Evaluation of Predisposing Risk Factors for Gallstone Formation Following Bariatric Surgery

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ABSTRACT:

BACKGROUND:

The risk factors for development of gallstones have been studied extensively in the general population. They are different when it comes to patients who underwent bariatric operations. Obesity and rapid weight loss induced by weight-reducing surgery are well recognized for the development of gallbladder stones. There is no standard policy whether to perform prophylactic cholecystectomy at the time of the bariatric operation or to give postoperative treatment to decrease the risk.

OBJECTIVE:

The aim of the study is to evaluate the predictors of gallstone formation post-Bariatric surgery and associated risk factors. The implication behind it will help decide how to follow up postoperatively and whom are at increased risk to develop cholelithiasis.

METHODS:

This prospective study was performed on 100 patients who underwent weight-reducing operations at Al-Imamain Al-Kadimiyen Teaching Hospital. They were followed for 12 months postoperatively. Ultrasonography examination was done for those who developed symptoms suggestive of gallstone formation.

RESULTS:

Twenty percent of them were found to have gallstones. Of the the parameters enrolled in the study (age, gender, type of surgery, preoperative body mass index, percentage of excess body weight loss), only the factor of the percentage of excess weight loss was the most significant of predicting development of gallstone post-bariatric procedures (p value = 0.002). The preoperative BMI, age, gender and type of operation were found were not found to be statistically significant in terms of its relationship with gallstone formation.

CONCLUSION :

Concomitant cholecystectomy along with the bariatric procedure is not recommended. Surveillance by ultrasonography for those with excess weight loss more than 25% of their original weight is advised for 1 year postoperatively.

KEYWORDS: gastric bypass, sleeve gastrectomy, gallstones, risk factors, obesity.

INTRODUCTION:

Cholelithasis is so prevalent worldwide affecting 10% of men and 20% of women in the USA, rendering cholecystectomy to be one of the most common elective surgeries performed [(1)] . Gallstones are common in the community and represent a greater problem in the obese population. Diagnosis of cholelithiasis in overweight patients is relatively less sensitive by ultrasonography and clinical Murphy's sign when gallstones become symptomatic is less reliable [(2)] . The risk of gallstone formation is directly related to the level of obesity and when the body mass index (BMI) is > 40, the risk rises to be 5 to 6 times that of the general population. It is also known that the risk increases following very low caloric diets [(3)] .

The formation of gallbladder calculi is attributed to changes to the gallbladder motility as well as bile composition where it becomes supersaturated with cholesterol secreted in the bile resulting in more cholesterol nucleation and crystallization. Increased mucin gel secretion is also got implicated leading to an inflammatory state. Obesity by its own has an association with biliary cholesterol hypersecretion which is enhanced by insulin resistance already developed in obese subjects. Insulin causes increased cholesterol production in hyperinsulinemic subjects. The slow gallbladder emptying in obesity gives more time for the cholesterol to crystalize and nucleate along

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with increased mucin gel secretion. Gallbladder emptying postprandially depends on cholecystokinin (CCK) release stimulating the CCK receptors in the smooth muscle cells of the gallbladder. The motility of the gallbladder is impaired probably because of the cholesterol deposition in the muscularis propria layer rendering it less sensitive to the activity of CCK. For all of these, obese subjects are more prone to cholelithasis and subsequent acute and chronic cholecystitis [4] .

The pathogenesis of gallstone formation after bariatric surgery is similar. The concentration of biliary cholesterol is increased due to weight loss, and the decreased dietary fat which reduces CCK release resulting in delayed gallbladder emptying. The increased mucin production during weight loss, leads to increased cholesterol crystallization and nucleation, thus enhancing formation of cholesterol gallstones. It has been found that there is mucosal abnormalities in specimens retrieved from gallbladders of obese persons even in the absence of stones sonographically. The most common abnormality is cholesterolosis. Cholesterolosis of the gallbladder is the accumulation of cholesterol esters and triglycerides in the macrophages at the gallbladder wall mucosal level [5] . It has been postulated that increased gallbladder secretion of mucin and calcium and increased presence of prostaglandins and arachidonic acid in bile have remarkable attribution to gallstone formation [6] . Accordingly, three strategies in management have been suggested and developed:

1.one approach is to perform simultaneous cholecystectomy along with the bariatric surgery. It does not need to have any modifications in the access. This would also prevent likely complications such as gallstone pancreatitis and common bile duct stones which will become more challenging to treat after bypassing the duodenum in some bariatric procedures including the Roux-en-Y Gastric Bypass.

2. A second approach is to wait and see in which cholecystectomy is performed for symptomatic gallstones developed post-bariatrically.

3.Some utilizes ursodeoxycholic acid postoperatively to decrease incidence of gall calculi formation postoperatively.

It remains controversial which approach to be standardized and it is up to the surgeon's discretion which to choose perioperatively [7] .

Routine cholecystectomy at the time of the weight-reducing surgery, is justified based upon histologic findings of vesicular disease in 90% of cholecystectomy specimens, the technical difficulties in re-operation, and the cost-effectiveness of a second hospitalization. It may help anticipating complications of biliary pancreatitis, deranged liver function test or acute cholecystitis. Those in favor of not performing routine cholecystectomy have a point in that there is a longer operating time with potential increase in complications, the intraoperative difficulties in excessively obese patients, the relatively low incidence of symptomatic gallstones and the fact that cholecystectomy becomes technically easier with weight reduction. Most studies assessing the ursodeoxycholic acid treatment showed insignificant results thus the role of it may need further evaluation [8]

PATIENTS AND METHODS:

This is a prospective study of a 100 patients who underwent Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) and Laparoscopic Sleeve Gastrectomy (LSG) at Al-Imamain Al-Kadhimain Medical City between January 2014 and January 2015. The study included patients of both sexes with morbid obesity, who completed a minimum 12-month postoperative follow-up. All were having preoperative abdominal ultrasonography study showing no cholelithasis. Those who had undergone cholecystectomy prior to their bariatric operation were excluded from the study as well as those who had symptomatic gallstones at the time of their weight reduction surgery where they were managed with simultaneous cholecystectomy. During follow up, the patients who were symptomatic for acute cholecystitis, acute cholangitis, abnormal liver function tests, and/or biliary pancreatitis as first presentation, were examined by ultrasound along with liver function tests. The demonstration of gallstones in symptomatic patients during the follow-up period led in all cases to cholecystectomy after consenting the patients.

The data of sex, age, preoperative BMI, and percent of excess weight loss (%EWL) were utilized and compared with other similar studies.

RESULTS:

Out of these 100 patients, 20 of them developed symptomatic gallstones diagnosed by transabdominal ultrasonography mandating cholecystectomy where all were performed laparoscopically. Overall rate of symptomatic gallstones formation was 20% and mean time for its development was 10 months postop (range 2-12). The asymptomatic patients were not included in the study.

It has been shown that 16 out of 64 females (25% of all females) developed post-bariatric gallstones while 4 of the 36 males (11% of all males) had gallstones (Table 1).

Table 1 : Relationship of Gender risk factor and Gallstone Formation

	Males	Females	Total
No Gallstones	32	48	80
Gallstones	4	16	20
Total	36	64	100

Regarding type of the weight-reducing procedure employed, there were 20 out of 96 LSG cases (21% of all LSG cases) with postop cholelithasis and none following the LRYGB (Table 2).

Table 2 : Type of Operation and Gallstone formation

	LRYGB	LSG	Total
No Gallstones	4	76	80
Gallstones	0	20	20
Total	4	96	100

Twelve of 40 (30%) patients aged between 40-49 years, had gallstones whereas only 4 of the 16 (25%) of those between 20-29 years of age and between 50-59 developed cholelithiasis following the procedures. Those with ages between 30-39 and between 60-69 did not get gallstones postoperatively (Table 3).

Table 3 : Age Relationship to Gallstone Formation

Age	No Gallstones	Gallstones	Total
20- 29	12	4	16
30-39	24	0	24
40- 49	28	12	40
50- 59	12	4	16
60- 69	4	0	4
Total	80	20	100

Those with preoperative BMI of less than 45 who were 96, 16 developed gallstones, while all those with BMI equal to or more than 45 who were 4, got postoperative gallstones. The rest of patients with other BMI values showed mixed resultsas follows: 4 of the 24 (17%) whose BMIs were between 40.0-40.9, 4 of the 36 (11%) with preop BMI of 42.0-42.9, 4 of the 8 (50%) where their BMI falls between 43.0 and 43.9, and 4 of the 12 (33%) having a BMI value residing between 44.0 and 44.9, were found to form gallstones after their operations (Table 4).

Table 4 : BMI Relationship to Gallstone Formation.

BMI	No Gallstones	Gallstones	Total
= < 39.9	4	o	4
40- 40.9	20	4	24
41- 41.9	4	0	4
42- 42.9	32	4	36
43- 43.9	8	4	12
44- 44.9	12	4	16
= > 45	0	4	4
Total	80	20	100

The results of gallstone formation when applying the percentage of excess weight loss parameter were found to be as follows: Those whose percentages of excess weight loss (%EWL) of their original weight were less than 24.9% did not form postop stones except 4 out of the 32 (12.5%) with %EWL was between 22.0-22.9, whereas 16 of the 20 (80%) whose %EWL was equal or more than 25% (Table 5).

Table 5: %EWL Relationship to Gallstone Formation.

% EWL/ 1Year	No Gallstones	Gallstones	Total
= < 19.9	8	0	8
20-20.9	20	0	20
21-21.9	0	0	0
22- 22.9	28	4	32
23- 23.9	12	0	12
24- 24.9	8	0	8
25- 25.9	0	12	12
= > 26	4	4	8
Total	80	20	100

Table 6 : Risk factors for Gallstone formations and their significance(p < 0.05 is considered to be statistically significant).

Risk Factors	No Gallstones	Gallstones	P value
Age mean(years)	40.2(25-50)	40.35(20- 64)	0.49
Gender			0.10
male	32	4	
female	48	16	
Preoperative BMI mean	42.8(42- 45)	41.75(38-44)	0.10
Type of operation			0.31
LRYGB	0	4	
LSG	20	76	
%LWS mean	24.6%(22-26%)	21.65%(18-26%)	0.002

LRYGB: Laparoscopic Roux-en-Y Gastric Bypass, LSG: Laparoscopic Sleeve Gastrectomy, %EWL: Percent of Excess Weight Loss

DISCUSSION:

Risk factors for cholelithiasis in the general population such as age, obesity, female gender and parity are well recognized to surgeons and clinicians. They are not those only in case of patients following bariatric surgery [9] .From published series of Brethauer using ultrasound surveillance after gastric bypass, the rate of asymptomatic gallstone formation ranged from 38 to 58% within 12 months after the procedure [10] . In this study, the incidence of gallstones formed postoperatively detected by ultrasound (20%) was lower than what is found in most studies. This can be explained, by higher weight loss obtained with LRYGB which is a malabsorptive as well as a restrictive type of bariatric surgery employed mostly worldwide resulting in increased %EWL as compared with purely restrictive procedures as LSG employed more at our institution. The finding of more female patients developing the condition as compared to males (25% vs 11%) appears to be consistent with the well-known female gender risk factor regardless of being subjected to bariatric surgery or not. This difference was also seen in similar studies as that of Li [11] .

Age was also found to be relatively significant when it is in the forties to be a well-established gallstone risk factors in literature and that what was found in sister studies.

In this study, there is a tendency that higher preoperative BMI was associated with higher rates of cholelithiasis postoperatively which reflects again the general tendency of obese patients to develop gallstones irrespective of operative status. This finding was comparably found in other studies. In those patients who developed symptomatic gallstones after the operation, there were significantly more patients with weight loss of more than 25% of original weight than those without symptomatic gallstones (p = 0.002803).

This study is similar to the study of Li [11] who found that %EWL > 25% was statistically significant in predicting postoperative symptomatic cholithiasis. De Oliveira et al [12] did not find any significant differences in age, excess weight loss and preoperative BMI between patients who formed and did not form gallstones.

Fobi et al found, in 425 patients with negative preoperative ultrasonographic findings who underwent cholecystectomy concomitantly with bariatric operations, an 86.2% incidence of vesicular pathology, 12.3% of which corresponded to cholelithiasis [13] .

Shiffman et al. found that 40% of those with asymptomatic cholelithiasis will develop symptoms [14] .

CONCLUSION:

1. There is a significant association between rapid weight loss (expressed as percentage of excess weight loss) and gallstone formation. This may

help selecting patients for postoperative ultrasound surveillance for gallstones on follow-up.

2. Since no preoperative risk factors can be isolated, selection criteria for interventions such as prophylactic cholecystectomy will be difficult to formulate.

3. The approach of wait and see can be adopted with emphasis on those with rapid weight loss. When the operative approach is considered, the increased operating time adding simultaneous cholecystectomy with its own perioperative risks increases morbidity and mortality.

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