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BRIEF ARTICLE

A population-based cohort study of symptomatic gallstone disease in diabetic patients

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Abstract

AIM: To investigate the prevalence of gallstone disease (GSD) and to evaluate the risk of symptomatic GSD among diabetic patients.

METHODS: The study was conducted by analyzing the National Health Research Institutes (NHRI) dataset of ambulatory care patients, inpatient claims, and the updated registry of beneficiaries from 2000 to 2008. A total of 615 532 diabetic patients without a prior history of hospital treatment or ambulatory care visits for symptomatic GSD were identified in the year 2000. Age- and gender-matched control individuals free from both GSD and diabetes from 1997 to 1999 were randomly selected from the NHIR database (n = 614 871). The incidence densities of symptomatic GSD were estimated according to the subjects' diabetic status. The distributions of age, gender, occupation, income, and residential area urbanization were compared between diabetic patients and control subjects using Cox proportion hazards models. Differences between the rates of selected comorbidities were also assessed in the two groups.

RESULTS: Overall, 60 734 diabetic patients and 48 116 control patients developed symptomatic GSD and underwent operations, resulting in cumulative operation rates of 9.87% and 7.83%, respectively. The age and gender distributions of both groups were similar, with a mean age of 60 years and a predominance of females. The diabetic group had a significantly higher prevalence of all comorbidities of interest. A higher incidence of symptomatic GSD was observed in females than in males in both groups. In the control group, females under the age of 64 had a significantly higher incidence of GSD than the corresponding males, but this difference was reduced with increasing age. The cumulative incidences of operations for symptomatic GSD in the diabetic and control groups were 13.06 and 9.52 cases per 1000 person-years, respectively. Diabetic men exhibited a higher incidence of operations for symptomatic GSD than did their counterparts in the control group (12.35 *vs* 8.75 cases per 1000 person-years).

CONCLUSION: The association of diabetes with increased symptomatic GSD may provide insight to the treatment or management of diabetes in clinical settings.

Key words: Gallstone disease; Diabetes; Symptomatic; Incidence density; Hazard ratio

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INTRODUCTION

Gallstone disease (GSD) is one of the most common and costly digestive diseases worldwide, and it is more prevalent in Europe and America than in Asia and Africa. Symptomatic GSD and its related complications inflict heavy economic costs and social burdens[1-3] because surgical gallbladder removal, usually by laparoscopic cholecystectomy, is often required. GSD affects 10%-15% of the United States population (over 25 million people). Approximately 25% of the patients require treatment, at a cost of several billion dollars annually[4]. The prevalence of GSD in Taiwan is 4.3%-10.7% and increases significantly with age, which is consistent with reports from other countries[5]. In addition, an increasing trend in the incidence of severe GSD among patients aged 20-39 years has been reported in Taiwan[6]. Published epidemiological studies of GSD have revealed a steady upward trend in the admission rates for treatment of gallstones since the 1990s[7]. However, the reported prevalence of GSD varies considerably depending on study design, patient ethnicity, and geographic region[8-11]. A number of factors, including old age, female gender, genetics, diet, obesity, diabetes, and the use of oral contraceptives or hormone therapy, have been associated with increased risk of GSD[12,13].

Diabetic patients appear to have an increased risk of developing gallstones[14,15]. Although previous studies reported mixed results regarding the temporal relationship between GSD and diabetes, the reciprocal relationship between GSD and diabetes suggests a common etiological or biological mechanism[16] that may be reflected in gallstone composition. Gallstones are generally classified as either cholesterol stones or pigment stones according to their morphology and composition. The composition of cholesterol stones varies widely across different populations. For example, gallstones consist of more than 50% cholesterol in Western patients and an overwhelming 95% in Germany[17-20]. A mechanistic link between diabetes and GSD was recently defined using an animal model with increased cholesterol secretion and insulin resistance[21].

The inconsistent reports of the prevalence of GSD in diabetic patients have been attributed primarily to variations in study design[22-26]. One case-control study reported an estimated GSD rate of 32.7% in patients with diabetes and 20.8% in corresponding non-diabetic controls[14]. In contrast, Persson *et al*[22] reported no differences in the prevalence of GSD between diabetic patients and controls. Another case-control study reported that diabetes increased the prevalence of gallstones in females but not in males (47% *vs* 26%)[23]. To our knowledge, few studies have investigated the incidence of GSD in diabetic and non-diabetic patients using a cohort design. Furthermore, the majority of studies have been hospital-based or community-based, which might compromise the representativeness of the study sample, thus reducing the statistical power for comparisons of GSD risk in patients with and without diabetes. A population-based follow-up study conducted in Kinmen, Taiwan, reported that the incidence of GSD was 3.56% per year among type 2 diabetics[24-27]. However, it seems to be inappropriate to generalize the results from this small sample (n = 281) to the entire Taiwanese population.

Examining the co-occurrence of medical conditions related to diabetes and GSD may shed light on a common etiology and enable the identification of common biological mechanisms or pathways, which may greatly contribute to clinical interventions for GSD. Furthermore, diabetic patients with a number of complications must be aware of the symptoms and treatment for all of these diseases[28]. Given that most patients with GSD are asymptomatic and are not aware that they have gallstones, although the assessment of GSD risk among diabetic patients may add disease burden to policy makers responsible for planning health care resources, this may draw attention to the importance of managing diabetes *per se* and its related complications in clinical settings[1,29,30].

This study aimed to examine the risks of developing GSD among diabetic patients. The presence of comorbidities associated with diabetes was also evaluated in the representative diabetic cohorts retrieved from the Taiwanese National Health Research Insurance (NHRI) database.

MATERIALS AND METHODS

Data source

The Department of Health in Taiwan created the universal National Health Insurance (NHI) system in 1995, and approximately 96% of the Taiwanese population

had been covered in the NHI program by the end of 1996[28]. The Bureau of NHI (BNHI) has contracts with 97% of hospitals and 90% of clinics across the island[31,32]. To ensure the accuracy of the claim data, the BNHI conducts expert reviews of a random sample of 50-100 ambulatory and inpatient claims from each hospital and clinic quarterly. The computerized administrative claims and datasets compiled by the NHRI are made available to investigators for research purposes after the individual health information is encrypted to ensure privacy[33]. This study was conducted using the NHRI dataset of ambulatory care claims, inpatient claims, and the updated registry of beneficiaries from 2000 to 2008.

Study cohorts and comorbidities

Diabetic ambulatory care claims record the patients with diabetes-related diagnoses (ICD-9: 250 or A-code: A181). An individual was classified as a diabetic patient if she or he had an initial diabetes-related diagnosis at any time in 2000 and then experienced one or more additional diagnoses within the subsequent 12 mo. The first and last outpatient visits within a given year must be at least 30 d to avoid the accidental inclusion of miscoded patients[34]. To detect newly diagnosed gallstone cases, we excluded patients who sought hospital or ambulatory care treatment for gallstones (ICD-9: 574) from 1997 to 1999. A total of 615 532 diabetic patients were identified in the year 2000.

Subjects in the control group were selected from all beneficiaries insured in 2000 who were free from both diabetes and GSD from 1997 to 2000. A total of 614 871 control individuals were randomly selected to generate an age- and gender-matched control population for the diabetic group.

Once the study subjects were identified, we examined the ambulatory care visits and hospitalization claims for selected comorbidities including hypertension (ICD-9: 401, 405), gout (ICD-9:274), hyperlipidemia (ICD-9: 272.0-272.9, A182), cystic fibrosis (ICD-9: 277.0), sickle cell anemia (ICD-9: 282.6), cirrhosis (ICD-9: 571.2, 571.5, 571.6), cholangitis (ICD-9: 576.1), Caroli's disease (ICD-9: 576.2), Crohn's disease (ICD-9: 555.9), and hemolytic anemia (ICD-9: 282-283). The comorbidities mentioned above were counted only when the initial diagnosis had been made during the study period (2000-2008).

Study endpoints

The study subjects from the diabetic and control groups were linked to ambulatory care visits and hospitalization claims from 2000 to 2008 for possible gallstone episodes (ICD-9-CM 574). Person-years (PYs) of follow-up were calculated for each diabetic patient from the time of his/her first diagnosis of diabetes in 2000 to the date of the first ambulatory care visit or hospitalization due to gallstones prior to the end of 2008. The PYs for control subjects were defined as the period between the first day of insurance coverage by NHI in 2000 and the date that the first gallstone symptoms developed and were diagnosed.

Statistical analysis

The age, sex, occupation, income, and residential urbanization level were compared between diabetic patients and control subjects. The differences in the rates of selected comorbidities were assessed in the two groups. We also estimated the incidence densities of symptomatic GSD according to the subjects' diabetic status.

Cox proportion hazards models were generated to assess the gender- and age-specific effects of diabetes on the risk of developing gallstones. Hazard ratios (HR) and 95% CI were calculated to estimate the relative risk of developing symptomatic GSD. All analyses were performed using SAS statistical software (version 9.1 for Windows; SAS Institute, Inc., Cary, NC), and the results were considered to be statistically significant when two-tailed *P* values were less than 0.05.

RESULTS

A total of 615 532 diabetic patients and 614 817 control participants who were initially free of symptomatic GSD were included in this study (Table 1). The two groups had similar baseline age and gender distributions, with a mean age of 60 years and a greater proportion of females. Although the average insurance premium was lower for patients in the diabetic group, the Charlson score was extraordinarily higher. The geographical distributions and urbanization scores of diabetic patients were also similar to those of the control group.

The diabetic group exhibited significantly higher baseline rates for all comorbidities of interest (Table 2). The largest discrepancy in prevalence was noted for hyperlipidemia (73.4% *vs* 37.8%), followed by hypertension (86.7% *vs* 61.8%) and gout (32.4% *vs* 23.3%).

Over the 8-year follow-up period, 60 734 diabetic patients and 48 116 controls developed symptomatic GSD and underwent operations. The cumulative operation rates for the diabetic and control groups were 9.87% and 7.83%, respectively (Table 3). A higher incidence of symptomatic GSD was also found in females than in males in both groups. Particularly, females under the age of 64 in the control group had a significantly higher incidence of GSD (20% and 22% more) than the corresponding males, but this difference decreased with increasing age. A similar but less significant pattern was also observed in the diabetic group (Table 3). Figure 1 shows that the cumulative incidence rates of operations for symptomatic GSD in the diabetic and control groups were 13.06 and 9.52 cases per 1000 PYs between 2000 and 2008. Diabetic men had a higher incidence of operations for symptomatic GSD than did their control counterparts (12.35 *vs* 8.75 cases per 1000 PYs), representing a significantly increased adjusted hazard ratio of 1.12 (95% CI: 1.07-1.16) for diabetic men. Furthermore, diabetic women also had a modest but significant additional risk of developing GSD during the 8-year follow-up period (HR = 1.05; 95% CI: 1.01-1.08).

Table 1 Characteristics of diabetic and control groups in this study, 2000-2008, Taiwan, China

Variables[1]	Control group		Diabetic group	
	n	%	*n*	%
Age, yr				
< 45	69 617	11.3	69 825	11.3
45-64	296 810	48.3	297 142	48.3
> 64	248 444	40.4	248 562	40.4
Mean age (± SD)	60.0 ± 12.8		60.1 ± 12.7	
Sex				
Female	319 308	51.9	319 310	51.9
Male	295 563	48.1	295 566	48.1
Insurance premium (NTD)[2]				
Dependent	156 296	25.4	169 761	27.6
< Median (19 200)	135 948	22.1	137 408	22.3
⩾ Median	322 627	52.5	308 363	50.1
Mean premium (± SD)[3]	20 142.6 ± 15 269.4		19 307.7 ± 14 454.7	
Charlson score				
0	551 094	89.6	0	0.0
1	49 777	8.1	444 658	72.2
⩾ 2	14 000	2.3	170 874	27.8
Mean score (± SD)	0.1 ± 0.4		1.4 ± 0.8	
Geographic area				
Northern	269 239	44.2	269 920	44.4
Central	151 693	25.0	141 321	23.2
Southern	168 995	27.8	178 627	29.4
Eastern	17 938	3.0	17 944	3.0
Urbanization status				
Metropolis	243 808	39.8	255 467	42.0
Satellite city/town	163 515	26.8	159 687	26.2
Rural area	202 343	33.2	193 949	31.8
Total	614 871	100.0	615 532	100.0

[1]The inconsistencies between the total population and the sums of the populations for individual variables are due to missing information; [2]NTD: New Taiwan Dollars; [3]Dependent insurers were not included.

Table 2 Prevalence of selected comorbidities at baseline in diabetic and control groups, 2000-2008, Taiwan, China

Variables[1]	Control group		Diabetic group		*P* value[2]
	n	%	*n*	%	
Hypertension					< 0.001
No	235 138	38.2	81 913	13.3	
Yes	379 733	61.8	533 619	86.7	
Gout					< 0.001
No	471 346	76.7	416 400	67.6	
Yes	143 525	23.3	199 132	32.4	
Hyperlipidemia					< 0.001
No	382 560	62.2	163 598	26.6	
Yes	232 311	37.8	451 934	73.4	
Cystic fibrosis					0.006
No	614 836	99.9	615 470	99.9	
Yes	35	0.1	62	0.1	
Cirrhosis					< 0.001
No	589 838	95.9	569 024	92.4	
Yes	25 033	4.1	46 508	7.6	
Cholangitis					< 0.001
No	605 197	98.4	602 604	97.9	
Yes	9674	1.6	12 928	2.1	
Caroli's disease					< 0.001
No	612 979	99.7	613 326	99.6	
Yes	1892	0.3	2206	0.4	
Crohn's disease					< 0.001
No	590 912	96.1	590 404	95.9	
Yes	23 959	3.9	25 128	4.1	
Hemolytic anemia					< 0.001
No	612 100	99.6	612 111	99.4	
Yes	2771	0.4	3421	0.6	
Total	614 871	100.0	615 532	100.0	

[1]Hypertension (ICD-9: 401-405, A260, A269), gout (ICD-9: 274), hyperlipidemia (ICD-9: 272.0–272.4, A182), cystic fibrosis (ICD-9: 277.0), cirrhosis (ICD-9: 571.2, 571.5, 571.6), cholangitis (ICD-9: 575.8, 576.1), Caroli's disease (ICD-9: 576.2), Crohn's disease (ICD-9: 555.0, 555.1, 555.9), hemolytic anemia (ICD-9: 282–283); [2]Based on χ^2 test.

DISCUSSION

This study aimed to explore the risk of developing symptomatic GSD in diabetic patients compared with the general population and to examine the risk of comorbidities related to diabetes. The study revealed a higher incidence of symptomatic GSD in patients with diabetes in all age groups. Furthermore, the cumulative incidence trends were more marked in women than in men. The prevalence of selected comorbidities was higher in the diabetic group with symptomatic gallstones than in those without gallstones.

A previous study in an Italian population reported that the cumulative incidence of GSD was 0.67% per year, and GSD was more common in females than in males[13]. Another study reported that the 5-year incidence of gallstone disease was approximately 2%-3% among Danish individuals over the age of 40[12]. Our analysis of the Taiwanese NHRI datasets revealed that the incidence and the incidence density of symptomatic GSD in non-diabetic patients were approximately 7% and 9% per year, respectively. These incidence estimates are slightly higher than those measured in Western countries. Previous evidence has shown that both incidence and prevalence increase with age[1,9-12]. Therefore, one potential explanation for this discrepancy might be that the control group in this study, which was age- and gender-matched to the diabetic group, was older than the study cohorts in previous reports.

Despite the controversies about the prevalence of GSD in diabetic *vs* non-diabetic groups, GSD is not uncommon in patients with diabetes. Previous studies have reported that roughly 14%-30% of diabetic patients develop GSD[14,22-25]. One population-based follow-up study indicated that 3.56% of type 2 diabetic patients developed GSD per year. However, no conclusions about relative risk can be made based on these estimated incidence rates because no control groups were included in these studies[27]. Our study, based on a population-based dataset in Taiwan, illustrated that approximately 9.52% of the Taiwanese population developed symptomatic GSD annually, and the incidence density was higher in diabetic group than in the general population (13.06% *vs* 9.52%). In addition, females and older individuals were more likely to develop symptomatic GSD, regardless of their diabetes status. The results were consistent with the previously described epidemiology of GSD. It is noteworthy that gender differences in symptomatic GSD in-

Table 3 Overall age- and sex-specific incidence densities and relative hazards of gallstone disease (ICD-9: 574) in diabetic and control groups, 2000-2008, Taiwan, China

Variables[1]	Control group				Diabetic group				aHR[2] (95% CI)[2,4] in association with diabetic group
	No. of patients	No. of events	ID[2] (per 1000 patient-years) (95% CI)[2,3]		No. of patients	No. of events	ID[2] (per 1000 patient-years) (95% CI)[2,3]		
Men									
< 45	40 537	1467	4.25 (4.24-4.25)		40 537	2360	7.06 (7.06-7.07)		0.80 (0.66-0.96)[4]
45-64	141 899	9184	7.59 (7.58-7.59)		141 899	12 561	11.23 (11.22-11.23)		1.03 (0.96-1.09)[4]
> 64	113 127	10 241	12.31 (12.30-12.31)		113 129	12 224	16.40 (16.39-16.40)		1.20 (1.14-1.27)[4]
Total	295 563	20 892	8.75 (8.75-8.76)		295 566	27 145	12.35 (12.34-12.35)		1.12 (1.07-1.16)[5]
Women				Increased % *vs* males				Increased % *vs* males	
< 45	29 080	1292	5.11 (5.11-5.12)	+ 20.8%	29 079	1898	7.69 (7.69-7.70)	+ 8.9%	0.75 (0.60-0.94)[4]
45-64	154 911	12 596	9.30 (9.29-9.30)	+ 22.5%	154 911	15 989	12.59 (12.58-12.59)	+ 12.1%	0.96 (0.90-1.02)[4]
> 64	135 317	13 336	12.61 (12.60-12.61)	+ 20.8%	135 318	15 685	16.81 (16.81-16.82)	+ 2.5%	1.13 (1.07-1.18)[4]
Total	319 308	27 224	10.21 (10.21-10.22)	+ 2.4%	319 310	33 572	13.70 (13.70-13.71)	+ 10.9%	1.05 (1.01-1.08)[5]
Overall	614 871	48 116	9.52 (9.52-9.53)		615 532	60 734	13.06 (13.06-13.07)		1.08 (1.05-1.10)[6]

[1]Inconsistencies between the total population and the sums of populations for individual variables are due to missing information; [2]ID: Incidence density; aHR: Adjusted hazard ratio; [3]Based on poisson assumption; [4]Based on Cox proportional hazard regression adjusted for all variables, except for age and sex; [5]Based on Cox proportional hazard regression adjusted for all variables, except for sex; [6]Based on Cox proportional hazards regression adjusted for age, sex, insurance premium, Charlson score, geographic area, urbanization status, and status of diabetes, hypertension, gout, hyperlipidemia, cystic fibrosis, cirrhosis, cholangitis, Caroli's disease, Crohn's disease and hemolytic anemia.

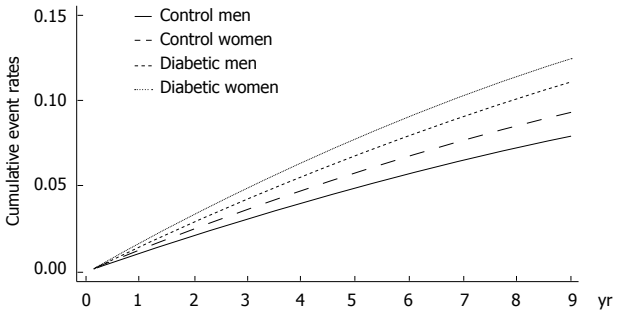

Figure 1 Cumulative incidence of gallstone disease in patients with or without diabetes over the study period.

cidence were not significant in patients over 64 years of age in either the diabetic or the control group, suggesting that age is a more important variable than gender.

Our findings indicate that subjects in the diabetic group suffer from more comorbidities than those in the control group, which was not surprising, but the significantly higher incidence rates of hypertension and hyperlipidemia were particularly noteworthy. Gallbladder function and bile acid metabolism are the two major factors associated with gallstone formation[35]. Diabetes or insulin resistance may affect gallbladder motility or contractility, further promoting the formation of gallstones[36-40]. This may be explained by the fact that diabetes tends to lower the levels of high-density-lipoprotein cholesterol and raise the triglyceride and low-density-lipoprotein levels, that may subsequently affect gallbladder dysmotility[35,37,39]. Previous evidence has shown that hypersecretion of hepatic cholesterol and altered lipid profiles derived from diabetic dyslipidemia may also be linked to the super-saturation of bile with cholesterol, thereby altering bile acid metabolism and cholesterol crystallization[40,41]. The higher incidence of symptomatic GSD in diabetes may be attributable to the higher prevalence of hypertension and hyperlipidemia among diabetic patients.

Considerable clinical evidence has indicated that an array of abdominal manifestations is likely to be associated with GSD and diabetes, including cystic fibrosis, cirrhosis, cholangitis, Caroli's disease, and Crohn's disease[5,11,42-48]. Calcium salts of unconjugated bilirubin in the enterohepatic circulation have been suggested to underlie these co-occurring manifestations. For instance, bilirubin excretion may be related to an increased risk of calcium bilirubinate precipitation, especially in chronic hemolytic disorders. Chronic bacterial infections of the bile ducts may also contribute to gallstone formation by increasing the combination of unconjugated bilirubin with calcium[41,46]. Based on the results of this study (Table 2), we strongly suggest that gallstones developed in diabetic patients were primarily cholesterol stones; this hypothesis will be examined directly in future studies.

Gallstone formation may be caused by many etiological factors, each of which may produce different clinical consequences. Most patients remain asymptomatic for a long period, frequently for life. Gallstones may traverse the cystic duct with or without symptoms of obstruction. Transient cystic duct obstruction causes periodic painful episodes, whereas persistent obstruction usually produces inflammation and acute cholecystitis, leading to the onset of symptomatic GSD. However, there is little information regarding the direct mechanisms that underlie the increased onset of GSD in diabetes. Because elderly patients are more likely to develop symptomatic GSD, it is important to diagnose GSD early in patients with diabetes. Patients may benefit from the early detection of GSD and the underlying comorbidities that may promote both GSD and diabetes, which could subsequently enhance the effectiveness of diabetes management.

Urban-rural differences were also detected in this study. Diabetic patients in metropolitan areas had a higher incidence of symptomatic GSD than patients from rural areas. The observed urbanization-level differences likely reflect the differences in the distribution of medical resources and/or treatment-seeking behaviors[49]. Future research is needed to explain the urban-rural variations and enable policy-makers to promote policies that will reduce or eliminate these differences.

There were several limitations that should be noted in this study. First, potential misclassification might arise due to our exclusive reliance on claims datasets. A previous report showed that the accuracy of diabetes diagnoses in the NHI claims data was only 74.6%[50]. In order to avoid this bias, we included and analyzed only the patients that had been diagnosed with diabetes at least twice, with the first and the last outpatient visits at least 30 d but less than one year apart. It is also possible that newly diagnosed or undiagnosed diabetic cases without records of ambulatory care visits were included in the control group. Therefore, the overall difference in incidence of GSD could have been underestimated[51]. Second, type 1 and type 2 diabetes were not differentiated in this dataset, which limited our interpretation of the study findings. However, other studies have shown that type 2 diabetes accounted for the majority of diabetic patients in Taiwan; as a result, the interpretations of our results are likely to be most relevant for type 2 diabetes[52,53]. Third, other factors that might confound our results were not available, such as body mass index, socioeconomic status, duration and treatment of diabetes, smoking, alcohol use, family history of GSD, *etc*. Fourth, the incidence of symptomatic GSD among diabetic patients with/without comorbidities was not reported; therefore, these differences in prevalence could not be analyzed.

Despite the above-mentioned limitations, this is one of very few studies to examine the risk of symptomatic GSD in patients with diabetes using a Taiwanese population-based cohort study design. Given the high coverage rate of National Health Insurance in Taiwan, the likelihood of non-response and loss to follow-up was relatively limited, ensuring the representativeness of the sample. In addition, we took advantage of the longitudinal nature of the NHI dataset to follow up the incidence rate of symptomatic GSD and related comorbidities in diabetic and control groups.

In conclusion, an increased risk of symptomatic GSD in diabetic patients over an 8-year study period was observed in this study. Diabetes and GSD may share a number of common risk factors or etiologies. A crucial link between insulin resistance and increased cholesterol predisposed the diabetic patients to gallstone formation[21]. These results may provide insight into the treatment or management of diabetes in clinical settings. Future research is needed to facilitate public health prevention or intervention programs to reduce the incidence of symptomatic GSD[54].

COMMENTS

Background

Gallstone disease (GSD) is a one of the most common of all digestive diseases worldwide. Symptomatic GSD and related complications necessitate surgical removal of gallbladder, inflicting a heavy economic costs and social burdens. Most patients with GSD are asymptomatic and unaware of having gallstones. Diabetic patients with complications particularly require an adequate awareness for care management of GSD. The apparent incongruity for GSD prevalence in diabetic patients should be attributable to varied study designs.

Research frontiers

This study aimed to investigate the incidence of GSD and examined the risks of developing symptomatic GSD among the diabetes using a cohort design and retrieving data from the National Health Insurance Research database of Taiwan.

Innovations and breakthroughs

The results showed that the cumulative operation rates for diabetes and controls were 9.87% and 7.83% among 615 532 diabetic patients and 614 817 control participants over the 8-year follow-up period. Diabetic patients also tended to have significantly higher prevalence in developing comorbidities, most notably hyperlipidemia and hypertension. Higher incidence of symptomatic GSD was found in females than in males in both groups. Females aged < 64 years in control group had a significantly higher incidence than corresponding males, but the difference reduced with increasing age. A similar but less significant pattern was also observed in diabetic group. Both diabetic men and women were characterized with higher incidence of symptomatic GSD operation than their corresponding counterparts after 8-year follow-up. The authors concluded that higher incidence of symptomatic GSD was found in patients with diabetes in all age groups and the trends of cumulative incidence were more marked for women than men. In addition, the prevalence of selected comorbidities in diabetic group with gallstone was also higher than those without symptomatic GSD.

Terminology

GSD is caused by gallstones that block the normal flow of bile if they lodge in any of the ducts that carry bile from the liver to the small intestine. Severe damage or infections affecting the gallbladder, liver, or pancreas can occur if any of these ducts remain blocked for a significant period of time, which necessitate surgical removal of gallbladder, usually by laparoscopic cholecystectomy.

Peer review

This is a good study in which authors analyzed incidence of symptomatic GSD in patients with diabetes by using a representative database over a long period of time. The results are interesting and suggest that diabetes is associated with increased risk of developing symptomatic GSD. The investigators also drew a conclusion that patients with diabetes developed more symptomatic GSD in all age groups and were more notable for women than men. This study was based on a nationwide population-based datasets, which illustrated that about 9.52% population in Taiwan developed symptomatic GSD per year and the incidence density was higher in diabetic patients (13.06%). Diabetes associated with increased risk of developing symptomatic GSD was observed over an 8-year study period. Being female and with older ages were associated with increased incidence of symptomatic GSD, however, the potential importance of gender was overridden by aging.

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