

Original Article

Gallstone disease founded by ultrasonography in functional dyspepsia: prevalence and associated factors

Yaser Froutan¹, Ahmad Alizadeh¹, Fariborz Mansour-Ghanaei², Farahnaz Joukar², Hossein Froutan³, Faeze Berenji Bagheri¹, Mohammad Reza Naghipour², Seyed Ali Chavoshi⁴

¹Department of Radiology, Guilan University of Medical Sciences, Rasht, Iran; ²Department of Gastroenterology, Gastrointestinal and Liver Diseases Research Center (GLDRC), Guilan University of Medical Sciences, Rasht, Iran; ³Department of Internal Medicine, Tehran University of Medical Sciences, Tehran, Iran; ⁴Department of Radiology, Shahid Beheshti Hospital, Qum, Iran

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Abstract: The aim of this study was to evaluate the frequency of gallbladder stone in functional dyspepsia (FD) by abdominal ultrasonography and to determine the factors associated with this frequency in Guilan province. A total of 195 subjects who referred to outpatient clinic of Razi Hospital, a tertiary referral center (Guilan, Iran) to evaluate FD were included in this study. They were interviewed by using a questionnaire and underwent ultrasonography. Among the 195 subjects were 18.5% male and 81.5% female. The overall frequency of Gallstones (GS) was 19% (37/195) with 17% males and 83% female. In patients with dyspepsia, the presence of fatty liver evidenced by ultrasonography was 67% (131/195). From 131 patients with fatty liver disease 24 (18.3%) have been reported GS. The most frequent symptom in all participants as well as patients with GS and patients with fatty liver was abdominal pain (69.7%, 81% and 66%, respectively) followed by excess flatus. Risk factor associated with increased odds ratios (ORs) for the development of gall stones was diabetes mellitus (OR = 2.63). It also showed that gallbladder wall thickening was more common in patients with GS (OR = 36.63). GS disease was not significantly related to the age, gender, fatty liver, renal stone, history of hypertension (HTN) and hyperlipidemia (HLP), alcohol consumption and smoking status. Patients with FD especially if they have diabetes should be referred for upper abdominal ultrasonography for screening and early detection of GS disease.

Keywords: Functional dyspepsia, gallstone, fatty liver, ultrasonography

Introduction

The prevalence of dyspepsia varies between 10-40% in different populations [1-3]. Chronic or recurrent dyspeptic symptoms have been reported by nearly 20% to 30% of people each year [4]. The management of dyspepsia costs £1.1 billion in the UK per year [5]. In several community surveys have been reported that only 20% of people with dyspeptic symptoms had sought physicians and more than 50% of dyspeptic patients were taking medication most of the time [6-8].

“Dyspepsia” is the medical term for difficult digestion. Various symptoms in the upper abdomen, such as fullness, discomfort, early satiation, bloating, heartburn, nausea, vomiting or epigastric pain and also lack of appetite is pre-

sented as dyspepsia [9]. The potential causes of dyspepsia are known to include peptic ulcer disease, gastro-esophageal reflux, Hiatus hernia, Gallstones (GS) and functional dyspepsia (FD) [9]. FD is defined as the presence of chronic or recurrent pain or discomfort thought to relate the gastroduodenal region, in the absence of any organic, systemic, or metabolic disease that is likely to explain the symptoms [4, 10]. Hence, correct differentiation between FD and other disease like peptic ulcer and gallstone related symptom are required. Several interventions have been performed for diagnosis of functional dyspepsia, including upper gastro-intestinal endoscopy, upper abdominal ultrasonography, and routine hematology and biochemistry screening blood tests [11]. Although, functional dyspepsia is not a life-threatening disease, because of the high costs

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Table 1. Study population characteristics (N = 195)

Characteristics	
Age (mean) ± SD	48 ± 11.4
Age distribution (yr)	
20-39 n (%)	50 (25.5)
40-59 n (%)	117 (59.8)
≥ 60 n (%)	28 (14.4)
Sex	
Male n (%)	36 (18.5)
Female n (%)	159 (81.5)
With hypertension n (%)	41 (21)
With hyperlipidemia n (%)	46 (23.5)
With diabetes n (%)	23 (11.8)
Fatty liver (%)	131 (67)
Renal stone (%)	22 (11.2)
TGW* (%)	8 (4.1)

*Thickened gallbladder wall.

of diagnostic and treatment intervention [7], it is required to select a cost effective management.

GS are extremely common in worldwide. The prevalence of asymptomatic gallstone was reported between 10%-15% [12, 13]. The average risk of developing symptomatic disease were estimated 2-2.6% annually [14]. Approximately 10% and 20% of asymptomatic patients became symptomatic within 5 and 20 years of diagnosis, respectively [14, 15]. GS associated symptoms may be non-specific, it could be difficult to distinguish between symptomatic disease and FD. On the other hands, most GS is incidentally found during clinical evaluation of dyspepsia or routine ultrasonography [16]. Studies suggested Transabdominal ultrasonography as a gold standard test for the diagnosis of gallbladder stones with more than 95% sensitivity and specificity [17, 18].

The aim of the current study to examine the frequency of GS founded by ultrasonography in patients with dyspeptic symptom attending Razi hospital, Guilan, Iran.

Material and methods

Subjects and study design

This cross-sectional study was carried out on patients with functional dyspepsia, which referred to the gastroenterology clinic of the Razi hospital between December, 2012, and

January, 2014. The study design was approved by Medical Ethics Committee of Guilan University of Medical Sciences (GUMS).

A convenience sample with chronic or recurrent pain or discomfort centered in the upper abdomen with or without heartburn, vomiting or nausea for at least 3 months were included. Patients with any evidence of organic disease on the upper endoscopy examination or clinical assessment, prior history of cholecystectomy or gastric surgery, history of peptic ulcer disease and any evidence that dyspepsia related to irritable bowel syndrome (IBS) were excluded.

All the subjects were familiar in detail with the study and they all signed a written consent. After selecting patients based on the inclusion and exclusion criteria, abdominal ultrasonography was performed by an expert radiologist in order to find: gallstones, wall thickness (>3 mm), evidence of fatty liver and renal stone.

All participants were asked to come to a morning examination after an overnight fast of ≥ 8 h. Abdominal ultrasonography was conducted using a scanner equipped with a 2.0-5.0-MHz transducer (Voluson 730, GE Health-care, Pittsburgh, PA, United States).

The ultrasonographer was unaware of the participants' clinical characteristics. All subjects were interviewed by using a questionnaire that covered the demographic features, symptoms and history of hypertension (HTN), diabetes and hyperlipidemia (HLP).

Statistical analysis

Categorical variables were presented as absolute frequencies and percentages.

Univariate analysis methods were used at the 5% level of significance. To evaluate potential predictive variables associated with gallbladder stones, variables with *P*-values of < 0.2 were added to multivariate logistic regression models (adjusted OR; 95% CI). Statistical analysis was carried out with the SPSS (version 20).

Result

During study period, a total of 195 patients with FD acquired the inclusion criteria, and were underwent abdominal ultrasonography to detect GS. Patient characteristics are present-

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Table 2. Uni and multivariate analyses of predictive variables in functional dyspeptic patients with and without gallstone

Variables	with gallstone (37) N (%)	without gallstone (158) N (%)	OR*	P**	Adjusted OR (95% CI***)
Risk factors					
Age (yr)					
20-39	11(24.4)	34 (75.6)	1	0.202	1 (Reference)
40-59	18 (15.0)	102 (85.0)	1.833	0.160	0.207 (0.024-1.803)
>60	8 (26.7)	22 (73.3)	0.890	0.828	0.076 (0.008-0 .753)
Sex					
Male%	6 (16.7)	30 (83.3)	1.21	0.696	
Female%	31 (19.5)	128 (80.5)			
Smoking	1 (11.1)	8 (88.9)	0.521	0.545	
Alcohol	0 (0)	5 (100)	-	0.999	
Hypertension	7 (17)	34 (83)	0.851	0.727	
Diabetes	8 (34)	15 (66)	2.63	0.045	18.044 (1.917-169.856)
Hyperlipidemia	7 (15.2)	39 (85)	0.712	0.459	
Ultrasonography finding					
Wall thickness	7 (87.5)	1 (12.5)	36.63	0.001	144.925 (9.428-2227.762)
Fatty liver	24 (18.3)	107 (81.7)	1.136	0.739	
Renal stone	4 (18.2)	18 (81.8)	1.061	0.920	

*OR: odds ratio, **P-values of < 0.05. ***CI: confidence interval; Adjusted OR: Adjusted odds ratio.

ed in **Table 1**. There were 36 (18.5%) men and 159 (81.5%) women with mean age 48 ± 11.4 years. The frequency of GS was 19% (37/195) in patients with dyspepsia which, 83% of them were women. The age group of 40-59 y/o reported the highest proportion of dyspepsia (117/195). Only 4.6% of dyspeptic patients were smoker. Similarly, the overall prevalence of alcohol drinker was small (2.6%, 5/195). 21%, 23.5% and 11.8% of study population reported HTN, HLP and diabetes respectively.

In patients with dyspepsia, the overall prevalence of fatty liver was 67% (131/195). From 131 patients with fatty liver disease 24 (18.3%) have been reported GS.

In univariate analysis (**Table 2**), GS disease was common among patients with diabetes (OR = 2.63), It also showed that gallbladder wall thickening was more common in patients with gallstone (OR = 36.63). GS disease was not significantly related to the age, gender, fatty liver, renal stone, a history of HTN and HLP, alcohol consumption and smoking. At multivariate analysis (**Table 2**), it was clear that people with a past history of diabetes were 18 times more likely to have GS disease (adjusted OR =

18.044; 95% CI: 1.917-169.856) than people with no history of diabetes.

The most reported symptom in all study population as well as patients with GS and patients with fatty liver was abdominal pain (69.7%, 81% and 66%, respectively) followed by excess flatulence (**Figure 1**).

Discussion

We have reported the frequency of GS founded by ultrasonography in patients with functional dyspepsia. The results of our study showed among patients whose functional dyspepsia 19% had GS with more prevalent in women. In other studies, the frequency of GS in patients with functional dyspepsia varies from 2% to 16.% [19, 20]. Similarly, Eldon A. Shaffer reported the prevalence of Cholelithiasis founded by ultrasonography in several American and European population was ranging from 4.6% to 61.5% [12]. Studies indicated that female gender is an important risk factor for GS disease [21, 22].

We founded the low percentage of smoker and alcohol drinkers in our study population. In several population based studies, smoking [23-25]

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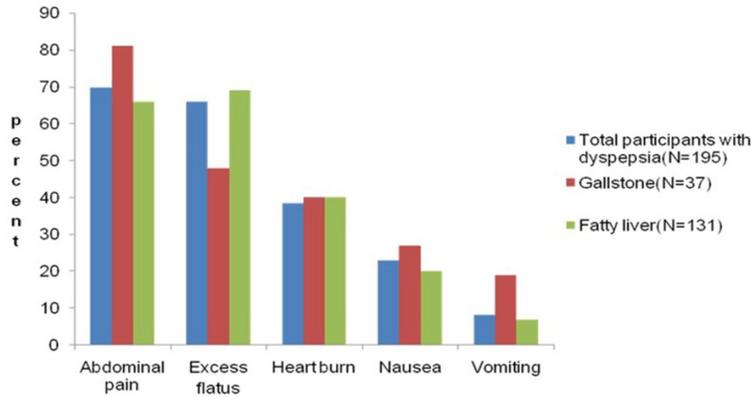


Figure 1. Percentage of participants reporting symptoms

and alcohol [23, 26, 27] has not been shown to be a risk factor for functional dyspepsia.

In our study, from 131 patients with fatty liver disease 24 (18.3%) have been reported GS. In other words, more than half of patient with GS disease had fatty liver. Paola Ioria & et al in 2005 reported the overall prevalence of gallbladder disease in fatty liver disease was 19.8% with higher proportion in female [28]. The pathophysiologic basis of the increased prevalence of gallbladder disease in fatty liver is multifactorial, with an interaction of supersaturation, gallbladder hypomotility, and nucleation of cholesterol microcrystal [29]. Patients with fatty liver, often overweight-are at risk for GS disease [30]. It is obvious that obesity and hypertriglyceric condition may increase biliary cholesterol secretion, and alter gallbladder motility.

We reported the frequencies of gallstone were not significantly different in terms of history of HTN, HLP and renal stone. Similarly, a study indicated no further frequency of hypertension in patients with GS [31], while other studies reported hypertension was significantly associated with gallstones [32, 33]. In fact, unhealthy lifestyle may be considered as a predisposing factor for obesity, HTN and hypertriglyceridemia (HTG) and then cholelithiasis [33].

Several studies showed that HTG levels have been associated with gallstones [34, 35], whereas several prospective studies of gallstones reported no associations with total cholesterol and LDL [36, 37]. In fact, Patients with visceral obesity and dyslipidemia are at increased risk for GS disease and this may particularly as a result of disturbed triglyceride

metabolism [38]. In our study, we assessed the HLP just by taking history of HLP. So, we cannot differentiate between Hypercholesterolemia and HTG.

Our results show that GS disease was common among patients with diabetes. Several studies have shown the increased incidence of gallstone disease in diabetic patients [39-42]. In a cross-sectional community study in a rural village of Taiwan, diabetes mellitus was also a risk factor for GS disease in women [43].

Diabetic patients seem to have an increased incidence of gallstones and gall bladder problems, but these, much like fatty infiltration of the liver, are primarily related to the obesity associated with type 2 diabetes and not to the diabetes itself. Obesity leads to secretion of bile by the liver that is supersaturated with cholesterol, leading to crystallization and stone formation [44].

Although, both renal stone and GS disease are associated with a variety of diseases including obesity and metabolic syndrome, the coexisting of renal stone and gallstone disease is still controversial. However, Chia-Hsiang Li & et al. [45]. In a nationwide cohort study showed that the probability of renal stones is significantly higher in GS patients, compared with the general population.

The two most common symptoms reported in our study population were abdominal pain followed by excess flatus. Other studies indicated the majority of dyspeptic patients had upper abdominal pain, fullness after eating, upper abdominal discomfort, upper abdominal bloating, belching, nausea and vomiting [2, 23]. As well as, dyspeptic patients with GS experienced the same symptoms such as abdominal pain, nausea and upper abdominal discomfort [9, 15].

In the present study, patients with GS have been reported more frequently of gallbladder wall thickening in ultrasonography. This is in line with the result of a recent study which showed that inflammation of the gallbladder wall is related to progression of cholesterol GS disease [46].

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This study provides evidence of the frequency of GS founded by sonography in patients with FD. Our study, while having much strength, involved a limitation that should be considered. In this study, we assess the frequency of chronic disease such as diabetes, HLP and HTN, just by taking history instead of laboratory data.

In conclusion, this study showed that gallstone has been founded by ultrasonography in 19% of FD. Physicians should pay more attention to patients with FD especially if they have diabetes mellitus. They should be referred for upper abdominal ultrasonography for screening and early detection of GS disease.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Fariborz Mansour-Ghanaei, Gastrointestinal and Liver Diseases Research Center (GLDRC), Guilan University of Medical Sciences, Razi Hospital, Sardarjanga Ave, Rasht 41448-95655, Iran. Tel: +98-131-5535116; Fax: +98-131-5534951; E-mail: ghanaei@gums.ac.ir

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