



# Bactobilia Among Patients with Uncomplicated Cholelithiasis Undergoing Laparoscopic Cholecystectomy: The Risk Factors and Effects on Postoperative Infectious Complications

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## Abstract

**Background:** Determining the rate of bactobilia among patients under going laparoscopic cholecystectomy (LC) and its correlations with predisposing factors and postoperative infections, which help evaluate the need for prophylactic antibiotic.

**Methods:** In this prospective study, 85 consecutive patients with uncomplicated cholelithiasis who underwent LC were enrolled from 2012 to 2013. Routine bile culture was done at the time of LC. Patients were divided into 2 groups, 1 with negative bile culture and another with bactobilia. Demographic and laboratory data were compared. Patients were followed up 10 days after their laparoscopy and 1 month after discharge to monitor the presence of infection.

**Results:** A total of 7 cultures of bile were positive for bacteria (8.2%). The patients' age was the sole factor with a significant relationship with the rate of bactobilia ( $P = 0.016$ ). Within 10 days after surgery, fever and surgical site infection were detected in 10.6% of patients, which was not significantly different in the 2 groups. There were no complications in the 30-day follow-up.

**Conclusions:** Detecting bactobilia with low frequency and the lack of correlation between bactobilia and postoperative infectious complications did not support prescribing prophylactic antibiotic in respective patients. The older age was the sole predisposing factor for the development of bactobilia.

**Keywords:** Bactobilia, Laparoscopic Cholecystectomy, Gallstone, Postoperative Complication, Antibiotic Prophylaxis

## 1. Background

Bile is usually sterile in healthy individuals, however, in the presence of gallstones in the gallbladder or biliary ducts, it could be colonized with bacteria (bactobilia) (1, 2). In symptomatic gallstone diseases, bactobilia has been reported in 20% - 46% of the patients who undergo a cholecystectomy (3).

In some studies, bactobilia has been shown to be a risk factor predisposing to postoperative infectious complications, which are one of the most important concerns of surgeons, especially in laparoscopic surgery (4, 5). The rate of post-operative wound infection after elective cholecystectomy in uncomplicated symptomatic gallstone ranges from 2.3% to 20% (6-9).

Detecting bactobilia could be valuable for planning the antibiotic prophylaxis and treatment of postoperative infections. Obtaining bile culture during biliary surgery

is mainly advised only in patients with some predisposing factors that could increase the risk of such infections. These risk factors include pyrexia, previous biliary instrumentation, previous biliary sepsis, bilioenteric anastomosis, immune suppression status, a palpable gallbladder, elevated WBC count, and elevated serum levels of alkaline phosphatase and old age (2, 5, 8, 10, 11). However, reports are still conflicting over the use of bile culture at biliary surgery (6, 12).

Microflora causing bactobilia and their antibiotic sensitivity profile has not yet thoroughly been studied among patients with uncomplicated gallstone, particularly in relation to the laparoscopic procedure. Therefore, the aim of this study was to determine the nature of bacteriain bile and their antimicrobial susceptibility in patients with uncomplicated symptomatic cholelithiasis who underwent elective laparoscopic cholecystectomy (LC). We also studied the relationship between bactobilia and the presence

of some predisposing factors as well as developing postoperative infectious complications.

## 2. Methods

### 2.1. Patients and Surgical Procedure

Between September 2012 and September 2013, 85 consecutive patients with uncomplicated symptomatic cholelithiasis admitted to the surgical wards of Shahid Faghihi teaching hospital affiliated to Shiraz University of Medical Sciences, were included. Diagnosis of cholelithiasis was confirmed by abdominal ultrasonography. None had evidence of the presence of *gallstone* in the *common bile duct*. All patients underwent elective LC. Demographic and laboratory data including age, sex, body mass index (BMI), and preoperative data including history of smoking (defined as water pipe smoking with respective frequency and smoking history of any number of cigarettes per day during the previous 6 months), duration of abdominal pain and severity mentioned the history of previous abdominal surgery (appendectomy, cesarean section, tubal ligation, hemorrhoidectomy), the presence of underlying medical conditions (hypertension, diabetes mellitus, hyperlipidemia, underlying liver disease, inflammatory bowel diseases, and hypothyroidism), hemoglobin level, white blood count (WBC), aspartate transaminases, alanine transferases, and fasting blood sugar (FBS) were collected. We followed up with patients 10 days after laparoscopy and then 1 month after discharge from the surgical clinic to identify patients with fever or wound infection. Fever was defined as a temperature above 37.8°C at least twice a day.

Patients with acute cholecystitis in the last 6 months, autoimmune disorders, cirrhosis, obstructive jaundice, cholangitis, biliary pancreatitis, usage of corticosteroids or other immune suppressive drugs, the history of endoscopic or percutaneous biliary intervention before operation, history of antibiotic usage in the last 1 month, leukocytosis or fever 1 month before operation, abnormal liver enzymes (greater than twice the upper limit of normal), C-reactive protein (CRP) level higher than 6 mg/dL, erythrocyte sedimentation rate (ESR) higher than 20 mm/hour, and total bilirubin level higher than 4 mmol/L were excluded. None of the patients received prophylactic antibiotics.

### 2.2. Bile Culture

A total of 5 - 10 mL of biliary sample from gallbladder was collected under aseptic conditions at the time of operation and were inoculated immediately into BACTEC 9240 (Becton Dickinson diagnostic instrument systems,

Sparks, Md.) bottles for adults plus aerobic/F aseptically and were processed as per the manufacturer's instructions in Professor Alborzi clinical microbiology research center (PACMRC). Bacteria growing from subcultures were identified to the species level on the basis of colonial morphology and by using standard microbiological tests including gram staining and biochemical profiles. Antibacterial susceptibility was determined according to the standard disk diffusion (Kirby-Bauer) method, using Mast Co. (Mast Co, Merseyside, UK). Antibacterial susceptibility pattern was interpreted, as recommended by clinical laboratory standards institute (CLSI). Blood culture sample was aseptically obtained after induction of *anesthesia* and before starting the operation from all patients and processed in PACMRC, as described for biliary samples. It is important to notice that all samples were obtained from the internal orifice and gram negative bacteria as well as anaerobic ones should be mentioned.

### 2.3. Statistical Analysis

The data were analyzed by SPSS (SPSS 11.0, Chicago, Illinois, USA). The study population was divided into bile culture-positive and bile culture-negative groups and the collected parameters were compared between the groups. Chi-square test or Fischer's exact test was used to compare categorical and ordinal variables. The student's t-test was used to compare quantitative variables. P value less than 0.05 was considered as significant. Ethical approval was obtained from the ethical review committee of the Shiraz University of Medical Sciences. The informed consents were obtained from all patients.

## 3. Results

### 3.1. Clinical Findings

A total of 85 participants, 77 women and 8 men, aged 20 - 82 years with a median age of 43.35 years were included. The mean BMI was  $26.3 \pm 4.58$  (ranged 17.9 - 36.9). In 85 bile samples, 7 (8.2%) were shown to have bacterial isolates. Evaluation of comorbidities showed that 18 patients (21.2%) had hyperlipidemia, 16 (18.8%) diabetes mellitus, 14 (16.5%) hypertension, and 9 (10.6%) hypothyroidism. Out of the patients, 14 (16.5%) were smokers. None had underlying liver disease or inflammatory bowel diseases. In the 10-day follow-up, 9 patients developed a fever (10.5%), 1 of whom had bacteremia with *Escherichia coli* (*E. coli*) and 2 others developed wound infection over the period. Overall, in the 10-day follow-up, 8 patients developed a wound infection, however, in the 1-month follow-up, no complications were detected.

### 3. 2. Bacteriologic Profile of Bile Cultures

The overall bacterial isolates from bile samples showed 3 strains of *Escherichia coli* (*E. coli*) (42.8%), 1 strain of *Klebsiella spp.*, 1 *Enterobacter spp.*, 1 *Acinetobacter spp.*, and 1 *Viridans streptococci* (each 14.8%).

All 6-gram negative bacteria strains were sensitive to amikacin and all except 1 strain of *Acinetobacter* were sensitive to imipenem. All except 2 strains of *E. coli* were sensitive to gentamycin. All strains were sensitive to ciprofloxacin and cefuroxime except 1 strain of *E. coli* and one *Klebsiella* strain. Also, all strains except 1 strain of *E. coli* and 1 *Enterobacter* strain were sensitive to colistin. Only, 3 strains were sensitive to ceftriaxone and cefepime including 2 strains of *E. coli*, and 1 *Acinetobacter* strain. A total of 3 strains were sensitive to ampicillin including 2 strains of *E. coli*, and 1 *Acinetobacter* strain. Also, 3 strains were sensitive to cefexime, 2 strains of *E. coli*, and 1 *Enterobacter* strain. Only 2 strains were sensitive to co-trimoxazole, 1 strain of *E. coli*, and 1 *Enterobacter* strain. Also, only 2 strains were sensitive to cefotaxime, 1 strain of *E. coli*, and 1 *Acinetobacter* strain.

### 3. 3. Predictors of Bactobilia and Its Influence

The data about patients with positive and negative bile culture results are shown in Table 1. Patients with bactobilia had significantly higher mean age ( $P = 0.016$ ). However, a statistically significant association between bactobilia and patient gender, BMI, history of smoking, hypertension, hyperlipidemia, or hypothyroidism was not detected. In addition, there was no statistically significant difference between those groups when comparing the rates of occurrence of fever or surgical site infection in the 10-day follow-up.

## 4. Discussion

Usually, about 15% of patients with gallstones undergo surgery (laparoscopic or open cholecystectomy) for uncomplicated symptomatic gallstones. Post-operative infectious complications are one of the important causes of morbidity and mortality among these patients, which could lead to significantly longer lengths of hospital stay (13).

Our results showed that the overall prevalence of bacteria within bile sampled at uncomplicated LC was 8.2% while it was 2.8% - 25 % in different reported studies (7, 14-16). The lower rate of bactobilia has been reported among patients who underwent LC (2.8%), when compared to the overall rate of 13.3% in patients undergoing open cholecystectomy (7).

In the present study, there was no correlation between bactobilia and postoperative infectious complications, which is in agreement with some other studies (6, 7, 12, 17). On the contrary, some studies have reported a higher incidence of postoperative infectious complications in patients in where bactobilia was detected, especially when cholecystectomy is performed in patients with complicated gallstone disease (13).

Some clinical trials suggest that antibiotic prophylaxis may not be necessary in LC, especially in patients with uncomplicated gallstones who underwent elective LC (9, 10). Either way, the better knowledge about the nature of bacteria in bile and their antimicrobial susceptibility patterns could play an important role in the proper selection of antibiotics for prophylaxis, especially in high-risk patients. In one patient, we isolated acinetobacter the risk factor, and the possibility of this type of contamination related to the hospital, and it is not expected to be isolated from healthy non-hospitalized patients. It was shown recently that prolonged bile duct obstruction leads to an impaired intestinal wall barrier and as a result, bacteria can colonize bile easier, thus, it is not surprising that gram-negative enteric bacteria, especially *E. coli*, are the most common bacteria causing bactobilia in many studies including ours (13-18). In our study, imipenem and aminoglycosides, especially amikacin, were the most effective antibiotics. Third-generation cephalosporins such as ceftriaxone and ceftazidime, which have been reported to be effective in antibiotic prophylaxis, had good activity against only 50% of the isolates in this study (12, 18). Cefuroxime, a 2nd generation cephalosporins, had been reported to be less effective in prophylaxis than 3rd generation cephalosporins; however, it had better activity than 3rd generation cephalosporins in the present study. Oral gyrase inhibitor antibiotics such as Ciprofloxacin reported to be feasible and safe for perioperative antibiotic prophylaxis in LC in a randomized double-blinded clinical trial and had a good activity against isolated gram-negative bacteria in our study (12). Colistin was also effective on most of the isolates; however, it should be reserved for the treatment of nosocomial infections caused by multi-resistant gram-negative bacteria (19).

In conclusion, the overall rate of bactobilia and postoperative infectious complications following LC performed on the patients with uncomplicated symptomatic gallstone was low, and no correlation was found between bactobilia and postoperative infectious complications. The age was the sole risk factor for developing bactobilia in such patients.

**Table 1.** Several Variables Compared Among Patients with Uncomplicated Gallstone Underwent Laparoscopic Cholecystectomy Based on the Result of Bile Culture

Variable	All Patients (85)	Bile Culture Result		P Value
		Positive (7)	Negative (78)	
<b>Demographic data and comorbidities</b>				
Mean age, year;(SD)	43(15)	56 (19)	42 (14)	0.016
Female (%)	77 (91)	7 (100)	70 (90)	0.487
Obese (body mass index $\geq$ 30) (%) <sup>a</sup>	5 (6)	1 (17)	5 (83)	0.341
Overweight (body mass index= 25 - 29.9) (%) <sup>a</sup>	32 (42)	2 (6)	30 (94)	0.659
Smoking (%)	14 (16)	2 (14)	12 (86)	0.324
Diabetes mellitus (%)	16 (19)	1 (6)	15 (94)	0.607
Hypertension (%)	14 (16)	2 (14)	12 (86)	0.324
Hyperlipidemia (%)	18 (21)	2 (11)	16 (89)	0.460
Hypothyroidism (%)	9 (11)	1 (11)	8 (89)	0.557
Previous abdominal surgery (%)	54 (63)	5 (9)	42 (91)	0.496
Appendectomy (%)	5 (6)	1 (20)	4 (80)	0.356
Hemorrhoidectomy (%)	6 (7)	1 (17)	5 (83)	0.413
Tubal ligation (%)	12 (15)	3 (25)	9 (75)	0.069
Cesarean section (%)	26 (33)	1 (4)	25 (96)	0.414
Hysterectomy (%)	2 (3)	0 (0)	2 (100)	0.828
<b>Laboratory data</b>				
Hemoglobin level, mean, g/dL; (SD)	12.5 (1.4)	12.9 (0.8)	12.4 (1.4)	0.423
White blood cells/ $\mu$ L; (SD)	7912 (2003)	7800 (1927)	7923 (2023)	0.878
Aspartate aminotransferase, U/L; (SD)	69 (108)	20 (4)	38 (113)	0.692
Alanine aminotransferase, U/L; (SD)	69 (115)	14 (9)	45 (121)	0.527
Alkaline phosphatase, U/L; (SD)	218 (81)	119 (38)	220 (84)	0.552
Fasting blood sugar, mg/dL; (SD)	65 (30)	89 (6)	94 (31)	0.656
Hemoglobin level, mean, g/dL; (SD)	12.5 (1.4)	12.9 (0.8)	12.4 (1.4)	0.423
White blood cells/ $\mu$ L; (SD)	7912 (2003)	7800 (1927)	7923 (2023)	0.878
Aspartate aminotransferase, U/L; (SD)	69 (108)	20 (4)	38 (113)	0.692
<b>Postoperative infectious complications</b>				
Wound infection during 10 days (%)	8 (9.4)	1 (12.5)	7 (87.5)	0.513
Fever during 10 days (%)	9 (10.5)	2 (25.0)	7 (75.0)	0.129

<sup>a</sup>Data of 77 patients were available.

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## Footnote

**Conflict of Interest Disclosure Statement:** There is no conflict of interest.

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