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Original Research Article

Study the predicators and risk factors for formation of gallstones in a sample of asymptomatic Iraqi patients in Baghdad

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ABSTRACT

Background: A gallbladder stone (GBS) is a foremost reason of morbidity worldwide. Majority of the cases are asymptomatic (>80%). Gallstones can be divided into three main types: cholesterol, pigment and mixed stones. The documented risk factors for GBS mostly are the advanced age, female gender, obesity, high-caloric diets and oral contraceptive, all of these can increase the lithogenicity of bile.
Methods: This is a cross-sectional study was conducted at general surgical consultation departments in two major multispecialty hospitals in Baghdad (Al-Yarmook and Al Karama Teaching Hospitals) and in different health centers in Baghdad and through an online survey between February 2022 and February 2023. The study sample included 225 participants of both genders. The study questionnaires were sent through electronic format to the participants and the questions were asked to the others directly with enough time to respond well. The target population was all segments of society in the city of Baghdad.
Results: The 225 patients were collected which their age range from 18 to 80 years of age. According to the collected data which showed that the percentage of GBS higher in female than male in value (54.2%) while for male (45.8%). Additionally, also it was found that the residence place has an important impact for this study and it presented that residency in urban places was (96.9%) which is higher than rural places which was only (3.1%). Also, most of patients were with: collage education (73.8%), non-employed (52.9%), middle-income class (72.4%). The results showed significant result ($p<0.05$) and good association between age, and type of stones present (solitary or multiple); but for the gender, education level, occupation status, residence, socioeconomic class the results was non-significant ($p>0.05$).
Conclusions: The prevalence of asymptomatic gallstone was relatively high in this region. Female gender, age, high cholesterol level, family history of gallstones, and increased BMI independent risk factors for gallstones formation.

Keywords: Asymptomatic gallstones, Baghdad, Diabetes mellitus, GBS, Predictors, Physical activity, Risk factors

INTRODUCTION

A gallbladder stone (GBS) is a foremost reason of morbidity worldwide.[1] Clinical studies introduce that GBS affect 10-15% of the population in Western societies. Majority of the cases are asymptomatic (>80%). About 1-2% of asymptomatic patients will develop symptoms requiring surgery per year, thus cholecystectomy considered one of the most common operations made among different countries.[1] GBS can be divided into three main types: cholesterol, pigment and mixed stones. In the USA and Europe 80% of GBS composition either cholesterol or mixed stones, while in Asia 80% of GBS are pigment stones.[2]

The process of GBS formation is complex and remains blurred but it mainly due to 1/the disequilibrium in the composition of bile such as more cholesterol,

accumulated amount of pigment material and/or decreased amount of bile acid. 2/ GBS may also result from dysfunction of gallbladder contraction.[3]

The documented risk factors for GBS mostly are the advanced age, female gender, obesity, high-caloric diets and oral contraceptive, all of these can increase the lithogenicity of bile.[2,4]

Previous studies were recognized to evaluate prevalence and risk factors of GBS in Iraq.[5,6] The study aimed at assessing predicators and risk factors for formation of GBS among asymptomatic adult patients in Baghdad.

METHODS

Study design

This is a cross-sectional questionnaire designed study. The study was conducted at general surgical consultation departments in two major multispecialty hospitals in Baghdad (Al-Yarmook and Al Karama Teaching Hospitals) and in different health centers in Baghdad and through an online survey between February 2022 and February 2023. This study was conducted for all age groups, gender (male, female) and social statuses. The data was collected from the participants through 32 questions using Arabic and English languages that designed online based questionnaire or directly was collected from the participants (Directly collected from surgical departments and health centers).

Sample and setup

The study sample included 225 participants of both genders 45.8% male and 54.2% female), whom ages ranged between 18-80 years. The study questionnaires were sent through electronic format to the participants and the questions were asked to the others directly with enough time to respond well. The target population was all segments of society in the city of Baghdad.

Inclusion criteria

The age of the covered subscribers shall not be less than 18 years and not more than 60 years. Patients attending the general surgical consultation department during the study period who were presented for abdominal ultrasound examination for other complaints not related to gallstone disease. The study includes all social situations and all educational levels were included.

Exclusive criteria

The participants excluded who were more than 80 years old, the participants excluded who were less than 18 years old, patients with symptoms related to gallstone disease, patients with history of cholecystectomy and pregnant women were excluded.

Patient's selection and data collection

Interviewing the patients or through electronic format to the patients was done using a detailed socio-demographical information's to collect data (such as age, gender occupation, education), family history of gallstone disease, history of diabetes and hypertension, history of the use of oral contraception, and number of children for females, history of hemolytic diseases, and history of smoking (current or past). The body mass index (BMI) was calculated. Overweight and obesity were defined as BMI-25-29.9 kg/m^2, BMI≥30 kg/m^2 respectively.[7]

Variables such as number of family members, medication profiles, stone type, stone content, type of operation, type of cholecystectomy were considered in this questionnaire. Detailed medical history, together with dietary habits and family background, were obtained from the parents. All patients underwent biochemical investigations with fasting blood glucose: (FBG), serum cholesterol (mg/100 ml), and HbA1C%, serum HDL (mg/100 ml), serum triglyceride (mg/100 ml), serum bilirubin and liver enzymes.

The ethics and research committees of college of medicine, Baghdad university, and the general directorate of health approved the study. An informed agreement was obtained from each participant before inclusion in the study.

Statistical analysis

Analysis of data was carried out using the available statistical package of SPSS-24 (statistical packages for social sciences-version 24) for data input and analysis. Data were presented in simple measures of frequency, percentage. The significance of difference of different percentages (qualitative data) was tested using Chi-square test with application of Yate's correction or Fisher exact test whenever applicable. Multivariate logistic regression analysis was carried out to identify independent risk factors for gallstones. Statistical significance was considered whenever the p value was equal or less than 0.05.

RESULTS

Socio-demographic characteristics for the study patients

The current study was designed for the purpose of evaluating the risk factors for GBS. 225 patients were collected which their age range from 18 to 80 years of age. Table 1 presented socio-demographic data for patients including: age, gender, education level, occupation, residence and socioeconomic class. According to the collected data which showed that the percentage of GBS higher in female than male in value (54.2%) while for male (45.8%). Furthermore, according to the age division that was made for this study, the percentage for (18-30) was (66.7%) and for (30-50) was

(27.1%) while for (50-80) was only (6.2%). Additionally, also it was found that the residence place has an important impact for this study and it presented that residency in urban places was (96.9%) which is higher than rural places which was only (3.1%). Also, most of patients were with-collage education (73.8%), non employed (52.9%), middle-income class (72.4%), single (63.1%), number of children/0-3 (93.8%), number of pregnancies/0-3 (93.8%).

Table 1: Socio-demographic characteristics for the study patients.

Characters	N	Percentage (%)
Age (years)		
18-29	150	66.7
30-49	61	27.1
50-80	14	6.2
Range (18-80) (years)		
Gender		
Male	103	45.8
Female	122	54.2
Education level		
No education	7	3.1
Primary education	4	1.8
Secondary education	48	21.3
Collage education	166	73.8
Occupation status		
Governmental job	54	24.0
Private job	36	16.0
Retired	6	2.7
Non employed	119	52.9
Housewife	10	4.4
Residence		
Urban	218	96.9
Rural	7	3.1
Socioeconomic class		
High-income class	36	16.0
Middle-income class	163	72.4
Low-income class	26	11.6
Material status		
Divorced	8	3.6
Married	75	33.3
Single	142	63.1
Number of children		
0-3	211	93.8
>3	14	6.2
Number of pregnancies		
0-3	211	93.8
>3	14	6.2

Physical activity characteristics and diet for the study patients

Table 2 showed the physical activity (PA) characteristics and diet for the study patients include physical activity, diet, BMI and change in weight. According to collected data which show that the percentage of the normal BMI higher than the overweight in value (73.3%) for normal BMI to (20.4%) for overweight BMI. the percentage for the type of diet were high for omnivorous (87.1%), and percentage for type of physical activity were high for the moderate intensity (44.9%).

Table 2: Physical activity characteristics and diet for the study patients.

Characters	N	Percentage (%)
Physical activity		
No activity	46	20.4
Low intensity	66	29.3
Moderate intensity	101	44.9
High intensity	12	5.3
Diet		
Omnivorous	196	87.1
Vegetarian	13	5.8
Mixed feed	16	7.1
BMI in (kg/m^2)		
Normal	165	73.3
Overweight	46	20.4
Underweight	14	6.2
Change in weight		
No change	153	68.0
Gain	37	16.4
Loss	35	15.6
If change in weight is present specify amount and type?		
>5 kg	36	15.9
<5 kg	189	83.9

Clinical presentation characteristics for the study patients and type of cholecystectomy

Table 3 showed the clinical presentation characteristics for the study population and type of cholecystectomy include: History of colic pain, postmenopausal status, diagnosis and type of cholecystectomy. According to the collected data which show that the percentage of laparoscopic higher than open cholecystectomy in value (66.3%) for laparoscopic to (33.7%) for open cholecystectomy, while percentage for the most common diagnosis (acute) was 58.7%.

Table 3: Clinical presentation characteristics for the study population and type of cholecystectomy.

Characters	N	Percentage (%)
History of colic pain		
No	63	28
Yes	162	72
Diagnosis		
Acute	132	58.7
Chronic	61	27.1
Acute on chronic	32	14.2
Type of cholecystectomy		
Open	76	33.7
Laparoscopic	149	66.3

Medical conditions characteristics for the study population

Table 4 showed that medical conditions characteristics for the study patients including: medical history (diabetes mellitus DM 8.5%, CVA 4.4%, IBS 1.2%, etc.), postmenopausal status percentage for non-menopause patients was 93.8 percentages, family history of gallstone (percentage for not present was 65.3%) as well as the smoking percentage for non-smoker was 65.3 percentages.

Table 4: Medical conditions characteristics for the study patients.

Characters	N	Percentage (%)
Medical history		
Not presence	153	67.3
Presence of diabetes mellitus	16	8.5
Presence of hypertension	11	4.9
Presence of CVA	10	4.4
Presence of CAD	6	2.7
IHD	2	0.9
COPD	1	0.4
Presence of hyperlipidaemia	10	4.4
Presence of renal disease	5	2.2
Presence of liver disease	1	0.4
Presence of IBS	4	1.2
Presence of peptic ulcer	2	0.9
Presence of the anemia	4	1.8
Family history of the gallstone		
No	147	65.3
Yes	78	34.7
Postmenopausal status		
No	211	93.8
Yes	14	6.2
Smoking		
Current	88	39.1
Non smoker	137	60.9

Laboratory investigation for the study patients

Table 5 showed the laboratory investigation for the study population including: FBG percentage for normal results was 85.7 percentages, serum cholesterol percentage for normal results was 52.4 percentages, serum triglycerides percentage for normal results was 83.1 percentages, LDL percentage for normal results was 77.8 percentages, HDL percentage for normal results was 89.8 percentages, HBA1c percentage for normal results was 84 percentages, elevated liver enzyme percentage for normal results was 77.3 percentages.

Table 5: Laboratory investigation for the study patients.

Characters	N	Percentage (%)
Fasting blood glucose (normal 70-100 mg/dl)		
Normal	193	85.7
Elevated	32	14.3
Serum cholesterol (normal less than 200 mg/dl)		
Normal	118	52.4
Eevated	107	47.6
Serum triglycerides (normal less than 150 mg/dl)		
Normal	187	83.1
Elevated	38	16.9
Serum LDL (normal less than 110 mg/dl)		
Normal	175	77.8
Elevated	50	22.2
Serum HDL (normal 60 mg/dl)		
Normal	202	89.8
Elevated	23	10.2
HbA1C% (normal 4-6.5%)		
Normal	189	84
Elevated	36	16.0
Serum bilirubin (normal 1.2 mg/dl)		
Normal	185	82.2
Elevated	40	17.8
Elevated liver enzymes		
Yes	51	22.7
No	174	77.3

Association of socio-demographic features and gallstones type

Table 6 showed the association between socio-demographic features and gallstone number (solitary stone, multiple stone). The results showed significant result $p<0.05$ and good association between age, and type of stones present (solitary or multiple); but for the gender, education level, occupation status, residence, Socioeconomic Class the results was non-significant $p>0.05$.

Association of medical condition and gallstones content

Table 7 showed the association of medical condition and gallstones content (pigment stone, cholesterol stone, and mixed stone). The results showed significant result [P-value<0.05] and good association between all medical condition and stone content (pigment stone, cholesterol stone, and mixed stone).

Logistic regression analyses

Table 8 showed the multivariate logistic regression analysis showed that gallstone disease is more probable to be associated with the following conditions: increased age (p=0.004); increased female gender (p=0.023); family history of gallstones (p=0.001), S. cholesterol level; (p=0.001), and BMI (p=0.003); means significant risk for development of asymptomatic gallstones in next years.

Table 6: Association of socio-demographic features and gallstones type.

Characters	Solitary stone (%)	Multiple stone (%)	P value
Age (years)			
18-30	74.0	57.8	0.032
30-50	22.0	33.3	
50-80	4.1	8.8	
Gender			
Male	44.7	47.1	0.725
Female	55.3	52.9	
Education level			
No education	3.3	2.9	0.990
Primary education	1.6	2	
Secondary education	22	20.6	
Collage education	73.2	74.5	
Occupation status			
Governmental job	28.5	31.4	0.066
Private job	16.3	15.7	
Retired	4.1	1	
Non employed	50.4	45.1	
Housewife	2.4	6.9	
Residence			
Urban	95.9	98	0.365
Rural	4.1	2	
Socioeconomic class			
High-income class	15.4	16.7	0.183
Middle-income class	76.4	67.6	
Low-income class	8.1	15.7	
Material status			
Single	66.7	58.8	0.148
Married	28.5	39.2	
Divorced	4.9	2	
No. of children			
0-3	96.7	90.2	0.227
4+	3.3	9.8	

Table 7: Association of medical condition and gallstones content.

Characters	Pigment stone (%)	Cholesterol stone (%)	Mixed stone (%)	P value
Medical history				
DM	100	0	0	0.009
Hypertension	33.3	16.7	50	0.001
Anaemia	0	100	0	0.019
Presence of CVA	0	0	100	0.123
Presence of CAD	0	0	100	0.011
Presence of renal disease	25	50	25	0.512
Presence of liver disease	0	0	100	0.003
Presence of IBS	100	0	0	0.002
Family history of gallstone				
No	22.4	59.2	18.4	0.009
Yes	28.2	46.2	25.6	

Table 8: Logistic regression analyses.

Variables	B coefficient	P value
Age (years)	0.027	0.004
Female gender	0.628	0.023
Family history of gallstones	2.233	0.001
S. Cholesterol (mg/100 ml)	0.398	0.001
BMI (kg/m^2)	0.091	0.003

DISCUSSION

The present study aimed to evaluate predicators and associated risk factors of GBS in patients visited consultation surgical departments in Baghdad. The prevalence of gallstones may be related to the cultural variances or may be to other sociodemographic factors that showed in the present study such as the younger age, this agreed with Novacek which showed that the present finding of increase prevalence of gall stones with younger age at menarche suggests that gall stone disease is associated with the length of fertility period.[8]

Female gender is one of main risk factors for gallstone disease, which is in agreement with Zamil et al.[6] In view of that, females patients are more predisposed to GBS because of female's sex hormones and pregnancy hormones increase the incidence of GBS formation; since these hormones may increase cholesterol excretion in the bile thus increasing casual of GBS formation.[9,10] The study results for increase GBS formation also agreed with Khan et al study which showed that urbanization together with increases in BMI are accompanying with an increase in symptomatic cholelithiasis .These factors with decreasing age of cholecystectomy patients all together provide additional support to above hypothesis.[11]

Also, most of patients were with: collage education (73.8%), middle-income class (72.4%), this compatible with Völzke et al study.[10]

The study results for the number of children /0-3 (93.8%), number of pregnancies/0-3 (93.8%), agreed with previous study showing that the likelihood of having gallstones associated with two or more pregnancies was considerably higher in younger than in older women making lithogenic risk related to multiple pregnancies may be much more in younger women.[12]

According to collected data which show that the percentage of the normal BMI higher than the overweight in value for normal (73.3%) for overweight BMI to (20.4%) for overweight BMI. This come with previous Iraqi study showed that an increased BMI is an avoidable risk factor, which associated with a higher risk of gallstones.[5,13,14]

The present study results agreed with Park et al showed that percentage for the type of diet were high for omnivorous (87.1%). Which generally result from the eating of meat from beef and pork, and animal fat was definitely associated with the risk of cholesterol gallstone.[15]

The present study showed that the percentage for type of physical activity were high for the moderate intensity (44.9%). This agreed with Henao-Morán et al found that PA duration affects the level of protection against GBS with 150 min per week of moderate to vigorous physical activity. Although the mechanisms by which PA protects against GBS are not clear but it's mainly related to: 1: prevention of insulin resistance, 2: the increases in cholesterol low density lipoprotein receptors in the liver that may also be protective by reducing bile cholesterol saturation and increasing HDL-cholesterol, 3: increasing mucin production in the gallbladder wall and mitigating gallbladder contraction, 4: decreases in triglyceride levels related to physical activity promote diminished mucin production and thus lower the risk of gallstones, 5: it has also been observed that prolonged intestinal transit time is a risk factor for GBS. This may be due to increased deoxycholic acid formation in, and absorption from, the large bowel. And PA will stimulate intestinal motility.[16]

According to the collected data which show that the percentage of laparoscopic higher than open cholecystectomy in value (66.3%) for laparoscopic to (33.7%) for open cholecystectomy, this agreed with Pimpale et al study which showed that Laparoscopic cholecystectomy offers best surgical management.[17]

The medical conditions characteristics for the study patients including: medical history for patients with (DM=8.5%) which agreed with previous research shown that the prevalence of gallstones was significantly more in diabetics (21.5%) as compared with non-diabetics (12.6%).[5]

Family History of Gallstone (percentage for not present was 65.3%) and smoking percentage for non-smoker was 65.3%, these results agreed with Palermo et al. Moreover, risk factors for GBS formation may suppose that age, smoking, fatty liver and a family history of GBS which are strongly associated with an increase in the prevalence of this condition.[18]

The laboratory investigation results for the study population found that serum cholesterol percentage for normal results was 52.4% and most of patients presented with normal cholesterol level in agreement with other studied presented that high serum cholesterol concentrations were independently associated with the risk of gallstones.[19,20]

The association between socio-demographic features and gallstone number (solitary stone, multiple stone). The results showed significant result ($p<0.05$) and good association between age, and type of stones present (solitary or multiple); but for the gender, education level, occupation status, residence, socioeconomic class the results was non-significant ($p>0.05$), which agreed with previous study results.[5]

The association of medical condition and gallstones content (pigment stone, cholesterol stone, and mixed stone). The results showed significant result ($p<0.05$) and good association between all medical condition and stone content (pigment stone, cholesterol stone, and mixed stone), which agreed with previous study results.[5]

The multivariate logistic regression analysis showed that gallstone disease is more probable to be associated with the following conditions: increased age (p=0.004); increased female gender (p=0.023); family history of gallstones (p=0.001), S. cholesterol level; (p=0.001), and BMI (p=0.003); means significant risk for the development of asymptomatic gallstones in next years in compatible with many other prior researches for a positive significant association between diabetes and gallstones was noticed.[21,22] Positive family history is associated with increased risk for asymptomatic gallstones, the same results were found in other studies directed previously for this cause which showed that there is a strong familial tendency for gallstone formation in relatives of gallstone disease patients. This enhances the knowledge of genetic as risk factor for gallstone, or shared same environmental factors such as diet.[23,24]

CONCLUSION

The prevalence of asymptomatic gallstone was relatively high in this region. Female gender, age, high cholesterol level, family history of gallstones, and increased BMI were independent risk factors for gallstones.

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