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ASYMPTOMATIC GALLSTONES IN DIABETIC PATIENTS

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Abstract

Diabetes was reported to be frequently associated with inflammation of biliary tract and cholelithiasis. The definite cause of gallstones in diabetics is not well clarified. However, due to autonomic neuropathy, the contraction of gallbladder is poor resulting in hypomotility, impaired gallbladder emptying and biliary stasis resulting in increased gallbladder volume, which to predispose to gallstone formation.

This study aimed to determine the prevalence of asymptomatic gallstones and its associated factors among diabetic patients in Basrah.

This cross sectional study was carried out in diabetic Centre in Al-Fayhaa Hospital, Basrah, Iraq from November 2014 to February 2015. We recruited 210 patients with diabetes (type1 and 2), 89 males and 121 females, questionnaire used to include the sociodemographic features. BMI measurement and ultrasound examination to find gallstone was done.

Blood samples were taken for HbA1C, FBS, Lipid profile and the association between duration of diabetes, lipid levels, FBS, with gallstone was evaluated.

Gallstone was seen in 25.2% of diabetic patients. Gallstone was higher in patients with increased duration of diabetes, in patients with BMI more than 25kg/m, with increased cholesterol and triglycerides levels and with high level of HbA1C.

In conclusion, the prevalence of asymptomatic gallstones in diabetic patients in Basrah increases with increased duration of DM, high level of HbA1C, BMI, cholesterol, and triglyceride levels and with hyperglycemia. No significant association was found with; age, parity, gender and type of diabetes.

Introduction

Although the association between diabetes mellitus (DM) and gallstones is controversial, many studies revealed that diabetic patients are two to three times more risky for gallstones than non-diabetics[1]. Diabetes was reported to be frequently associated with inflammation of biliary tract and cholelithiasis[2]. The definite cause of gallstones in diabetics is not well clarified. However, due to autonomic neuropathy, the contraction of gallbladder is poor resulting in hypomotility, impaired gallbladder emptying and biliary stasis[3,4] resulting in increased gallbladder volume, which predispose to gallstones formation[5]. Obesity, hypertriglyceridemia[6], and hyper-insulinemia[7], which are frequently reported in diabetic patients, are proposed to be contributing factors for gallstones formation.

The prevalence of gallstones in diabetic patients differs from one study to another. Chapman et al[8] in their case-control study found a higher prevalence of gallstones in diabetic patients than controls (32.7% vs. 20.8%; P<0.001). In Libya (2013)[9], the prevalence was 39.8%, and in Nigeria (2013) was 17.5%[10]. In Italy, a study showed that the prevalence of gallstones in diabetic patients was significantly higher than in the general population (24.8% vs.13.8%)[11]. In Iraq (Baghdad), a case-control study revealed that 33% of type 2 diabetic patients had gallstones compared to

17% of non-diabetic patients[12]. Little is known about the prevalence of asymptomatic gallstones among diabetic patients in Basrah. This study was conducted to determine the prevalence of asymptomatic gallstone disease and its associated factors among diabetic patients (type1 and 2) in Basrah.

Patients and Methods

This is a cross-sectional study conducted in Diabetic Center in Al-Fayhaa General Hospital, which is a multispecialty hospital and one of the five major hospitals in Basrah in the period from November 2014 to February 2015.

The study population included known diabetic patients attending the diabetic center during the study period who were asymptomatic for gallstones or did not receive any treatment for gallstones previously. Patients with history of hepatic disorders, cholecystectomy or haemo-globinopathies, and pregnant women were excluded.

The minimum sample size needed was calculated assuming a prevalence rate of 20% with a precision degree of 0.05 at 95% confidence interval[13]. Consecutive patients who fulfilled the inclusion criteria and agreed to participate were included in the study.

Data were collected using a questionnaire covering socio-demographic aspects, medical history and possible risk factors of gallstones. Weight and height were measured and body mass index (BMI) was calculated. Blood sample was collected after 12 hours fasting and all laboratory investigations were done in the same hospital. The laboratory investigations included fasting plasma glucose, Serum cholesterol, Low-density lipoprotein (LDL), high-density lipoprotein (HDL), Triglycerides, and HbA1C.

Ultrasonography which is considered as a method of choice for diagnosis of gallstones with a diagnostic accuracy of 93%[14] was used to diagnose gallstones. A radiologist did all ultrasound examinations.

The Ethics and Research Committee of College of Medicine, Basrah University approved the study, and an informed consent was obtained from each participant before inclusion in the study.

Statistical analysis

The data were analyzed through Statistical Package of Social Sciences (SPSS) version 19. Frequencies and percentages were calculated for categorical variables and Chi squared (X2) or Fisher Exact tests were used for assessment of differences between these variables. Means and standard deviations were calculated for quantitative data and t-test or Mann Whitney tests were used for comparison. P-value of <0.05 was considered as a statistical significant level.

Results

Out of 246 targeted patients, 210 consented to participate in the study giving a response rate of 85.4%. The mean age of the participants was 50.3±10.9 years (Range: 13-75 years). Females constituted 57.6% of the study population. The majority (91.4%) were with type 2 diabetes mellitus, and 28.1% of the diabetic patients had a more than 10 years duration of diabetes.

The prevalence of asymptomatic gallstones among the studied population was 25.2% (95% CI, 19.2 -30.3). A significantly higher prevalence rate of gallstones was found among low educated patients, obese, women with high parity, and patients with a longer duration of the disease. The prevalence of gallstones increased significantly with age and it reaches its peak at age group 40-49 years then declined after that. Gender was not found to be significantly associated with the prevalence of gallstones. However, females showed higher rates of gallstones than males as demonstrated in table I.

Table I: Prevalence of gallstones according to socio-demographic and clinical characteristics

Character	Gallstones +ve No. (%) 53 (25.2)	Gallstones -ve No. (%) 157 (74.8)	P-value
Socio-demographic			
Age (years), No. (%)			0.002
< 30	0 (0.0)	12 (100.0)	
30 – 39	2 (11.8)	15 (88.2)	
40 – 49	26 (43.3)	34 (56.7)	
50 – 59	15 (19.7)	61 (80.3)	
≥ 60	10 (22.2)	35 (77.8)	
Gender			0.151
Male, No. (%)	18 (20.2)	71 (79.8)	
Female, No. (%)	35 (28.9)	86 (71.1)	
Education			0.026
< 12 years, No. (%)	48 (28.6)	120 (71.4)	
≥ 12 years, No. (%)	5 (11.9)	37 (88.1)	
Smoking			0.408
Smokers, No. (%)	6 (33.3)	12 (66.7)	
Non-smokers, No. (%)	47 (24.5)	145 (75.5)	
Parity (n= 121)			0.086
0 – 3	4 (15.4)	22 (84.6)	
4 &more	31 (32.6)	64 (67.4)	
Clinical characteristics			0.149
Type 1 DM, No. (%)	2 (11.1)	16 (88.9)	
Type 2 DM, No. (%)	51 (26.6)	141 (73.4)	
Duration of diabetes in years	No.(%)		0.002
≤ 5 years	16 (17.2)	77 (82.8)	
6-10 years	12 (20.7)	46 (79.3)	
> 10 years	25 (42.4)	34 (57.6)	
BMI (Kg/m^2), No. (%)			< 0.001

< 25	0 (0.0)	43 (100.0)	
25 - 29.9	10 (16.9)	49 (83.1)	
≥ 30	43 (39.8)	65 (60.2)	

Levels of fasting plasma glucose, serum cholesterol, glycosylated hemoglobin (HbA1C), and triglycerides were significantly higher in patients with gallstones than those without gallstones. Low level of high-density lipoprotein (HDL) was significantly associated with gallstones, while no significant association was found between low-density lipoprotein (LDL) and gallstones as shown in table II.

Table II: Comparison of levels of biochemical parameters between diabetic patients with and without gallstones

Laboratory investigations	Gallstones +ve 53 (25.2) Mean±SD	Gallstones -ve 157 (74.8) Mean±SD	P-value
Fasting plasma glucose, mg/100 ml	252.1±73.9	210.9±73.1	0.005
HbA1C, %	11.1±2.1	9.6±2.2	< 0.001
Serum Cholesterol, mg/100 ml	272.8±46.0	183.0±42.2	< 0.001
Serum LDL, mg/100 ml	114.1±44.8	111.9±32.7	0.462
Serum HDL, mg/100 ml	35.3±9.2	44.3±12.9	0.002
Serum Triglycerides, mg/100 ml	254.4±144.4	174.4±99.6	0.003

On logistic regression analysis, the factors that significantly predict gallstones were; duration of diabetes, fasting plasma glucose, serum cholesterol, triglycerides, HbA1C, and body mass index as demonstrated in table III.

Table III: Logistic regression analyses

Variable	B-Coefficient	P-value	OR	95% CI	
				Lower	Upper
Duration of diabetes	1.442	0.011	4.23	1.39	12.79

Fasting plasma glucose	1.565	0.021	4.78	1.27	18.06
S. Cholesterol	0.054	<0.001	1.06	1.03	1.08
S. Triglycerides	0.012	0.009	1.03	1.02	1.06
BMI	3.483	0.006	3.56	2.66	8.11
HbA1C	0.307	0.001	1.43	1.17	1.75

Discussion

Gallstones disease is thought to be a benign disease since about 70-80% of patients were found to be asymptomatic at the time of diagnosis[15,16], and only 10-25% of them will progress to be symptomatic[17].

In this study, the prevalence of asymptomatic gallstones in diabetic patients was 25.2% while a study in Baghdad, Iraq revealed a prevalence of 33%[12]. Other studies from different countries showed different figures. In Taiwan (2004), the prevalence was 14.4%[2], Italy (2004): 24.8%[11], Nigeria (2013) 17.5%[10]. Such considerable variation in prevalence of gallstones in diabetic patients could be attributed to differences in study design, geographical variation, and ethnicity[18,19].

Cholelithiasis is a disease of all age groups, but the incidence peak in diabetic patients was found in age group 60-69 years and declined in the eighth decade[20]. Our study revealed that the peak prevalence of gallstones was in the age group 40-49 years, a result which is consistent with that of another study in Iraq (Tikrit)[21], and Sudan[22]. In agreement with other studies[23,24], the current study showed a higher prevalence of gallstones among female patients particularly among those aged 40-49 years. Women in reproductive age group are 2-3 times more risky to have gallstones than non-reproductive aged women. It is due to the high estrogen level which causes bile super-saturation with cholesterol and consequently increasing its excretion[23].

In this study, diabetic patients who are overweight and obese with body mass index more than 25kg/m^2 showed increment in the prevalence of gallstones compared with diabetic patients with body mass index less than 25kg/m^2 (normal level) and this result is similar to the findings of Al-Bayati[12], Miscingna et al[25], Pagliarulo et al[11] and Grigor'eva[26] who found that high body mass index sustained significance of association at multivariate analysis, and also this result is in agreement with that of a study done in Nigeria[10]. Another study also showed a strong association between obesity and diabetes especially non-insulin dependent diabetes mellitus[2], obesity by itself may be considered as risk factor for gallstones[27,28].

Our study found that duration of DM was strongly associated with increased frequency of gallstones and this is in agreement with other studies[10,12,29] but it is inconsistent with that of a case control study done in Benghazi[9], which reported that the duration of diabetes did not affect the prevalence of gallstones in diabetic patients. The strong positive association may be explained by increment of insulin resistance with increased length of diabetes mellitus[12,25] or may be the effect of autonomic neuropathy on gall bladder function with increased duration of diabetes[30].

The high level of HbA1C reflects poor control of diabetes and this study showed positive association between HbA1C and gallstones prevalence which is consistent with other study[12] which showed a high prevalence of gallstones among diabetic patients with high level of HbA1C in comparison with diabetic patients of low level of HbA1C. This may be explained by

the response to hyperglycemia by reducing bile salt output and reducing motility of gall bladder[26,31]. Also the result of this study indicates that there was a high significant association between gallstones frequency in diabetic patients and the cholesterol and triglycerides level and such association was maintained after multivariate logistic regression analysis, a result that agreed with other studies done by Hung et al[32], Al-Saadi and Al-Ardhi[33]. It is believed that increased cholesterol and triglycerides levels will decrease and corrupt the function of gallbladder[34], while other study reported that the gallstone disease was not significantly associated with cholesterol or triglycerides level[11] which means that other factors may be participated in the gallstone formation.

At last, there was a significant association between gallstones prevalence and hyperglycemia, the chronic hyperglycemia reflects poor control condition of diabetes and has its bad complications on multiple organs in the body. The study done by Liu et al[35] de Boer et al[36] suggested that chronic hyperglycemia affects the movement of bile duct and this may lead to hold the bile and then to gall stone disease.

Conclusion

The prevalence of asymptomatic gallstones in diabetic patients in Basrah doesn't differ greatly from what was reported in Iraq and some countries. It increases with; increment of duration of diabetes, high levels of HbA1C, body mass index, cholesterol and triglycerides and with hyperglycemia. No significant association was found with age, parity, gender and the type of diabetes.

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