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The effect of high serum lipid level on benign gallbladder diseases

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Abstract

There is a positive correlation between serum lipid levels and benign gallbladder diseases. We wanted to evaluate whether there is a relationship between the preoperative lipid profiles results with the presence of cholesterolosis, cholesterol polyps and cholelithiasis in the pathological examination. Patients who presented with various symptoms and underwent cholecystectomy surgery in a tertiary university hospital were retrospectively analyzed. Pathological examination records of 331 patients who had undergone cholecystectomy between 2016 and 2020 were obtained retrospectively. The latest lipid profiles results before the cholecystectomy were recorded. Patients were divided into groups according to their lipid profiles periods before cholecystectomy. The cholecystectomy reports of the patients were examined in terms of cholesterolosis, cholesterol polyp, and cholelithiasis. There was no difference between lipid profiles and the pathological subtypes in the patients whose lipid profiles were measured between 0-30 days and 0-90 days preoperatively. There was a significant difference in triglyceride levels between patients with cholesterol polyps and those without polyps, whose lipid profiles were measured within 90-180 days before surgery (p=0.031). There were significant differences in total cholesterol, triglyceride, LDL, and non-HDL levels between patients with and without cholesterolosis (p=0.017, p=0.037, p=0.048, p=0.019, respectively). There was a significant difference in triglyceride levels between patients with cholesterol polyps and those without polyps, whose lipid profiles were was measured within 0-180 days before surgery (p=0.023). There was a significant difference in total cholesterol, LDL, and non-HDL levels between patients with and without cholesterolosis (p=0.017, p=0.021, p=0.03, respectively). There is a positive correlation between preoperative serum lipid profiles and benign gallbladder diseases. The incidence of cholesterolosis and cholesterol polyps may increase after long-term exposure to high lipid concentrations.

Keywords: Cholesterolosis, gallbladder, cholelithiasis

Introduction

Benign lesions of the gallbladder generally do not cause symptoms. In some of the patients, severe and colic abdominal pain located in the right hypochondrium or epigastrium, less commonly nausea and vomiting, dyspepsia even intolerance against some food groups (oily foods, fried foods, cabbage, peas, etc.) may develop [1]. Especially woman gender, obesity, rapid weight loss, pregnancy, and estrogen are essential factors in the etiology of benign gallbladder diseases. A common disease, cholesterolosis, can be found in approximately 9-26% of cholecystectomy specimens [2]. Although many histological studies have been conducted on cholesterolosis, its etiology has not been elucidated. However,studies have revealed that inflammation of the gallbladder wall in cholesterolosis is typically absent or very mild and appearsto be a histomorphological feature [3-6]. Other gallbladder diseases frequently encountered in routine pathology practice are cholesterol polyps in the gallbladder and cholelithiasis. Cholesterol polyps are the most common form of gallbladder polypoid lesions and do not carry malignant potential [7]. Cholelithiasis is one of the most common problems affecting the gastrointestinal system. The prevalence of gallstones depends on many different factors such as age, gender, ethnicity. The incidence of gallstones increases with advanced age and reaches over 40% after the 7th decade. It is two times more common in women than men [8].

We aimed to evaluate whether there is a relationship between the preoperative lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride level) results with the presence of cholesterolosis, cholesterol polyps or cholelithiasis in the pathological evaluation.

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Materials and Methods

All procedures performed in this study were carried out following Recep Tayyip Erdoğan University Faculty of Medicine Clinical Research Ethics Committee approval (Number: 2021/224, Date:23/12/2021) and the 1964 Helsinki Declaration ethical principles.

Pathological examination records of patients who had undergone cholecystectomy between 2016 and 2020 were obtained from the hospital information system.

The latest lipid profile results before the cholecystectomy, age, and gender data were recorded.

We identified 331 patients with lipid profile results within 0-180 days before the surgery. Patients were divided into groups according to their lipid profile periods for precholecystectomy as 0-30 days, 0-90 days, 0-180 days, and 90-180 days. The cholecystectomy reports of the patients were examined in terms of cholesterolosis, cholesterol polyp, and cholelithiasis. It was evaluated whether there is a relationship between the presence of cholesterolosis, cholesterol polyp, cholelithiasis, and lipid profile parameters.

Statistical analyzes were performed with the IBM SPSS Statistics, Version 23.0 (SPSS Inc., Chicago, USA) program. Descriptive statistics of the groups were reported as frequencies and percentages (n, %). Difference analysis between the two groups in terms of numeric variables with normal distribution was performed using Student's t-test and the Mann-Whitney U test for those which did not show normal distribution. The relation of categorical data between the groups was evaluated with the Chi-square test. For significance, Pearson Chi-Square or Fisher's Exact Test p values were used, considering the number of patients in the categories. The significance level was accepted as $p < 0.05$.

Results

Of the total 331 patients, 242 (73%) were woman, 89 (27%) were man. Of the patients whose lipid profile was measured in the first 30 days before surgery, 77 (74%) were woman, and 27 (26%) were man. While 101 (98%) patients had chronic cholecystitis, 2 (2%) had acute suppurative cholecystitis. There was no significant difference between the patients' pathological subvariables and lipid profiles in the 0-30 day group. Data are presented in table 1.

Table 1. Lipid profile results of patients in 0-30 day before cholecystectomy

Cholesterol Polyps n:12 (11%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol (mg/dL)	212 (114-341)	219 (139-282)	0.954
Triglyceride (mg/dL)	121 (41-464)	164 (64-257)	0.497
HDL (mg/dL)	49 (31-75)	43 (29-75)	0.333
LDL (mg/dL)	132 (56-213)	134 (77-206)	0.889
LDL/HDL	2.82 (0.91-5.77)	2.87 (1.24-5.71)	0.409
non-HDL (mg/dL)	160 (69-290)	175 (93-246)	0.774
Age	56 (20-88)	53 (40-68)	0.24
Cholesterolosis n:26 (25%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	212 (114-341)	216 (139-282)	0.756
Triglyceride(mg/dL)	120 (41-464)	130 (42-320)	0.855
HDL(mg/dL)	49 (31-75)	45 (29-75)	0.291
LDL(mg/dL)	132 (56-213)	132 (77-206)	0.996
LDL/HDL	2.78 (0.91-5.11)	2.87 (1.24-5.77)	0.52
non-HDL(mg/dL)	160 (69-290)	170 (93-246)	0.947
Age	56 (20-88)	53 (30-73)	0.244
Cholelithiasis n:89 (85%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	226 (134-298)	211 (114-341)	0.623
Triglyceride(mg/dL)	127 (42-464)	123 (41-458)	1.000
HDL(mg/dL)	50 (31-75)	48 (29-75)	0.675
LDL(mg/dL)	135 (59-203)	132 (56-213)	0.821
LDL/HDL	2.66 (0.91-4.46)	2.83 (0.96-5.77)	0.791
non-HDL(mg/dL)	170 (69-257)	159 (72-290)	0.689
Age	55 (40-63)	54 (20-88)	0.289

mg/dL: milligrams per decilitre, HDL: high-density lipoprotein, LDL:low-density lipoprotein

Table 2. Lipid profile results of patients in 0-90 day before cholecystectomy

Cholesterol Polyps n:20 (8%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol (mg/dL)	208 (113-341)	217 (139-323)	0.336
Triglyceride (mg/dL)	128 (41-484)	179 (64-506)	0.103
HDL (mg/dL)	48 (21-94)	43 (29-75)	0.223
LDL (mg/dL)	128 (44-232)	134 (74-236)	0.446
LDL/HDL	2.78 (0.8-7.14)	2.95 (1.24-6.05)	0.32
non-HDL (mg/dL)	160 (58-290)	167 (93-284)	0.194
Age	57 (20-95)	54 (36-68)	0.115
Cholesterolosis n:52 (20%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	207 (113-341)	216 (139-323)	0.148
Triglyceride(mg/dL)	129 (41-474)	137 (42-506)	0.485
HDL(mg/dL)	47 (21-94)	50 (26-75)	0.951
LDL(mg/dL)	128 (44-225)	132 (74-236)	0.121
LDL/HDL	2.75 (0.8-7.14)	2.94 (1.24-6.05)	0.236
non-HDL(mg/dL)	159 (58-290)	167 (93-284)	0.106
Age	57 (20-95)	53 (28-77)	0.031
Cholelithiasis n:203 (80%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	206 (113-323)	209 (114-341)	0.252
Triglyceride(mg/dL)	134 (42-506)	129 (41-484)	0.491
HDL(mg/dL)	47 (31-82)	49 (21-94)	0.956
LDL(mg/dL)	130 (44-236)	129 (56-225)	0.273
LDL/HDL	3.04 (0.8-6.05)	2.77 (0.84-7.14)	0.233
non-HDL(mg/dL)	167 (58-284)	158 (68-290)	0.168
Age	56 (36-78)	56 (20-95)	0.427

mg/dL: milligrams per decilitre, HDL: high-density lipoprotein, LDL:low-density lipoprotein

Table 3. Lipid profile results of patients in 90-180 day before cholecystectomy

Cholesterol Polyps n:5 (6%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol (mg/dL)	210 (127-323)	235 (168-355)	0.065
Triglyceride (mg/dL)	123 (46-274)	209 (129-254)	0.031
HDL (mg/dL)	49 (23-87)	59 (27-75)	0.315
LDL (mg/dL)	133 (67-248)	144 (90-231)	0.263
LDL/HDL	2.73 (1.04-7.54)	3.09 (2.22-3.33)	0.798
non-HDL (mg/dL)	159 (78-290)	179 (141-280)	0.245
Age	58 (22-80)	50 (39-64)	0.287
Cholesterolosis n:17 (22%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	206 (127-323)	228 (168-355)	0.017
Triglyceride(mg/dL)	122 (46-274)	177 (85-254)	0.037
HDL(mg/dL)	47 (23-87)	51 (27-75)	0.706
LDL(mg/dL)	133 (67-248)	138 (90-231)	0.048
LDL/HDL	2.71 (1.04-7.54)	2.82 (2.02-5.73)	0.305
non-HDL(mg/dL)	156 (78-290)	179 (141-280)	0.019
Age	57 (22-80)	53 (39-75)	0.816
Cholelithiasis n:60 (77%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	219 (144-266)	209 (127-355)	0.355
Triglyceride(mg/dL)	125 (66-253)	124 (46-274)	0.82
HDL(mg/dL)	53 (30-68)	47 (23-87)	0.533
LDL(mg/dL)	141 (76-212)	133 (67-248)	0.325
LDL/HDL	2.69 (1.38-5.93)	2.86 (1.04-7.54)	0.806
non-HDL(mg/dL)	169 (89-229)	159 (78-290)	0.448
Age	64 (28-80)	53 (22-79)	0.034

mg/dL: milligrams per decilitre, HDL: high-density lipoprotein, LDL:low-density lipoprotein

Table 4. Lipid profile results of patients in 0-180 day before cholecystectomy

Cholesterol Polyps n:25 (8%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol (mg/dL)	209 (113-341)	228 (139-355)	0.102
Triglyceride (mg/dL)	126 (41-484)	181 (64-506)	0.023
HDL (mg/dL)	48 (21-94)	45 (27-75)	0.52
LDL (mg/dL)	130 (44-248)	137 (74-236)	0.247
LDL/HDL	2.76 (0.8-7.54)	2.95 (1.24-6.05)	0.337
non-HDL (mg/dL)	159 (58-290)	170 (93-284)	0.206
Age	57 (20-95)	52 (36-68)	0.044
Cholesterolosis n:69 (21%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	206 (113-341)	223 (139-355)	0.017
Triglyceride(mg/dL)	124 (41-474)	140 (42-506)	0.110
HDL(mg/dL)	47 (21-94)	50 (26-75)	0.729
LDL(mg/dL)	129 (44-248)	137 (74-236)	0.021
LDL/HDL	2.74 (0.8-7.54)	2.94 (1.24-6.05)	0.203
non-HDL(mg/dL)	158 (58-290)	170 (93-284)	0.03
Age	57 (20-95)	53 (28-77)	0.073
Cholelithiasis n:263 (80%)			
	No	**Yes**	
	Median (min - max)	**Median (min - max)**	**p**
Cholesterol(mg/dL)	210 (113-323)	209 (114-355)	0.111
Triglyceride(mg/dL)	129 (42-506)	127 (41-484)	0.61
HDL(mg/dL)	48 (30-82)	48 (21-94)	0.904
LDL(mg/dL)	136 (44-236)	130 (56-248)	0.192
LDL/HDL	2.95 (0.8-6.05)	2.79 (0.84-7.54)	0.373
non-HDL(mg/dL)	168 (58-284)	158 (68-290)	0.112
Age	57 (28-80)	56 (20-95)	0.566

mg/dL: milligrams per decilitre, HDL: high-density lipoprotein, LDL:low-density lipoprotein

Of the patients whose lipid profile was measured within 0-90 days before surgery, 182 (72%) were woman, and 71 (28%) were man. While 244 (97%) patients had signs of chronic cholecystitis, 7 (3%) had symptoms of acute suppurative cholecystitis. There was no significant difference between the pathological sub-variables and lipid profiles of the patients in the 0-90 day group. A significant difference was found only between age and patients with cholesterolosis (p=0.031). Data are presented in table 2.

Of the patients whose lipid profile was measured within 90-180 days before the operation sixty (77%) were woman and 18 (23%) were man. Among the patients in this group, there was a significant high triglyceride levels in cholesterol polyps (p=0.031). Also, in patients with cholesterolosis total cholesterol, triglyceride, LDL and non-HDL levels were significantly higher (p=0.017, p=0.037, p=0.048, p=0.019). While 75 (97%) patients had signs of chronic cholecystitis, 2 (3%) had acute suppurative cholecystitis. Patients with cholelithiasis were significantly younger (p=0.034). Data are presented in table 3.

Of the patients whose lipid profiles were evaluated within 0-180 days before the operation 242 (73%) of the were woman and 89 (27%) were man. While 319 (97%) of the patients had signs of chronic cholecystitis, 9 (3%) had signs of acute suppurative cholecystitis. Among the patients in this group, the triglyceride level was significantly higher in patients with cholesterol polyps (p=0.023). In patients with cholesterolosis, total cholesterol, LDL, and non-HDL levels were significantly increased at the presence of cholesterolosis (p=0.017, p=0.021, p=0.03). Data are presented in table 4.

Discussion

Gallbladder diseases are primarily benign, non-neoplastic diseases. Studies have shown that gallbladder diseases are approximately 2-3 times more common in women than men [9,10]. In our study, the woman/man ratio was around three times and was consistent with the literature. This difference between both sexes may be related to hormonal changes and recurrent pregnancies in women.

Cholesterolosis is reported to be found in 10-25% of cholecystectomy specimens, and it is emphasized that there is abnormal cholesterol ester accumulation in the macrophages and mucosal epithelium of the lamina propria of the gallbladder [11,12]. Our study detected cholesterolosis in 21% of the patients, consistent with the literature. Gallbladder polyps are seen in approximately 2-12% of patients who underwent cholecystectomy [13-15]. Roa et al. reported preoperative polyps in 12% of patients who underwent cholecystectomy and detected gallbladder polyps [16]. In our study, cholesterol polyps were detected in 8% of the patients, which was consistent with the literature. The incidence of cholelithiasis in the general population is 15-20% [17]. In our study, cholelithiasis was seen in 80% of the patients.

The coexistence of cholesterolosis and hypercholesterolemia is common in obese patients with gallstones. However, it has been reported that the coexistence of cholesterolosis with gallstones and high plasma cholesterol levels is not essential [18]. In a study, cholesterol supersaturation was observed in the bile of patients with cholesterolosis, but serum cholesterol levels were reported to be within normal limits [19]. The etiology of cholesterol polyps is thought to be cholesterolosis, which occurs after storing serum cholesterol in the gallbladder, aggregation of free sterols from the bile, or changes in liver cholesterol synthesis [20]. Demir et al. reported that LDL, HDL, and total cholesterol levels were

approximately ten units higher in patients with cholesterol polyps than in the control group [9]. In our study, however, no significant difference was observed between the patients whose lipid profile was evaluated within 0-30 days or within 30-90 days before surgery and the pathological subvariables of these patients. However, there was a significant difference between the triglyceride levels of those with and without cholesterol polyps in patients whose lipid profile was measured between 90-180 days. In addition, it was observed that the total cholesterol, triglyceride, LDL and non-HDL levels of patients with cholesterolosis were significantly higher than those without. These pathophysiological changes may be due to the long-term exposure of the patients to high lipid concentrations. In the same respect, it was reported that cholesterol and triglyceride ratios are higher in patients with gallstones than those without [21]. In addition, in the study of Duru et al., it was emphasized that high total cholesterol is associated with polycythemia, and this situation may form stones in the gallbladder [22]. In our study, however, no statistically significant relationship was found between gallstones and lipid profile at any time.

Limitations of the study

Since the study was retrospective, information on the use of lipid-lowering drugs, data on patients' lifestyles and comorbidities were unable to be obtained from the patients, since the study was retrospective, information on the use of lipid-lowering drugs and patients' lifestyles and comorbidities could not be obtained from the patients. Our case number may be insufficient in some groups because we separate them according to periods. For more accurate and reliable findings, prospective studies with large participation are required. However, there are not many studies similar to ours ın the lıterature. Exıstıng studıes also took into acoount the laboratory results immediately before cholecystectomy. Our data is considerable because this topic is a little-studies subjectc, and our examinations include preoperative long-term results.

Conclusion

It should be kept in mind that high serum lipid levels may also play an active role in benign gallbladder diseases. It should be considered that the incidence of cholesterolosis and cholesterol polyps may increase after long-term exposure to high lipid concentrations.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
All procedures performed in this study were carried out following Recep Tayyip Erdoğan University Faculty of Medicine Clinical Research Ethics Committee approval (Number: 2021/224, Date:23/12/2021) and the 1964 Helsinki Declaration ethical principles.

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