Prevalence of cholelithiasis in a Turkish population sample of postmenopausal women

Postmenopozal dönemdeki Türk kadın populasyon örneğinde safra kesesi taşı sıklığı

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Background/aims: *Gallstone disease is a global health problem worldwide. Potential risk factors for gallstone disease have not been well established except for age and gender. We aimed to investigate the prevalence and potential risk factors for gallstone disease in a population of postmenopausal women.* ***Methods:*** *A detailed Turkish questionnaire was prepared, and 474 of 502 postmenopausal women seen at the menopause clinic of Dr. Zekai Tahir Burak Hospital were included in the study. Sociodemographic, medical and reproductive characteristics were analyzed. Subjects were divided into two groups. The gallstone disease group (Group 1, n=73) was defined by both prior histories of gallstones diagnosis or cholecystectomy in the postmenopausal period and the presence of current sonographically diagnosed gallstones; Group 2 (n=401) included women with no gallstone disease.* ***Results:*** *The present study found a 15.4% prevalence rate of cholelithiasis in a Turkish population sample of postmenopausal women. The demographic characteristics were similar between the two groups. The mean gravidity was 5.25 in Group 1 and 4.9 in Group 2. The number of subjects with past oral contraceptive use was 17 (23.3%) in Group 1 and 56 (13.9%) in Group 2. The number of women who took hormone replacement therapy was 40 (54.8%) in Group 1 and 222 (55.3%) in Group 2. There was no significant difference related to mean total cholesterol levels (216.5±44.9 mg/dl versus 215.9±44.3 mg/dl; p=0.915) and mean triglycerides (134.5±54.8 mg/dl versus 143.2±77 mg/dl; p=0.202) between the two groups.* ***Conclusions:*** *No risk factors for developing gallstones were determined among the evaluated parameters in postmenopausal women.*

Key words: Menopause, gallstones, risk factor, prevalence

Amaç: *Safra taşı hastalıkları evrensel bir sorundur. Safra taşı hastalıkları için potansiyel risk faktörleri yaş ve cinsiyet dışında iyi belirlenmemiştir. Biz postmenopozal kadın popülâsyonunda safra taşı hastalıklarının prevalansını ve olası risk faktörlerini araştırmayı amaçladık.* ***Yöntem:*** *Detaylı bir Türkçe anket hazırlandı ve çalışmaya Dr. Zekai Tahir Burak Hastanesi Menapoz Polikliniğine başvuran 502 kadından 474'ü dahil edildi. Sosyo-demografik, medikal ve üreme karakteristikleri analiz edildi. Denekler iki guruba ayrıldı. Safra taşı hastalığı gurubu (Grup 1, n=73), postmenopozal dönemde tanı almış safra taşı hastalığı ya da kolesistektomi hikayesi olanlar ile sonografik olarak yeni tanı almış safra taşı olanlar olarak ve Grup 2 (n=401) ise safra taşı olmayanlar olarak tanımlandı.* ***Bulgular:*** *Çalışmamızda Türk postmenopozal kadın popülasyon örneğinde safra taşı prevalansı %15.4 olarak bulundu. Demografik karakteristikler her iki Grup arasında benzerdi. Ortalama gravite sayısı Grup 1'de 5.25 ve Grup 2'de 4.29 idi. Geçmişte oral kontraseptif kullanan denek sayısı Grup 1'de 17 (%23.3) ve Grup 2'de 56 (%13.9) idi. Hormon replasman tedavisi alan kadın sayısı Grup 1'de 40 (%54.8) ve Grup 2'de 222 (%55.3) idi. Her iki grup arasında ortalama kolesterol düzeyleri (216.5±44.9 mg/dl ile 215.9±44.3 mg/dl; P=0.915) ve ortalama trigliserid düzeyleri (134.5±54.8 mg/dl ile 143.2±77 mg/dl; P=0.202) açısından anlamlı farklılık saptanmadı.* ***Sonuç:*** *Postmenopozal kadınlarda safra taşı hastalığı gelişimi için değerlendirilen parametreler içinde hiçbir risk faktörü saptanmadı.*

Anahtar kelimeler: Menopoz, safra taşı, risk faktörü, prevalans

INTRODUCTION

Gallstone disease is a global health problem worldwide. Most patients are asymptomatic; hence, gallstones in these patients are mostly detected on ultrasonography during routine medical examination. Cholecystectomy is one of the most commonly performed operations in general surgery clinics. Because of this high prevalence, the costs related to treatment of gallstone disease are high.

The etiology and pathogenesis of gallstone disease are still unknown. If the prevalence and risk factors for gallstone disease can be understood, it can lead to development of preventive strategies. Sin-

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Manuscript received: 05.03.2010 **Accepted:** 22.06.2010

doi: 10.4318/tjg.2010.0129

ce the 1980s, there have been several large ultrasonographic screening studies on the prevalence of gallstones in different populations worldwide. The role of increasing age and female gender on the prevalence of gallstone disease has been well established (1,2). Therefore, prevalence of gallstones in postmenopausal women is estimated to be high. In the present study, we aimed to investigate the prevalence and potential risk factors for gallstone disease in a population sample of postmenopausal women.

MATERIALS AND METHODS

Of 502 women who were contacted during their routine menopause visit from May 2007 to November 2007, 474 were included in the study. Women who had diagnosed gallstone disease (n=8) or who had undergone cholecystectomy (n=20) in the premenopausal period were excluded.

A detailed Turkish questionnaire was prepared to obtain gynecologic history. The questionnaire covered the following issues: sociodemographic data, smoking habits, history regarding several diseases including diabetes mellitus and hemolytic and liver diseases, digestive symptoms including abdominal pain, obstetrical and gynecological history (gravidity and parity, abortion rates, menopause type and length), serum lipid levels, and history of past oral contraceptive use and hormone replacement therapy (HRT). Informed consent was obtained from all participants. Twenty-one of 474 women were already diagnosed with gallstone disease and underwent cholecystectomy in the postmenopausal period. These women were included in this study with data archived at the time of the operation. A total of 453 individuals were offered ultrasonography of the gallbladder. Stones (48 subjects) and cholesterolosis (4 subjects) in the gallbladder were detected in 52 individuals. Subjects were divided into two groups as: Group 1, individuals who had gallstone disease (n=73) and Group 2, individuals who had no gallstone disease (n=401).

Statistical Analyses

Data were evaluated using SPSS for Windows release 15.0 software (Chicago, IL). To compare two groups, chi-square test and Fisher's exact test were used for categorical data. t-test for independent sample was used for continuous data with normal distribution, and Mann-Whitney U test was used for continuous data without normal distribution. Frequency and percentage were given for categorical data and mean±SD for continuous data as descriptive statistics. A p value less than 0.05 was accepted as statistically significant.

RESULTS

Prevalence of cholelithiasis was detected as 15.4% in this study. The demographic characteristics of the subjects in the two study groups demonstrated no statistically significant differences (Table 1). The mean ages of Group 1 and Group 2 were 52.6±5.79 years and 52.2±5.38 years, respectively. Body mass index (BMI) measurements were similar between the two groups (p=0.194). There was no significant difference between Groups 1 and 2 regarding educational status (p=0.960), diagnosis of diabetes mellitus (p=0.591), diagnosis of hemolytic and chronic liver diseases (p>0.05), number of participants with smoking habit (p=0.793), mean duration of smoking (p=0.932), and heredity (p=0.750). Digestive symptoms including abdomi-

Table 1. Patient demographics and data related to several diseases and smoking

	Group 1 (n=73)	Group 2 (n=401)	p value
Age, y (mean ± SD)	52.58 ± 5.79	52.24 ± 5.38	NS
BMI, kg/m^2 (mean ± SD)	28.93 ± 4.33	28.20 ± 4.46	NS
Educational background, n (%)			NS
No education	11 (15.1%)	49 (12.2%)	
Primary school	38 (52%)	214 (53.4%)	
Secondary school	7 (9.6%)	38 (9.5%)	
High school	8 (10.9%)	42 (10.4%)	
University	9 (12.4%)	58 (14.5%)	
Diabetes mellitus, n (%)	7 (9.6%)	31 (7.7%)	NS
Hemolytic diseases, n (%)	0	1 (0.2%)	NS
Chronic liver diseases, n (%)	0	2 (0.4%)	NS
Heredity, n (%)	15 (20.5%)	76 (18.9%)	NS
Smoking habit, n (%)	12 (16.4%)	71 (17.7%)	NS
Duration of smoking, y (mean ± SD)	17.42 ± 3.21	17.13 ± 0.88	NS
Digestive symptoms, n (%)	13 (17.8%)	17 (4.2%)	p<0.001

Group 1: Individuals with gallstones. Group 2: Individuals with no gallstones. NS: Not significant.

nal pain were detected in 13 individuals in Group 1 and in 17 in Group 2. The rate of digestive symptoms was significantly higher in Group 1 than in Group 2 predictably (p<0.001).

Table 2 shows obstetrical and gynecological data of the two groups. There were no significant differences in terms of gravidity, parity, abortion rates, and menopause type and length. The number of participants with a prior history of oral contraceptive use and the length of this drugs use were similar between the groups. When subjects were queried regarding HRT use, similar results were detected between the two groups.

Table 3 shows the blood lipid values. There was no significant difference related to mean total cholesterol levels (216.5±44.9 mg/dl versus 215.9±44.3 mg/dl; p=0.915), mean high-density lipoprotein (HDL) cholesterol levels (51.6±14 mg/dl versus 55.7±19.3 mg/dl; p=0.105), mean low-density lipoprotein (LDL) cholesterol levels (138.3±38.3 mg/dl versus 130.7±40.7 mg/dl; p=0.157) and mean triglycerides (134.5±54.8 mg/dl versus 143.2±77 mg/dl; p=0.202) (in individuals with gallstone disease versus without gallstone disease, respectively).

DISCUSSION

The prevalence of gallstone disease is affected by multiple factors including ethnicity, age and gender. Since the 1980s, the effects of ethnic and geographical differences on the formation of gallstone have been well established in several studies. The overall prevalence of gallstone disease is higher in Europe and America than in Asia and Africa (3-6). Age and gender are other independent and important risk factors for developing gallstones as far as ethnicity. Older age and female sex have been shown to be strong risk factors for gallstone disease (7-9). In a series reported by Jensen et al. (7), the incidence of gallstone disease in men aged 30 years was 0.3%, while in those aged 60 years, it was 3.3%. These rates in women were 1.4% and 3.7%, respectively. Furthermore, they detected that the sex difference in gallstone incidence decreased with increasing age. In another study, Angelico et al. (10) reported similar results related to higher incidence in older ages.

The classical characterization of the patient with cholelithiasis is mentioned as the “4F rules” including fatty, forty, female and fair. However, several studies in the literature have included conflicting results and the effects of some parameters on developing gallstones have not been well established. We aimed to investigate the prevalence and potential risk factors for gallstone disease in a sample population of postmenopausal women.

Several putative risk factors have been analyzed in prevalence studies. De Santis et al. (11) found that diabetes mellitus increased risk for gallstone disease. They suggested that autonomic neuropathy caused by diabetes mellitus led to hypomotility of the gallbladder. Several (12, 13), although

Table 2. Obstetrical and gynecological history of the two groups

	Group 1 (n=73)	Group 2 (n=401)	*P* value
Gravidity, mean (range)	5.25 (0-14)	4.9 (0-15)	NS
Parity, mean (range)	3.19 (0-9)	3.09 (0-11)	NS
Abortion, mean (range)	0.64 (0-4)	0.54 (0-9)	NS
Menopause type			NS
Natural, n (%)	59 (80.8%)	90 (22.5%)	
Surgical, n (%)	14 (19.2%)	311 (77.5%)	
Duration of menopause, y (mean ± SD)	6.11 ± 4.76	5.77 ± 5.26	NS
History of oral contraceptive use, n (%)	17 (23.3%)	56 (13.9%)	NS
Length of oral contraceptive use, y (mean ± SD)	3.3 ± 2.39	2.86 ± 1.65	NS
HRT, n (%)	40 (54.8%)	222 (55.3%)	NS
Length of HRT, y (mean ± SD)	2.81 ± 2.31	3.14 ± 2.71	NS

Group 1: Individuals with gallstones. Group 2: Individuals with no gallstones. HRT: Hormone replacement therapy. NS: Not significant.

Table 3. Comparison of plasma lipid concentrations

	Group 1 (n=73)	Group 2 (n=401)	*P* value
Cholesterol (mg/dl), (mean ± SD)	216.52 ± 44.92	215.88 ± 44.35	NS
HDL-cholesterol (mg/dl), (mean ± SD)	51.66 ± 14.04	55.68 ± 19.34	NS
LDL-cholesterol (mg/dl), (mean ± SD)	138.33 ± 38.35	130.74 ± 40.67	NS
Triglycerides (mg/dl), (mean ± SD)	134.52 ± 54.83	143.25 ± 77.05	NS

HDL: High-density lipoprotein. LDL: Low-density lipoprotein.

not all (14), studies have shown a positive relationship with heredity. Murray et al. (15), in a large population-based study of women, suggested that smoking was an important risk factor for developing gallstone disease. Most studies have reported an increased risk associated with the number of pregnancies (16, 17); however, Halldestam et al. (14) showed no such association. The present study also found no relationships between gallstone disease and diabetes mellitus, heredity, smoking, or number of pregnancies.

Several prior studies have indicated an association between high blood lipid levels and increased risk of gallbladder disease (18, 19), but we did not find a relationship between serum lipid levels and increased incidence of gallstones. Gastric and enteric transit is delayed in the postmenopausal period and this is suspected to be a potential pathophysiological factor in the development of gallstones (20, 21). Petroianu et al. (22), in a prospective randomized trial, investigated the effect of the menopausal period on gallbladder emptying and cholelithogenesis. While delay in gallbladder emptying in women with gallstone disease was found, no association between the gallbladder emptying and menopause was determined. The effects of HRT on the gallstone formation were investigated and HRT was detected to increase the incidence of gallstones (23-25). The mechanism of this relation was pointed out as being due to HRT's effects of decreased bile acid synthesis, inhibited gallbladder motility and delayed gallbladder emptying. However, three observational studies reported no association between HRT and gallbladder disease (17, 26, 27). Furthermore, oral contraceptives were also cited for the same reason. While Evron et al. (28) noted an increased incidence of cholelithiasis among women exposed to oral contraceptives, La Vecchia et al. (29) found no significant increase in the relative risk of cholecystectomy due to contraceptive use. We did not identify an association between gallstone formation and HRT or oral contraceptive use.

In conclusion, the present study found a 15.4% prevalence rate of cholelithiasis in a Turkish population sample of postmenopausal women. None of the evaluated parameters (body mass index, additional systemic diseases, heredity, smoking habit, number of pregnancies, serum lipid level, and HRT and past oral contraceptive use) was detected as a risk factor for developing gallstone disease in our study.

REFERENCES

1. Shaffer EA. Gallstone disease: epidemiology of gallbladder stone disease. Best Pract Res Clin Gastroenterol 2006; 20: 981-96.
2. Acalovschi M. Cholesterol gallstones: from epidemiology to prevention. Postgrad Med J 2001; 77: 221-9.
3. Caroli-Bosc FX, Deveau C, Harris A, et al. Prevalence of cholelithiasis: results of an epidemiologic investigation in Vidauban, southeast France. General Practitioner's Group of Vidauban. Dig Dis Sci 1999; 44: 1322-9.
4. Everhart JE, Khare M, Hill M, Maurer KR. Prevalence and ethnic differences in gallbladder disease in the United States. Gastroenterology 1999; 117: 632-9.
5. Chung YJ, Park YD, Jeon SW, et al. Prevalence and risk factors of gallstones in a general health screened population. Korean J Med 2007; 13: 794-802.
6. Safer L, Bdioui F, Braham A, et al. Epidemiology of cholelithiasis in central Tunisia. Prevalence and associated factors in a nonselected population. Gastroenterol Clin Biol 2000; 24: 883-7.
7. Jensen KH, Jorgensen T. Incidence of gallstones in a Danish population. Gastroenterology 1991; 100: 790-4.
8. Chen CY, Lu CL, Huang YS, et al. Age is one of the risk factors in developing gallstone disease in Taiwan. Age Ageing 1998; 27: 437-41.
9. Jorgensen T. Prevalence of gallstones in a Danish population. Am J Epidemiol 1987; 126: 912-21.
10. Angelico F, Del Ben M, Barbato A, et al. Ten-year incidence and natural history of gallstone disease in a rural population of women in central Italy. The Rome Group for the Epidemiology and Prevention of Cholelithiasis (GREPCO). Ital J Gastroenterol Hepatol 1997; 29: 249-54.
11. De Santis A, Attili AF, Ginanni CS, et al. Gallstones and diabetes: a case-control study in a free-living population sample. Hepatology 1997; 25: 787-90.
12. Chapman BA, Frampton CM, Wilson IR, et al. Gallstone prevalence in Christchurch: risk factors and clinical significance. N Z Med J 2000; 113: 46-8.
13. Attili AF, De Santis A, Attili F, et al. Prevalence of gallstone disease in first-degree relatives of patients with cholelithiasis. World J Gastroenterol 2005; 11: 6508-11.
14. Halldestam I, Kullman E, Borch K. Incidence of and potential risk factors for gallstone disease in a general population sample. Br J Surg 2009; 96: 1315-22.
15. Murray FE, Logan RF, Hannaford PC, Kay CR. Cigarette smoking and parity as risk factors for the development of symptomatic gall bladder disease in women: results of the Royal College of General Practitioners' oral contraception study. Gut 1994; 35: 107-11.
16. Novacek G. Gender and gallstone disease. Wien Med Wochenschr 2006; 156: 527-33.
17. Jorgensen T. Gallstones in a Danish population: fertility period, pregnancies, and exogenous female sex hormones. Gut 1988; 29: 433-9.
18. Boland LL, Folsom AR, Rosamond WD, Atherosclerosis Risk in Communities (ARIC) Study Investigators. Hyperinsulinemia, dyslipidemia, and obesity as risk factors for hospitalized gallbladder disease. Ann Epidemiol 2002; 12: 131-40.
19. Attili AF, Capocacia R, Carulli N, et al. Factors associated with gallstone disease in the MICOL experience. Multicenter Italian Study on Epidemiology of Cholelithiasis. Hepatology 1997; 26: 809-18.

20. Keane P, Colwell D, Baer HP, et al. Effects of age, gender and female sex hormones upon contractility of the human gallbladder in vitro. Surg Gynecol Obstet 1986; 163: 555-60.
21. Grodstein F, Colditz GA, Stampfer MJ. Postmenopausal hormone use and cholecystectomy in a large prospective study. Obstet Gynecol 1994; 83: 5-11.
22. Petroianu A, Oliveira LC, Vieira MI. Delay in gallbladder emptying during the perimenopausal period. Braz J Med Biol Res 2000; 33(9): 1037-40.
23. Uhler ML, Marks JW, Judd HL. Estrogen replacement therapy and gallbladder disease in postmenopausal women. Menopause 2000; 7: 162-7.
24. Cirillo DJ, Wallace RB, Rodabough RJ, et al. Effect of estrogen therapy on gallbladder disease. JAMA 2005; 293: 330-9.
25. Dhiman RK, Sarkar PK, Sharma A. Alterations in gallbladder emptying and bile retention in the absence of changes in bile lithogenicity in postmenopausal women on hormone replacement therapy. Dig Dis Sci 2004; 49: 1335-41.
26. Kakar F, Weiss NS, Strite SA. Non-contraceptive use and risk of gallstone disease in women. Am J Public Health 1988; 78: 564-6.
27. Schwarz S, Volzke H, Baumeister SE, et al. Menopausal hormone therapy and gallbladder disease: the study of health in Pomerania. Clin Endocrinol 2007; 67: 51-9.
28. Evron S, Frankel M, Diamant Y. Biliary disease in young women and its association with pregnancy or oral contraceptives. Int Surg 1982; 67: 448-50.
29. La Vecchia C, Negri E, D'Avanzo B, et al. Oral contraceptives and non-contraceptive oestrogens in the risk of gallstone disease requiring surgery. J Epidemiol Community Health 1992; 46(2): 171-2.