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BILE INFECTION IN LOW RISK PATIENTS SUBJECTED TO ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY

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Abstract

In healthy individuals, the bile is usually sterile, however, in cases of cholecystolithiasis and/or choledocholithiasis, it could be colonized with bacteria (bactibilia) and may lead to surgical site infection after cholecystectomy. In our hospital, the local regimen is to use antibiotics prophylaxis only for patients with high-risk factors, while in case of low-risk patients, the antibiotics used as postoperative treatment; this local regimen has no demonstrated bacteriological or epidemiological basis.

The aim of this study is to determine the nature of bacteria in bile and their antimicrobial susceptibility in low-risk patients and the relationship between bactibilia and the presence of some predisposing factors as well as developing postoperative infectious complications.

This study was conducted in Al-shiffa General hospital, Basrah, Iraq from April 2018 to May 2019. Forty-three patients with uncomplicated symptomatic gallstones who were candidates for elective laparoscopic cholecystectomy and have no risk factors for infection were included in the study.

Under fully aseptic technique, a sterile laparoscopic needle connected to a sterile 10ml disposable syringe used to aspirate 5–7ml of bile from the fundus of gallbladder for culture and antibiotic sensitivity. In this study culture assessment of bile demonstrate that, 20 patients (46.51%) have infected bile; Klebsiella spp. 7(35%) and Pseudomonas spp. 7 (35%) are the most frequent causative agents. Factors like gender, age, duration of complaint and number of stones were found not significantly increase the risk of infection. Antibiotics sensitivity revealed maximum sensitivity to Meropenem (100%), Amikacin (90%) and less sensitivity to the most commonly used Ceftazidime. No cases of superficial or deep-seated surgical site infections were reported.

In conclusion, bile infection reported in a significant rate in low risk patients for infection subjected to elective laparoscopic cholecystectomy. Klebsiella spp. and Pseudomonas spp. are the most common isolate which shows high sensitivity to Meropenem and Amikacin and less sensitivity to third generation Cephalosporine; so we recommend the use of Amikacin as a prophylactic antibiotic instead of third generation Cephalosporine.

Keywords: *Bile infection, Cholecyctectomy, elective surgery, laparoscopy, low risk patients*

Introduction

In healthy individuals, the bile is usually sterile, however, in cases of cholecystolithiasis and/or choledocholithiasis, it could be colonized with bacteria (bactibilia)[1,2]. In symptomatic gallstone diseases, bactibilia has been reported in 20-46% of the patients who underwent cholecystectomy[3].

Bactibilia is a common finding in individuals at high risk(age >60 years, the presence of diabetes, acute colic within 30 days of operation, jaundice, acute cholecystitis, or cholangitis, non-functional gallbladder, and biliary prostheses). However, there is little data regarding the prevalence of bactibilia in

patients who underwent cholecystectomy due to uncomplicated cholecystolithiasis[4].

The most common cultured pathogens in the bile are the Gram-negative enteric aerobes such as Escherichia coli, Klebsiella species and Proteus species and the less common are Pseudomonas aeruginosa, Bacteroides fragilis and Enterococcus faecalis. The Gram-positive and anaerobic bacteria are uncommon pathogens and the viral and fungal infection are rare[5].

Bactibilia 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[6,7]. The rate of post-operative wound infection after elective cholecystectomy in uncomplicated symptomatic gallstone ranges from 2.3% to 20%[8-10].

Microbial resistance is a growing public health problem associated with increased morbidity and mortality. The inappropriate use of antibiotics is the principal cause of microbial resistance[11,12].

There are different guidelines in the literature on the correct use of antimicrobial prophylaxis in surgery. A recent meta-analysis of randomized controlled trials concluded prophylactic antibiotics does not prevent infections in low risk patients undergoing laparoscopic cholecystectomy, while the usefulness of prophylaxis in high risk patients remains uncertain[13].

In our hospital, the local regimen of preoperative and postoperative antibiotics treatment for patients undergoing elective laparoscopic cholecystectomy is to use antibiotics prophylaxis only for patients with high-risk factors, while in case of low-risk patients, the antibiotics used as postoperative treatment and in both cases, it will continue as a postoperative treatment for ten days. This local regimen has no demonstrated bacteriological or epidemiological basis regarding the specific bacterial predominance, its resistance or sensitivity. Therefore, the aim of this study was to determine the nature of bacteria in bile and their antimicrobial susceptibility in low-risk patients with uncomplicated symptomatic cholelithiasis who underwent elective laparoscopic cholecystectomy. We also studied the relationship between bactibilia and the presence of some predisposing factors (age groups less than 60 years, gender, number of gallstones and duration of complaint) as well as developing postoperative infectious complications.

Patients and Methods

This study was conducted in Al-shiffa General Hospital, Basrah, Iraq from April 2018 to May 2019 and was approved by a local ethical committee. Forty-three patients with uncomplicated symptomatic gallstones who are candidates for elective laparoscopic cholecystectomy and have no risk factors for infection were included in the study. All participants were provided with the particular details for their surgeries and informed consent was obtained from each patient.

Exclusion criteria included; patients at high risk for infection like those aged >60 years, history of diabetes, history of acute colic, patients with complicated cholecystolithiasis including obstruction of the biliary tract; choledocolithiasis, acute calculous cholecystitis, recent history of Endoscopic Retrograde Cholangiopancreaticography (ERCP) and patients with biliary prostheses. Patients with history of immunosuppressive diseases or the patients on immunosuppressive drugs including steroid and patients on antibiotics were also excluded.

The following data were recorded perioperatively: patients' demographics, history of associated medical diseases, drugs history, clinical diagnosis, duration of complaint, abdominal ultrasound findings, operative findings like presence of adhesion around gallbladder, the

results of bile cultures and antibiotic sensitivities and any postoperative infectious complications were also documented.

Technique of bile aspiration: All operations were performed under general anesthesia with standard 4 ports laparoscopic cholecystectomy procedure by the same surgical team. After Co_2 insufflation and visualization of gallbladder and under fully aseptic technique, a sterile autoclavable 35cm long 18-gauge laparoscopic needle connected to a sterile 10ml disposable syringe (figure 1) was introduced through the 5mm right subcostal laparoscopic port (figure 2) to aspirate 5–7ml of bile from the fundus of gallbladder (figure 3). The aspirated bile was injected directly to culture bottle containing broth solution (BacT/ALERT® FA Plus–bioMerieux Direct USA) (figure 4), which then transferred directly to the laboratory department in our hospital for culture and antibiotic sensitivity. In the laboratory; the culture bottles are used with the BacT/ALERT Microbial Detection System in qualitative procedures for recovery and detection of aerobic and facultative anaerobic microorganisms (bacteria and yeast).

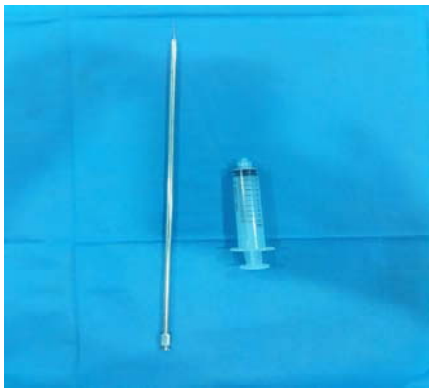

Fig.1: A sterile autoclavable 35cm long 18-gauge laparoscopic needle connected to a sterile 10ml disposable syringe

Fig.2: A needle introduced through the 5mm right subcostal laparoscopic port to aspirate 5–7ml of bile from gallbladder

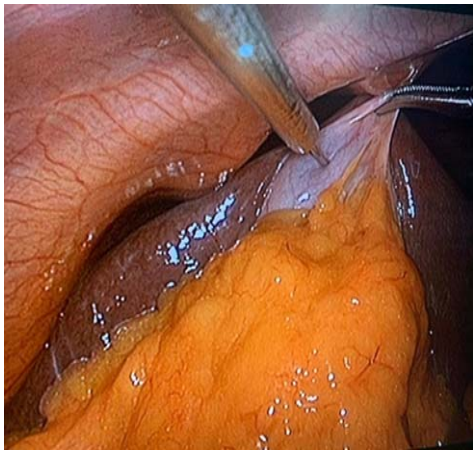

Fig.3: The needle was inserted in the fundus of the gall bladder for bile aspiration

Fig.4: The aspirated bile injected directly to Culture Bottle containing broth solution (BacT/ALERT® FA Plus–bioMerieux Direct USA)

At the end of the laparoscopic cholecystectomy, the gallbladder specimen was put in a retrieval endobag and extracted through the epigastric 10mm working port. The surgical field and the epigastric wound was washed with sterile normal saline if there is a bile leak from the site of aspiration in the gallbladder wall.

After recovery from anesthesia, the patients were transferred to the surgical ward for observation and follow-up. Injectable IV antibiotic was given in form of Ceftazidime 1g or Amikacin 500mg in case of penicillin allergy as a postoperative treatment, and treatment continues until the patients were discharged from the hospital when the vital signs were within normal range and could manage an oral diet. Instructions to continue oral antibiotics for 7 days were given. The patients were re-examined clinically and by abdominal ultrasound at the 10th postoperative day and then at the end of 4th week to detect any superficial or deep-seated surgical site infection.

Data were collected and statistically analyzed using Chi-square and Fisher exact tests using Koopman asymptomatic score and method of Katz to evaluate the relative risk ratio. Values with $p<0.05$ were significantly different. GraphPadPrism software for windows (version 7.0) was also used.

Results

In this study, most patients were females 36 (83.73%) and the remaining 7 (16.27%) were males as shown in fig.5.

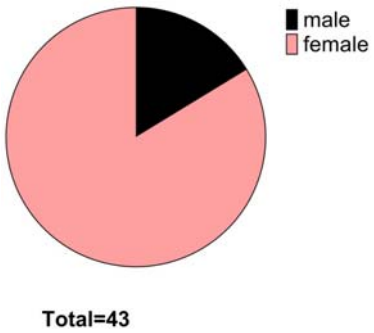

Figure 5: The gender distribution

In order to evaluate the rate of bactibilia in relation to different age groups, the patients were divided into three groups, group1 (20-34 years) included 16 patients (37.20%), group2 (35-49 years) included 21 patients (48.83%) and group3 (50-60 years) included 6 patients (13.95%) as shown in table I.

Culture assessment of bile demonstrated that; 20 (46.51%) patients had infected bile while 23 (53.48%) patients had sterile bile As shown in figure 6.

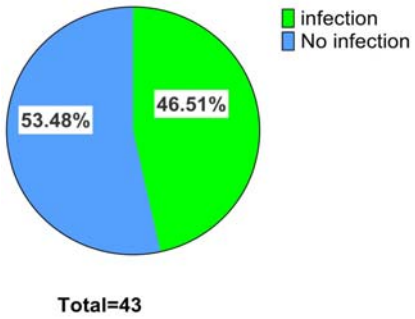

Figure 6: Percentage of infected bile

Regarding the types of found bacteria; Klebsiella spp. 7(35%) and Pseudomonas spp. 7 (35%) are the most frequent causative agents, while the less frequent causative agents were Staphylococcus spp.4(20%), Serratia marcescens 1(5%) and Raoultellaornithinolytica 1 (5%) as shown in figure 7.

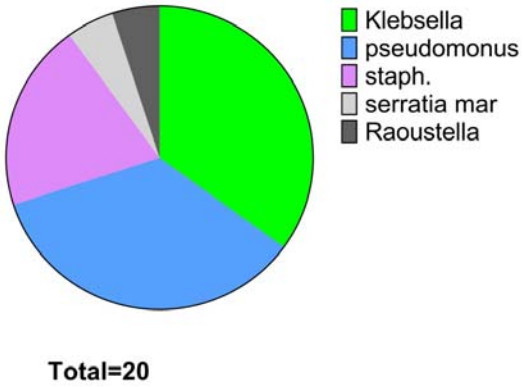

Figure 7: Types of bacteria that infect bile

The relationship between bactibilia (bile infection) and the presence of some predisposing factors are shown in table I. In this study no significant correlation was reported between gender and rate of bile infection (p-value 0.686), The relation between age groups and bile infection were also evaluated, in group 1 (20-34 years) 6 patients (13.95%) reported to have bile infection, in group 2 (35-49 years) 12 patient (27.90%) have bile infection and in group 3 (50–60 years) 6 patients, the rate of bile infection reported in 2 patients (4.65%). The statistical analysis of these results showed no statistical significance between these age groups and the rate of bile infection (p-value= 0.387).

In order to study the relation between duration of complaint of gallstone and the rate of bile infection, the duration was divided into three groups, group 1 (1-12 months) included 17 patients (39.53%), 9 of them (20.95%) have bile infection, group 2 (13-24 months) included 13 patients (30.23%), 7 of them (16.27%) have bile infection and group 3 (25-36 months) included 13 patients (30.23%), 4 of them (9.30%) have bile infection. The statistical analysis of these results showed no statistical significance as shown in table I.

Regarding the relation between the number of gallstones and the rate of bile infection, the ultrasound findings divided into two groups, group 1 (single stone) included 14 patients (32.55%), 7 of them (16.27%) have bile infection and group 2 (multiple stones) include 29 patients (67.44%), 13 of them (30.23%) have bile infection. The statistical analysis of these results showed no statistical significance between the number of gallstones and the rate of bile infection, (p-value= 0.745) as shown in table I.

Table I: Variable factors in relation to infection.

Variables		Number & %	infection	No infection	P-value
Gender	male	7(16.27%)	4(9.30%)	3(6.97%)	0.686
	female	36 (83.72%)	16(37.20%)	20 (46.51%)	
Age	(20-34) years	16 (37.20%)	6 (13.95%)	10 (23.25%)	0.387
	(35-49) years	21(48.83%)	12(27.90%)	9(20.93)	
	(50 – 60) years	6(13.95%)	2(4.65%)	4(9.30%)	
Duration of complaint	(1-12)months	17(39.53%)	9(20.95%)	8(18.60%)	0.394
	(13-24) months	13(30.23%)	7(16.27%)	6(13.95%)	
	(25-36)months	13(30.23%)	4(9.30%)	9(20.95%)	
Ultrasound findings; No. of stones	Single stone	14(32.55%)	7(16.27%)	7(16.27%)	0.750
	Multiple stones	29(67.44%)	13 (30.23%)	16 (37.20%)	

Regarding postoperative infectious complications, no cases of superficial or deep-seated surgical site infections were reported during the follow-up period.

In this study, the isolated bacteria showed high sensitivity to Meropenem and Amikacin 100% and 90% respectively, while Ceftazidime showed intermediate susceptibility 50%. The least sensitive one was Trimethoprim, Sulfamethoxazole was only sensitive in 20% of cases as shown in table II.

Table II: Antibiotics Susceptibility

Antibiotic	Susceptibility
Meropenem	100%
Amikacin	90%
Ciprofloxacin	70%
Cefepime	60%
Ceftazidime	50%
Gentamicin	50%
Piperacillin	50%
Ticarcillin	20%
Trimethoprim /Sulfamethoxazole	20%

Discussion

The rate of positive bile cultures differs significantly between different studies, ranging from 16% to 70%, this variation is believed to be due to the selection of patients that influenced by the presence of complications particularly cholecystitis, common bile duct disease, and cholangitis[14-16]. In this study we reported a similar rate of infected bile (46.51%).

Regarding the types of bacteria, Klebsiella spp. and pseudomonas spp., represent the most common isolated bacteria, this result is similar to the results published by Sahayam et al.[17] and Hazrah et al.[18], Whereas, most other studies reported that most common isolated organisms were E.Coli followed by either Klebsiella Spp. or Pseudomonas aeruginosa[19-22].

In our study, antibiotics sensitivity revealed maximum sensitivity to Meropenem (100%), Amikacin (90%) and Ciprofloxacin (70%). Intermediate sensitivity to Cefepime (60%), ceftazidime (50%), Gentamycin (50%), piperacillin (50%). low sensitivity to Ticarcillin and Trimethoprim, Sulfamethoxazole (20%). These results are similar to the results published by Ahmed et al.[23] and Sharma[24]. Other studies showed that high resistance to second generation Cephalosporins has increased while third and fourth generation Cephalosporins show a good promise against gram negative organisms which have high resistance to Ampicillins, Amoxicillin–clavulanic acid.[25-27]. In our results, the third generation Cephalosporins (ceftazidime) that was used as postoperative treatment showed intermediate susceptibility, so it is necessary to use another more effective antibiotic and because, Meropenem was preserved by local regimen for treatment of serious infections and not recommended for prophylaxis, so we recommended the use Amikacin which is the most effective antibiotic in our study after Meropenem.

Regarding surgical site infections, published studies reported an incidence ranging from 4% to 9%.[28-30]. In our study, no cases of superficial or deep-seated surgical site infections were reported, the absence of this complication may be due to effectiveness of postoperative antibiotic treatment that used in all cases or may be due to low risk patients.

Regarding the relationship between bile infection and the presence of some predisposing factors, published studies revealed that the risk of infected bile increases with increasing age (especially those with risk factors and those more than 60 years) and in female patients[31-33]. Our study reported different results that, age below 60 years, gender, number of gallstones and duration of complaint have no effect on the rate of bile infection, this difference may be due to relatively small sample of patients and may be due to exclusion of patients above 60 years.

Conclusion

Bile infection is reported in a significant rate in low risk patients subjected to elective laparoscopic cholecystectomy.

Klebsiella spp. and Pseudomonas spp. are the most common isolate which shows high sensitivity to Meropenem and Amikacin and less sensitivity to third generation Cephalosporine; so we recommend the use Amikacin as a prophylactic antibiotic instead of third generation of Cephalosporine.

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