PREVALENCE AND RISK FACTORS FOR GALL BLADDER POLYPS

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ABSTRACT

Objective: Polyps of gallbladder are tumour-like lesions of this organ. Little has been known about
factors associated with the occurrence of gallbladder polyps. We aimed to examine prevalence and
factors associated with gallbladder polyps in our region.
Design: Prospective clinical study.
Setting: Kocaeli University Teaching Hospital.
Subjects: Four hundred and thirty two patients were enrolled to the study.
Interventions: Subjects were screened for the presence of any pathological condition for gallbladder
by upper abdominal ultrasonography completed a questionnaire, and underwent a physical
examination and blood chemistry tests.
Results: Family history of gastrointestinal disease, gallbladder disease and any neoplastic disease
and abnormality in HDL-cholesterol levels had most consistent association at univariate analysis.
Multivariate logistic regression analysis showed that family history of any gastrointestinal disease
and abnormalities of HDL-cholesterol levels were significant.
Conclusions: Our findings suggest the formation of gallbladder polyps is associated with fat
metabolism. Other unknown factors may also influence the formation of this lesion. Relationship
between gallbladder polyps and family history of some diseases suggests us to perform some
genetic studies.

INTRODUCTION

Gallbladder polyps are one of the common
ultrasonographic findings in general population
(1). In general, polypoid lesions of gallbladder
refer to small protuberances such as cholesterol
polyps, ectopic gastric glands, adenomas, and
adenocarcinomas (2). The majority of the polypoid
lesions are benign (3,4). Ultrasonography has
improved the diagnosis of gallbladder diseases and
prompted many population studies of gallstone
disease (5-8). Endoscopic ultrasonography may
help differentiate non-neoplastic from neoplastic
gallbladder polyps (9). The results on the prevalence

distribution by age and sex for gallbladder polyps
have been extensively reported in previous studies
(6,10) and will be only briefly recalled here. Little has
been known of factors associated with the occurrence
of gallbladder polyps. This study analyses and
discusses the relationships between gallstone
disease and associated individual factors.

MATERIALS AND METHODS

This study was performed at the Department of
Internal Medicine of Kocaeli University Teaching
Hospital between January 2000 and March 2002. A
satisfactory upper abdominal ultrasonography was

performed in 432 patients for any reason. The study was conducted in accordance with the Declaration of Helsinki and was reviewed and approved by the local Ethics Committee. All patients gave their informed consent to participate.

The study included an interview with the administration of a standard questionnaire, followed by a physical and ultrasonographic examination of the upper abdomen, a blood sampling for biochemical analysis including a 75g oral glucose tolerance test for subjects who had polypoid protuberances at ultrasonography. Some of the questions asked were:

(i)   Did any one of your family members suffer from gallbladder disease or undergo cholecystectomy?

(ii)   Have you ever suffered from diabetes, gastric or duodenal ulcer, myocardial disease, hepatic cirrhosis or any other liver disease, pulmonary disease or other system disease?

(iii)   Have you ever smoked cigarettes or drunken alcoholic beverage?

(iv)   Have you ever regularly consumed serum lipid-lowering drugs, aspirin, and other drugs?

(v)   Women were also asked about the number of pregnancies and use of oral contraceptive drugs.

After subjects had fasted overnight, ultrasonography of gallbladder was performed by same group of radiologists using an instrument with a Toshiba Eccocee Duplex Ultrasonography. To estimate the prevalence of gallstone disease, the final gallbladder status was recorded as follows:

(i)   Normal at ultrasonography;

(ii)   Presence of gallstones at ultrasonography;

(iii)   Presence of biliary sludge at ultrasonography;

(iv)   Presence of polypoid protuberances at ultrasonography;

(v)   Previous cholecystectomy;

(vi)   Inconclusive or doubtful and

(vii)   Presence of two and four gallbladder polyps were diagnosed as immobile echoes protruding from inside the gallbladder wall into the lumen. The diameter of polyps was measured and then recorded. A blood sample was obtained from each subject, who had undergone upper abdominal

ultrasonography for any reason, after an overnight fast to measure serum glucose, total, low-density (LDL), very low-density (VLDL) and high density lipoprotein (HDL) cholesterol, triglyceride, alanine transaminase (ALT), aspartate transaminase (AST), gamma glutamyl transaminase (GGT) and alkaline phosphatase (ALP) levels. A glucose tolerance was classified as normal, impaired, and diabetic in accordance with the World Health Organization criteria (11).

The data were analysed by using the Statistical Package for Social Science (SPSS) for Windows version 6.0. In the preliminary analysis, univariate statistical methods were used to determine which factors were significant for gallbladder polyp. The chi-square test with Yates' correction or Fisher's exact test was used for categorical variables, and the student's t-test was used for quantitative measurements.

All the significant factors from the univariate analysis were subsequently included in the multivariate logistic regression procedure. The FORWARD automatic variable selection procedure was used to determine which of these variables were the predictors of gallbladder polyps. Presence of gallbladder polyps was the dependent variable.

RESULTS

Of the 432 patients who had upper abdominal ultrasonography performed, 305 were women and 127 were men. The age ranged from 24 to 69 years (42.1 ± 11.3 years). A satisfactory upper abdominal ultrasonography was performed in 432 patients including 26 patients who had a cholecystectomy.

Sixty had gallbladder stones; 27 had gallbladder polyps and 319 had a normal gallbladder. Twenty six out of 27 polyps were predicted to be cholesterol polyps on the basis of ultrasonographic appearance with the remainder classified as polypoid lesion of uncertain benignity. The overall prevalence rate of gallbladder polyps was calculated to be 6.3%. The prevalence of polyps was found to be 7.87% among males, insignificantly ($p > 0.05$) higher than the 5.57% in the females. In 14.8 % of cases, polyps were larger than 5 mm. Forty eight point one percent of our cases had polyps measuring 3 mm or less in diameters. The distribution of 27 patients on the basis of the number of the polyps was as follows: seventeen (63%) patients

had one polyp, eight (29.6%) patients had two and two (7.4%) patients had three or more. There were two gallbladders containing stones and polyps together. Some of personal and biochemical parameters in polypoid and non-polypoid groups are summarised in Table 1. All of the patients who had gallbladder polyps were asymptomatic or had minimal and non-specific symptoms. They were incidentally diagnosed by ultrasonography. In univariate analysis, blood albumin, globulin, cholesterol and HDL-cholesterol levels in both groups were statistically significant when compared to each other.

Age: In univariate analysis, an increased risk of gallbladder polyps was observed for increasing ages in females. But in multivariate analysis there was no differentiation with age in both sexes.

Serum lipids: Any significant relationship was not observed between total serum cholesterol levels and the risk of gallbladder polyps. Serum cholesterol was also negatively and insignificantly associated with gallbladder polyps in males and females. In multivariate analysis cholesterol level in both sexes was not associated with gallbladder polyps. With regard to HDL cholesterol levels, the risk of gallbladder polyps was higher in the lower level than

in the higher level. In males and females, an inverse association was observed for gallbladder polyps. In the multivariate analysis, there was an association with gallbladder polyps and HDL-cholesterol levels, regardless of the gender. Serum triglyceride levels were not associated with gallbladder polyps in men and women.

Obesity: There was no association with gallbladder polyps and increasing body mass index (BMI) in both genders.

Concomitant disease: On the survey, 72 women responded yes to the question: "Have you ever suffered from any heart disease?" The results indicated that there was no increased risk of gallbladder polyps.

In this study, 14 men and nine women were aware of lung diseases. In both sexes, any significant increase in the risk of gallbladder polyps was not evident. A total of 14 men and 11 women were aware of being diabetic. There was no higher risk for gallbladder polyps among diabetic men and women. The results were not different when 88 men and ten women with serum glucose levels above 110 mg/dl (although they had declared that they were not diabetic) were included.

Table 1

Comparison of some parameters in both groups

	Normal	Polyp	Significance
Age	41.9 ± 11.4	45 ± 9.6	p = 0.17
BMI	27.1 ± 5.0	27.1 ± 3.6	p = 0.96
Settlement time	25.1 ± 12.5	27.7 ± 17.4	p = 0.44
Blood glucose level	103 ± 25	108.1 ± 22.7	p = 0.3
Blood albumin level	4.0 ± 0.3	4.2 ± 0.4	p = 0.02
Blood globulin	3.1 ± 0.25	2.9 ± 0.39	p = 0.02
Total protein	7.1 ± 0.3	7.1 ± 0.4	p = 0.53
Triglyceride	184.9 ± 101.1	195.3 ± 192.4	p = 0.8
Cholesterol	207.3 ± 36.1	229.8 ± 53.2	p = 0.039
HDL	42.1 ± 10.2	50.4 ± 9.9	p = 0.05
LDL	122.6 ± 34.9	104.5 ± 47.8	P = 0.06
VLDL	39.1 ± 27.4	34.9 ± 14.4	p = 0.2
AST	22.4 ± 7.2	33.6 ± 49.6	p = 0.25
ALT	28.3 ± 14.3	37.7 ± 60.9	p = 0.42
ALP	87.8 ± 46.4	92.4 ± 38.3	p = 0.6
GGT	22.2 ± 10.8	21.0 ± 10.9	p = 0.66

Smoking: Both at univariate and multivariate analysis, smoking was not a factor associated with gallbladder polyps.

Alcohol use: No association was found between alcohol and gallbladder polyps by both univariate and multivariate analysis.

Family history: Each participant was invited to reply to the questions like "did any of your family members ever suffer from serious gastrointestinal disease, gallbladder disease, any neoplasm and diabetes mellitus?" Among those responding yes for the first three diseases, an increased risk of gallbladder polyps

was observed in both sexes. At the univariate analysis, women who had a family member clinically diagnosed with gastrointestinal disease, or gallbladder disease or any malignancy and diabetes mellitus also had an increased risk of gallbladder polyps.

Obstetrical history: An increasing risk for gallbladder polyps was not observed with the increasing number of pregnancies. Polyps and childbirth were also not associated, whereas the number of abortions showed no substantial association with polyps. At the univariate analysis, the use of oral contraceptives was not associated with gallbladder polyps (Table 2).

Table 2

Statistical analysis of risk factors for gallbladder polyps in all patients

Risk factor	Normal	Polyp	Significance		
			df	X^2	P-value
Age ($\geq$50 years)	92	9	1	1.59	0.92
Sex (Female)	288	27	1	0.81	0.37
Obesitiy (BMI $\geq$30)	231	18	1	0.96	0.33
Concomitant disease					
Heart disease	67	5	1	0.07	0.48
Lung disease	22	1	1	0.12	0.59
Endocrine disease	23	2	1	0.14	0.47
Alcohol use	30	5	1	4.20	0.056
Smoking habits	125	5	1	1.83	0.176
Settlement	339	19	1	3.17	0.075
Obstetric history	183	16	1	2.02	0.16
Family history of					
Gastrointestinal disease	134	18	1	12.52	0.004
Gallbladder disease	54	9	1	8.12	0.009
Any neoplasm	68	11	1	9.72	0.004
Diabetes mellitus	138	12	1	1.20	0.27
Elevated blood glucose	88	10	1	3.38	0.066
Abnormal cholesterol level	263	17	1	0.04	0.84
Abnormal HDL-cholesterol level	133	1	1	10.04	0.00153
Abnormal LDL-cholesterol level	126	5	1	1.90	0.168
Abnormal VLDL-cholesterol level	216	15	1	0.05	0.82
Abnormal triglyceride level	129	7	1	0.41	0.52
Albumin level	23	2	1	0.14	0.47

Table 3

In the total study population, jointly significant parameters and the predictive odds ratio of gallbladder polyps based on the multiple logistic regression analysis

Parameter	Odds ratio (OR)	95% confidence interval	P-value
Family history of gastrointestinal disease	4.04	1.77–9.24	0.0027
HDL-cholesterol level	0.079	0.1–0.59	0.0004

Multivariate logistic regression analysis on the remaining six variables showed that only two (family history of gastrointestinal disease and HDL-cholesterol levels) were jointly significant for the total study population (Table 3). The probability of gallbladder polyps is thus:

Log OR = -8.14 + (1.29 x family history of gastrointestinal disease) + (0.076 x HDL-cholesterol)

Family history of gastrointestinal disease = 1 if present or 0 if absent; family history of any tumoural disease = 1 if present or 0 if absent, HDL-cholesterol level if it is elevated or 0 if normal.

DISCUSSION

The overall study population in the present study was lower in number than that of previous epidemiological studies, but the results were to some extent useful. Polypoid lesions of the gallbladder are small protuberances, including benign tumours, malignant lesions and tumour-like lesions. The most common tumour-like lesion is cholesterol polyps (8,10,11). As reported previously (5,8), our study also showed that the prevalence of gallbladder polyps was high in middle-aged persons. Our observations suggests that age is not a related factor for gallbladder polyps. Gallbladder polyps were previously diagnosed by cholecystography, but the availability of ultrasonography makes differentiation of these lesions easy with other similar lesions, as we did (1,2,12). Gallbladder polyps were as prevalent in our study population (6.3%) as in previous studies (5,8,13). Furthermore, gallbladder polyps detected in our study seem to be similar to those in the previous studies with regard to size and number (13).

There was no significant association between polyps and sex, body mass index and diabetes mellitus. The lack of significant association between polyps and concomitant disease, smoking habit, alcohol use, living region, usage of exogenous female sex hormones and obstetric history were determined as described in the literature (5,8,13). With regard to serum lipids, our study shows there was no relationship between total cholesterol level and gallbladder polyps. Our results were similar to previous reports (5,13-15). As far as HDL cholesterol level is concerned, an inverse association was found at univariate analysis with gallbladder polyps in both sexes. In the multivariate analysis this association was observed if gender was not taken into consideration. Various mechanisms are said to underlie the accumulation of lipid in the gallbladder such as direct deposition of cholesterol from the blood (16,17), transfer of free sterol from the bile to gallbladder mucosa (16,18). Thus, an aetiologic association between fat metabolism and gallbladder polyps cannot be excluded. As seen in our present 27 patients, polyps of the gallbladder do not cause symptoms, except for unusual cases (10). On clinical grounds alone, it is certainly not possible to distinguish which histologic type of gallbladder polyp is present (19,20), nor can the ultrasonography or cholecystography reliably predict histology.

In this study, we found only two gallbladders containing stones and polyps together. This may be due to the mechanical factors that gallstones may destroy the cecile polyps or to the fact that a detailed evaluation of gallbladder wall in the stone containing gallbladder is difficult. This negative relationship in our study is similar to previous reports (21,22).

Reported risk factors for gallstone disease were unrelated to gallbladder polyps. Our findings suggest that the formation of gallbladder polyps is associated with fat metabolism. Other unknown factors such as family history of a gastrointestinal disease and neoplastic disease may also influence the formation of this lesion. These findings require us to make some genetic studies.

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