical variables were presented as proportion and percentage. Odd ratio was measured at 95% confidence interval. The difference in proportion was analysed by using chi square test and the difference in means among the groups was analyzed using the student-T Test. Binary logistic regression was used to find out the significant predictors of complicated gall stone. For all statistical tests, a P value less than 0.05 was considered statistically significant. Sample size was calculated 110 subjects in each group at 95% confidence limit.

RESULTS

This study was conducted in Department of Surgery, SMS Medical College and Hospital, Jaipur. Total 220 gall stone disease patients were included in this study. All patients were divided in two group CGSD and UGSD group. In each group, there were 110 patients.

Mean age was 47.2±13.2 years (range 20-85) in CGSD group and 46.7±13.8 years (range 20-75 year) in UGSD group. Female to male ratio was 8.2:1 in CGSD group and 4:1 in UGSD.

Table 1: Demographic, clinical and biochemical parameters.

	Complicated gall stone disease (CGSD) (n=110)	Uncomplicated gall stone disease (UGSD) (n=110)	P Value
Mean age±SD (years)	47.2±13.2	46.7±13.8	0.54
Female: Male	8.2:1	4:1	0.829
Mean CRP level ± SD (mg/l)	8.2±3.8	5.2±10.0	0.005
Large gall Stone (>2.5 cm) (n =26)	19 (17.3%)	7 (6.4%)	0.02
Mean duration of post-operative hospital stay (days)	2.2±0.5	1.9±0.5	0.015

Mean C-reactive protein (CRP) level was more in CGSD group (8.2 mg/ml) as compared to UGSD group (5.2 mg/ml) (p value 0.005). Of the total 220 patients, 26 patients had large gall stone (gall stone size > 2.5 cm). Of these 26 patients, 19 patients had CGSD and 7 patients had UGSD, which was statistically significant (p value 0.02). Mean duration of hospital stay was statistically significant longer in CGSD group as compared to UGSD group (2.2 days vs. 1.9 days, p value 0.015) (Table 1).

Metabolic syndrome was presented in 64 patients (58.2%) of CGSD group and 24 patients (21.8%) of UGSD patients, which was statistically significant (OR 4.986, CI 2.763-8.995, p value <0.001) (Table 2).

Table 2: Metabolic syndrome between CGSD and UGSD.

Metabolic syndrome	Complicated gall stone disease (CGSD) (n=110)	Uncomplicated gall stone disease (UGSD) (n=110)	Odd ratio at 95% confidence interval	P value
	N (%)	N (%)		
Present	64 (58.2)	24 (21.8)	OR 4.986 (CI: 2.763-8.995)	<0.001
Absent	46 (41.8)	86 (78.2)		

Table 3: Comparison of components of metabolic syndrome between CGSD and UGSD.

Components of metabolic syndrome	Complicated gall stone disease (CGSD) (n=110)	Uncomplicated gall stone disease (UGSD) (n=110)	Odd ratio at 95% confidence interval	P value
	N (%)	N (%)		
Hypertriglyceridemia (TG level ≥ 150 mg/dl) (n=92)	50 (54.4)	42 (45.6)	OR 1.031 (CI: 1.064-1.045)	0.71
Large waist circumference ≥102cm i men and ≥88 cm in women (n=85)	48 (56.5)	37 (43.5)	OR 0.90 (CI: 0.504-1.605)	0.834
Systolic hypertension (BP >130 mm Hg) (n=86)	49 (57)	37 (43)	OR 1.585 (CI: 0.918-2.735)	0.12
Diastolic hypertension (BP >85 mm Hg) (n=121)	57 (47.1)	64 (52.9)	OR 1.285 (CI: 0.818-1.735)	0.20
Lower serum HDL-C (≤30 mg/dl in men and ≤35 mg/dl in women) (n=145)	80 (55.2)	65 (44.8)	OR 1.846 (CI: 1.048-3.285)	<0.046
Fasting plasma glucose ≥100 mg/dl or previously diagnosed as type 2 DM (n=93)	60 (64.5)	33 (35.5)	OR 2.800 (CI: 1.609 to 4.874)	<0.001

Five components of metabolic syndrome were compared in both CGSD group and UGSD group. Hypertriglyceridemia (TG level ≥ 150 mg/dl), elevated systolic BP ≥130 mm Hg, elevated diastolic BP and abdominal obesities or large waist circumference ≥102cm (in men) and ≥ 88 cm (in women) had no statistically significant difference between both groups. Of the 220 patients, 92 patients had hypertriglyceridemia. Of these 92 patients, 50 patients (54.4%) had CGSD and 42 patients (45.6%) had UGSD. Large waist circumference was presented in 85 patients out of total 220 patients in both groups. Of these 85 patients, 48 patients (56.5%) had CGSD and 37 patients (43.5%) had UGSD.

Of the 220 patients, 145 patients had lower serum HDL-C level (≤ 30mg/dl in men and ≤ 35 mg/dl in women). Of these 145 patients, 80 patients (55.2%) had CGSD and 65 patients (44.8%) had UGSD. Hyperglycemias (fasting plasma glucose ≥100 mg/dl or previously diagnosed as type 2 DM) was statistically significant in CGSD group as compared to UGSD group (60 patients and 33 patients respectively, p value <0.001) (Table 3).

DISCUSSION

In the modern era, prevalence of obesity and metabolic syndrome is rapidly increasing in India and other South Asian countries, which result in increased morbidity and mortality due to cardiovascular disease and type 2 diabetes mellitus.[11,12] Metabolic syndrome should be recognized early so that complication of it can be prevented.[13]

Recent literature suggests that metabolic syndrome is a risk factor of gall stone disease. The association of gall stone disease with dyslipidemia, obesity, diabetes and hyperinsulinemia has supported the hypothesis that gall stone formation is a type of metabolic syndrome.[14,15]

Metabolic syndrome was first described by Archard and Thiers in 1921, in association with polycystic ovary syndrome.[16] Diagnostic criteria for the metabolic syndrome have been establish by the World Health Organisation (WHO) in 1998, by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP:ATP III) in 2001, and more recently by the International Diabetes Federation (IDF) in 2005.[17]

This study was conducted to find out the association between complicated gall stone disease and the metabolic syndrome. Both groups CGSD and UGSD were comparable according to age and sex. There was no statistically significant difference.

In our study, CGSD patients had statistically significantly more CRP level and longer post-operative hospital stays as compared to UGSD patients. Higher CRP level in CGSD may be due to inflammation of gall bladder as defined by definition of CGSD. Diaz-Flores A et al found out that preoperative CRP ≥11 mg/dL was associated with the highest odds ratio (OR = 17.9) of predicting difficult laparoscopic cholecystectomy.[18] Post operative hospital stay depends on intra-operative findings, difficult dissection of calot's triangle and duration of surgery. Bansal et al. observed that there were more inflammatory pericholecystic adhesions due to acute cholecystitis.[19]

Chen LY et al analyzed the association between prevalence of GSD and number of components of metabolic syndrome and found out that more the components of metabolic syndrome, higher the prevalence of gall stone disease, which was significant (P < 0.0001). The presence of all five components of metabolic syndrome increased the risk of gallstone disease by 3.4 times in male and by 5 times in female. Metabolic syndrome was more predominant in CGSD in compare to UGSD.[20,21]

We found that presence of metabolic syndrome (p<.05) is an independent predictor of CGSD after applying logistic regression analysis and Wald criteria. Metabolic syndrome was presented in 58.2% patient of CGSD group and 21.8% patients of UGSD patients, which was statistically significant (OR 4.986, CI 2.763-8.995, p value <0.001)

Sanchez NM et al, studied that total metabolic syndrome was associated with a more than three-fold risk of gallstone disease (OR = 3.20; 95%CI, 1.71-6.01; P = 0.0001).[22] They found that that presence of large waist circumference, lower HDL and DM confers a 7.89-fold increased risk of having gallstone disease.

Ching LI et al investigated that incidence of metabolic syndrome increased 1.99 times in gall stone disease patients (odd ratio 1.99; 95% CI = 1.70-2.33). On multivariate logistic regression analysis they found that age (OR = 1.037; 95% CI = 1.029-1.046), waist circumference, (OR = 1.013; 95% CI = 1.004-1.023) and HDL-C (OR = 0.985; 95% CI = 0.977-0.993) were associated with gall stone disease after adjusting for the other factors.[23]

Ata N et al had studied the relationship between complicated gall stone disease and the metabolic syndrome or its components. They found that fasting blood sugar was present statistically significant more in CGSD group as compared to UGSD group (47% and 24% respectively).[24]

Insulin resistance is associated with a low serum HDL-Cholesterol concentration and gallbladder dysmotility, which is a risk factor for gall stone disease.[25-27]

In the present study, Hyperglycemias and lower serum HDL-C level were more commonly presented in CGSD group as compared to UGSD. Hypertriglyceridemia, elevated systolic BP and large waist circumference although presented more in CGSD group, but there was no statistically significant difference.

Limitation of our study was that we didn't analyse body mass index, but we measured waist circumference, which is a component of metabolic syndrome.

CONCLUSION

Metabolic syndrome can be use to predict complicated gall stone disease. Hyperglycaemia and lower HDL-C associated with CGSD. One should be aware about possible metabolic syndrome background when dealing with gall stone disease patients. So that we can minimise the complications of metabolic syndrome by early diagnosis.

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