

Changes in Demographic Features of Gallstone Disease: 30 Years of Surgically Treated Patients

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Background/Aims: The aim of this study was to investigate changes in the clinical and demographical characteristics of gallstone disease in Korea, based on 30 years of surgically treated patients at a single institute. **Methods:** In total, 7,949 gallstone patients who underwent surgery between 1981 and 2010 were analyzed. Patients were divided into six time periods: period I (1981 to 1985, n=831), period II (1986 to 1990, n=888), period III (1991 to 1995, n=1,040), period IV (1996 to 2000, n=1,261), period V (2001 to 2005, n=1,651) and period VI (2006 to 2010, n=2,278). **Results:** The total number and mean age of the patients gradually increased, and the male/female ratio decreased. The proportion of gallbladder (GB)-stone cases increased, whereas the proportions of common bile duct (CBD)- and intrahepatic duct (IHD)-stone cases decreased. Differences in patient geographical origins also decreased. Based on the relationship between changes in the prevalence of gallstone disease and socioeconomic status, the prevalence of CBD stones showed a strong correlation with Engel's coefficient ($p < 0.001$). **Conclusions:** Our study indicates that although the total number of cases and the mean age of gallstone patients have continuously increased, there are trends of increasing GB-stone cases and decreasing CBD- and IHD-stone cases. (*Gut Liver* 2013;7:719-724)

Key Words: Cholelithiasis; Epidemiology; Surgery

INTRODUCTION

Gallstone disease is common worldwide, and its prevalence

has geographical and ethnic variations. The lowest prevalence is seen in Africans.^{1,2} In the National Health and Nutrition Examination Survey III study, the overall prevalence of gallstone disease in the United States was 7.9% in men and 16.6% in women.³ The prevalence of gallstone disease in Europe is reported to be 5% to 15%, according to several ultrasonographic surveys.⁴⁻⁷ In Asian countries, the prevalence of gallstone disease ranges from 3% to 10%. According to recent studies, the prevalences of gallstone disease were 3.2% in Japan,⁸ 10.7% in China,⁹ 7.1% in Northern India,¹⁰ and 5.0% in Taiwan.¹¹

Many recent studies have shown that gallstone disease is related to age, female sex, pregnancy, body mass index (BMI), alcohol consumption, dietary habits, and metabolic disorders such as hyperlipidemia and diabetes mellitus.^{1,11-14} Due to these risk factors and differences in socioeconomic status, the prevalences of pigment stones, common bile duct (CBD) stones, and intrahepatic duct (IHD) stones were higher in East Asian countries than in Western countries. However, as socioeconomic status and life-style have changed in Asian countries, the prevalence of gallstone disease is becoming similar to that of the Western world. This study was designed to explore the demographic features of gallstone disease in Koreans over the last 30 years.

MATERIALS AND METHODS

A total of 7,949 gallstone patients who had been treated surgically for gallstone disease at Seoul National University Hospital between 1981 and 2010 were analyzed in this study. Operations performed for gallstone disease were cholecystectomy, hepatectomy, choledocholithotomy, and T-tube insertion.

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Patients who were treated with endoscopic retrograde cholangiopancreatography (ERCP) without cholecystectomy for CBD stones were not included in this study. Information on age, the sex ratio, gallstone location, residential area, obesity according to BMI (kg/m^2), and the type of operation was collected. Patients were classified into three stone groups based on the stone location and seven subgroups (Table 1). Patients were also divided into six time periods for analysis: period I (1981 to 1985, $n=831$), period II (1986 to 1990, $n=888$), period III (1991 to 1995, $n=1,040$), period IV (1996 to 2000, $n=1,261$), period V (2001 to 2005, $n=1,651$), and period VI (2006 to 2010, $n=2,278$).

The number of cases, mean age, and the sex ratio were compared between the subgroups and between the stone groups. Differences in patient geographical origins, urban or rural areas, between the stone groups were analyzed. BMI (kg/m^2) was used to examine the correlation between the degree of obesity and gallstone location. A previous report from Koreans between 1961 and 1980¹⁵ were reviewed in addition to our study, in order to elucidate trends in the relative prevalences of gallstone disease over a longer period.

The significances of differences between the groups and be-

tween the periods were assessed using linear regression analysis. Pearson's linear function was used to examine correlations between the aforementioned factors. A $p<0.05$ was considered statistically significant. This study was approved by the Institutional Review Board of Seoul National University Hospital (H-1203-013-399).

RESULTS

1. Overall demographic characteristics of the patients

The number of surgically treated gallstone disease cases at Seoul National University Hospital has increased continuously over the last 30 years ($r=0.884$, $p=0.005$). The female/male ratio was 1.25 and 1.37 in periods I and II, respectively, showing a female predominance as in Western countries. However, the ratio started to decrease gradually from period III and it reached 1:1.02 in period VI ($r=0.759$, $p=0.024$). The mean age of the patients increased from 51.4 to 57.5 years during the study period ($r=0.906$, $p<0.001$) (Table 2).

2. Demographic characteristics of the seven subgroups

Patients were classified into seven subgroups: the gallbladder (GB) stone, CBD stone, IHD stone, GB+CBD stone, GB+IHD stone, CBD+IHD stone, and GB+CBD+IHD stone subgroups. The proportion of the GB stone subgroup increased gradually from 61.9% in period I to 89.8% in period VI ($r=0.949$, $p=0.001$). The proportions of the GB+CBD stone ($r=0.926$, $p=0.002$), CBD stone ($r=0.949$, $p=0.015$), and GB+CBD+IHD stone subgroups ($r=0.798$,

Table 1. Classification of Groups

7 Subgroups	
1: GB	
2: GB+CBD	
3: CBD	
4: GB+CBD+IHD	
5: IHD+GB	
6: IHD+CBD	
7: IHD	
3 Stone groups	
GB stone group: subgroup 1, 2, 4, 5	
CBD stone group: subgroup 2, 3, 4, 6	
IHD stone group: subgroup 4, 5, 6, 7	

GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct.

Table 2. The Total Number, Sex Ratio, and Mean Age of Patients according to Time Period (I to VI)

	I (80-'85)	II (86-'90)	III (91-'95)	IV (96-'00)	V (01-'05)	VI (06-'10)
No. of cases	831	888	1,040	1,261	1,651	2,278
F/M ratio	1.25	1.37	1.28	1.17	1.08	1.02
Mean age	51.4	53.2	53.3	54	55	57.5

F, female; M, male.

Table 3. Relative Prevalence and Age Distribution of Subgroups according to Time Period (I to VI)

	Relative frequency, %						Mean age, yr					
	I	II	III	IV	V	VI	I	II	III	IV	V	VI
1: GB	61.9	63.9	72.0	73.4	79.5	89.8	51.5	51.2	52.1	52.9	54.0	57.1
2: GB+CBD	14.8	12.7	11.3	8.2	8.1	2.2	55.5	61.6	60.0	59.8	60.8	63.3
3: CBD	10.3	8.6	5.0	5.2	2.8	1.6	51.7	56.4	57.8	61.8	62.3	65.6
4: GB+CBD+IHD	3.5	4.1	1.6	1.0	1.3	0.3	50.8	55.4	54.2	58.6	60.9	61.0
5: GB+IHD	0.8	1.0	0.7	0.1	0.8	0.3	41.3	51.2	54.7	52.0	53.0	63.4
6: CBD+IHD	5.4	4.8	5.8	5.3	2.9	0.8	44.7	49.2	53.7	51.8	58.5	55.5
7: IHD	3.2	5.1	3.6	6.7	4.5	4.9	40.5	41.5	47.5	51.5	53.7	58.5

GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct.

p=0.017) continuously decreased over time (Table 3). The mean ages of all subgroups showed an increasing tendency (Fig. 1). The greatest difference was seen in the GB+IHD stone subgroup, which was 22 years.

3. Demographic characteristics of the three stone groups

We classified patients into three stone groups: the GB stone, CBD stone, and IHD stone groups. The proportion of the GB stone group increased from 81% in period I to 92.6% in period VI (r=0.819, p=0.013), and the number of patients tripled over the last 30 years. In contrast, the proportion of the CBD stone (r=0.979, p<0.001) and IHD stone (r=0.694, p=0.039) groups decreased.

Female predominance was only seen in the IHD stone group. The female to male sex ratio in the IHD stone group reached 2.06:1 in period VI. In the GB stone group, GB stone disease occurred more frequently in males than in females, which resulted in a decrease in the sex ratio (r=0.851, p=0.009). The sex ratio of the CBD stone group also declined from 1.02 to 0.77 (Table 4).

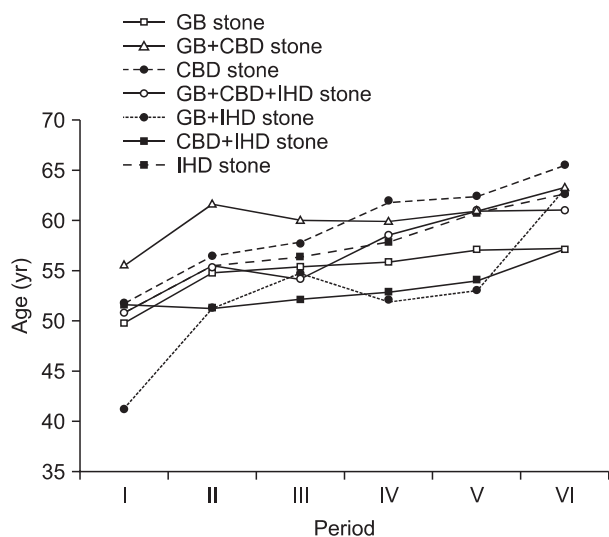


Fig. 1. Age distribution of the seven subgroups. GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct.

4. Geographical differences between three stone groups

Based on the relationships between the patients' residence and stone location, we found that during period I, the proportion of the GB stone group was higher in urban areas (67%) than that in rural areas (44.7%). In contrast, the proportions of the CBD and IHD stone groups were higher in rural areas (35.9% and 19.3%, respectively) than in urban areas (24.7% and 8.3%, respectively). However, this geographical difference narrowed over time. Chronological changes were similar in both the urban and rural areas: the proportion of the GB stone group increased continuously from period I to VI (r=0.935, p=0.002; and r=0.871, p=0.006, respectively), while CBD stone group decreased (r=0.964, p<0.001; and r=0.916, p=0.003, respectively), and the IHD stone group also showed a decreasing tendency (p=0.057 and p=0.086, respectively) (Fig. 2).

5. BMIs of the three stone groups

The BMIs (kg/m²) of the stone group patients were used to analyze the relationships between obesity and gallstone location. The mean BMIs of the GB and IHD stone groups increased during the study period (r=0.823, p=0.013; and r=0.663, p=0.049, respectively). The mean BMI of the CBD stone group increased until period V, but no significant change was seen in period VI. The mean BMI was higher in the GB stone group than in the CBD and IHD stone groups, which was similar to the result reported in Korean adults (Fig. 3). The mean BMI of males in the CBD and IHD stone groups was lower than that of Korean males overall. The mean BMI of females in the GB stone group was higher than that of Korean females overall (Fig. 4).

6. Socioeconomic status

The prevalence of gallstone disease and Engel's coefficient were compared to evaluate the relationship between chronological changes in gallstone disease and socioeconomic status by using the relative frequency of gallstone disease reported in Korean journals between 1961 and 1980 as references.¹⁵ Engel's coefficient, as reported by the Korea National Statistical Office, declined from 0.59 in 1961 to 0.21 in 2010, which strongly correlated with the changes in the proportion of the CBD stone group (r=0.980, p<0.001) (Fig. 5).

Table 4. Relative Prevalence of Stone Groups according to the Location of the Stones during Period I, II, III, IV, V, and VI

	GB stone group						CBD stone group						IHD stone group					
	I	II	III	IV	V	VI	I	II	III	IV	V	VI	I	II	III	IV	V	VI
Total no.	673	723	891	1,045	1,482	2,110	283	268	247	238	250	113	108	134	121	165	158	144
Total %	81.0	81.4	85.7	82.9	89.8	92.6	34.1	30.2	23.8	18.9	15.1	5.0	13.0	15.1	11.6	13.1	9.6	6.3
F/M ratio	1.32	1.33	1.34	1.12	1.07	0.98	1.02	1.25	0.86	0.98	0.85	0.77	1.16	1.73	1.16	1.75	1.55	2.06
Mean age	49.8	54.9	55.3	55.8	57.2	57.3	50.6	55.7	56.4	58.0	60.6	62.6	44.3	49.3	52.5	53.5	56.5	58.4

GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct; F, female; M, male.

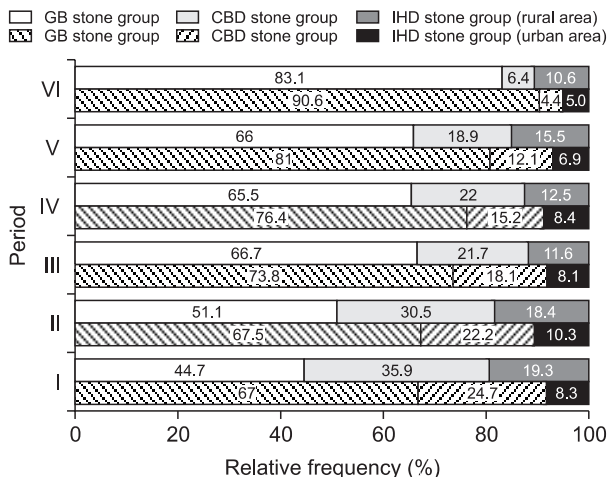


Fig. 2. Relationship between stone location and patient residence. GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct.

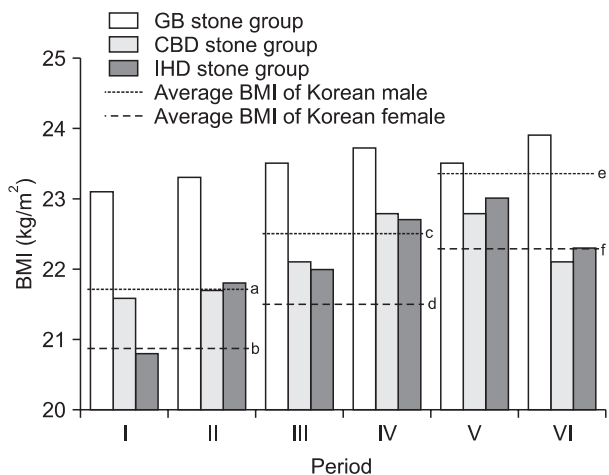


Fig. 3. Mean body mass index of each stone group in the evaluation period. a, 21.8 kg/m²; b, 20.9 kg/m²; c, 22.6 kg/m²; d, 21.7 kg/m²; e, 23.3 kg/m²; f, 22.4 kg/m². GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct; BMI, body mass index.

DISCUSSION

We reported on information regarding the epidemiology of gallstone disease based on the data obtained from our institute every 5 years since 1982.¹⁵⁻²⁰ Reports including this study are based on the data from surgically treated cases. Since there have been only a few reports on nationwide epidemiologic data and the prevalence of gallstone disease in Korea, this study may be useful for understanding demographical changes because it involves a large number of cases and has been conducted at regular intervals for 30 years at the same institute.

The total number of surgically treated gallstone patients tripled over the last 30 years, mostly due to the increase in the number of patients in the GB stone group. The number of patients in the GB stone group increased from 673 (81%) in period

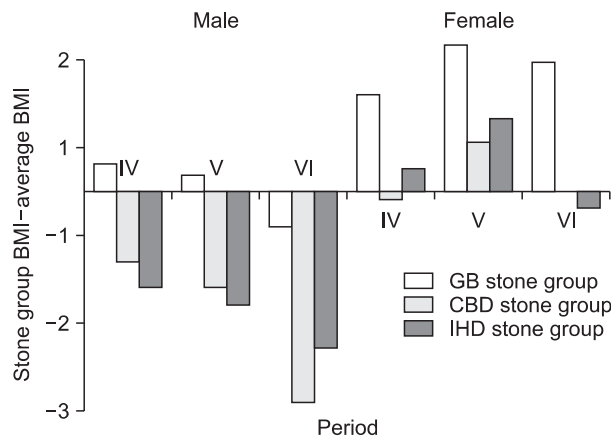


Fig. 4. Body mass index of each stone group, by sex, in the evaluation period. BMI, body mass index; GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct.

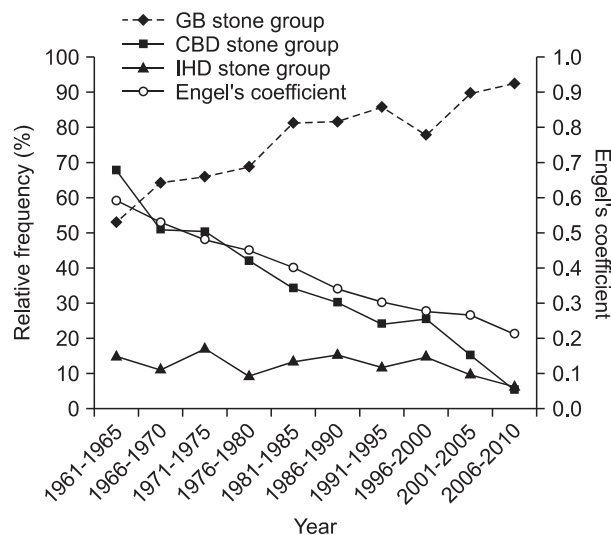


Fig. 5. Chronological changes in the proportions of the three stone groups and the relationships between the proportions and Engel's coefficients. GB, gallbladder; CBD, common bile duct; IHD, intrahepatic duct.

I to 2110 (92.6%) in period VI, whereas the numbers of patients in the CBD stone and IHD stone groups remained stationary. However, this increase does not necessarily mean that the prevalence itself has increased in Korea. This may be mainly due to the extension of indications for laparoscopic cholecystectomy since its introduction as well as the generalization of health screening in Korea. The aging of society may also contribute to the increase in the prevalence, which is a known risk factor of gallstone disease.^{1,2,21}

Only a few institutes have reported on the prevalence of gallstone disease in Korea. According to serial reports by a single institute, the prevalence changed from 4.9% to 2.0% based on ultrasonographic surveys of the adult population.^{22,23} Since those reports were not multicenter studies, they did not represent the

overall prevalence. Further multicenter studies are needed to determine the nationwide prevalence of GB disease and its epidemiologic changes.

The prevalence of surgically treated CBD stones decreased in both the urban and rural areas. The possible explanations are as follows. First, since a large proportion of CBD stones originate from GB stones, the prevalence of CBD stones decreases with the increasing frequency of cholecystectomies. In our study, the result which showed that CBD stone patients were 1 to 10 years older than GB stone-only patients may suggest the time required for stones to migrate naturally from the GB to the CBD. Second, since ERCP has widely been used for the treatment of CBD stones, the prevalence of surgical cases has markedly decreased. Third, the relative frequency of CBD stones decreased proportionately with Engel's coefficient, a socioeconomic index ($r=0.980$, $p<0.001$) (Fig. 4), which indicates that socioeconomic status is related to a decrease in the prevalence of CBD stones.

In this study, the relative frequency of IHD stones decreased continuously ($r=0.694$, $p=0.039$). This change, which was also reported in other Asian countries,^{24,25} may be attributed to decreases in risk factors, such as malnutrition, poor sanitation, and biliary parasite infestations, such as clonorchiasis or ascariasis,^{25,26} which have been reduced through improvements in socioeconomic status. However, our prevalence (6.3%) is still higher than those of Western countries (0.6% to 1.3%).^{27,28} A possible reason for this difference may be the incomplete westernization of rice-based dietary habits, and genetic factors reported in some previous studies.^{29,30}

Gallstone disease is known to be more common in older subjects.^{1,2,21} The mean age of the Korean gallstone patients, as well as the total number of such patients, has steadily increased over the study period as the Korean society continues to age. The mean age of patients with gallstones increased from 51.4 years in period I to 57.5 years in period VI. The mean age of the patients with IHD stones, which are known to develop at relatively younger ages, was 14 years older in period VI than in period I. Patients with CBD stones were 1 to 10 years older than those with GB stones, indicating that it may take several years for GB stones to migrate from the GB to the CBD.

Women are affected by gallstone disease 2- to 3-fold more frequently than men in Western countries, which may correlate with oral contraceptive use.^{1,2,7} In our study, the overall female/male ratio declined to 1:1.02, but the female/male ratio of the GB stone group in period VI was 0.97:1. This may be explained by the higher prevalences of CBD and IHD stones in males. In addition, Korean males receive health screenings more often than women, at a ratio of 1:0.78 to 1:0.87.^{22,23} The lack of female predominance in Korea may also be explained by the difference in obesity rates between American and Korean women. Approximately 35.8% of the American women had BMI higher than 30 kg/m², according to the data from the National Health and Nutrition Examination Survey of 2009 and 2010, whereas

only 28% of the Korean women had BMI higher than 30 kg/m² according to data from the Ministry of Health and Welfare of Korea in 2005.

Obesity is known to increase the prevalence of GB stones, especially cholesterol stones.^{1,2} In our study, the mean BMI was higher in the GB stone group than in the CBD and IHD stone groups and was also higher than the mean BMI of Korean adults. The number of GB stone patients and their mean BMIs are increasing because Koreans are increasingly consuming high-calorie, high-fat diets, which are closely related to obesity and GB disease.

The main drawback of this report is that the incidence was based on the data from surgically treated cases. As mentioned previously, the increased number of patients with GB stone is influenced by the generalization of laparoscopic surgery. ERCP procedure took a role in the decrease of number of patients in CBD stone group. Therefore, this report does not provide the actual incidence of gallstone disease and further study is needed.

In conclusion, the total number and mean age of surgically treated gallstone patients continuously increased during a period of the past 30 years. The increasing tendency of GB stones and decreasing tendency of CBD and IHD stones were also observed. The results of this study suggest that female predominance in gallstone disease and the difference in its prevalence between urban and rural areas have been decreasing in Korea.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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