ORIGINAL ARTICLE

BACTERIOLOGICAL PATTERNS AND ANTIBIOTIC SENSITIVITIES IN CALCULUS CHOLECYSTITIS

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Background: Calculus cholecystitis with its complications dominates the diseases of the biliary tract. There is an inherent difficulty in identifying patients having infected gall bladders who may have the risk of wound infection or gram negative septicaemia after cholecystectomy. This study was conducted to ascertain the bacteriological patterns and antibiotic sensitivities of bile in calculus cholecystitis patients presenting at a tertiary care hospital and formulate guidelines for prophylactic antibiotic therapy. **Methods:** This descriptive study was conducted in Combined Military Hospital, Rawalpindi from 20th Dec 2006 to 19th Sep 2008. A total number of 150 patients presenting at CMH Rawalpindi for elective cholecystectomy were included in the study. Prophylactic antibiotics were given after the induction of anaesthesia, 5 ml of bile was aspirated from their intact gall bladder was subjected to bacteriological examination at Armed Forces Institute of Pathology. A *pro forma* was designed to record all the information regarding isolated bacteria and their sensitivities to various antibiotics. Data was analyzed using SPSS-11. **Results:** Growth of bacteria was seen in 57 (38%) cases and no growth was seen in 93 (62%). Most common organism cultured was: *Pseudomonas aeruginosa* followed by *Escherichia coli (E. Coli)* and *Klebsiella pneumoniae*. The most effective antibiotic was Imipenem followed by Piperacillin-Tazobactum combination and Amikacin. **Conclusions:** Imipenem, Piperacillin-Tazobactum combination and Amikacin should be used for prophylaxis in cases of cholelithiasis undergoing elective cholecystectomy.

Keywords: Cholecystectomy, bile culture, cholelithiasis, prophylactic antibiotics

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INTRODUCTION

Cholecystitis and cholelithiasis with its complications dominate the disease of the biliary tract,[1] most common biliary tract disease being chronic calculus cholecystitis.[2] It is more common in females than in males[1] and more common in the age group of 40–49.[1,2] These diseases can cause severe infection or sepsis. In addition to surgical treatments, prompt administration of appropriate antibiotics is important to control the biliary tract infections.[3]

Gall bladder surgery is a common surgical procedure and the laparoscopic cholecystectomy became the method of choice in the treatment of cholelithiasis[4] showing a significant reduction in incisional complications in comparison with open surgery.[5]

Death of the patient is the ultimate disaster in any form of surgery, a rare event in the treatment of gallstones for which mortality rates less than 0.5% are published[6], morbidity being mainly due to septic complications in biliary surgery.

Antibiotic prophylaxis has been shown to markedly decrease the incidence of septic complications in biliary surgery, with the published rate ranging from 0–4%.[7] There is a difficulty in identifying patients having infected gall bladders.[8] Different radiological as well as biochemical parameters like gall stones, sludge, gall bladder wall thickness, peri-cholecystic fluid and raised white blood cell count are not predictive of infected bile.[8,9] Colonization of human biliary tracts with aerobic and anaerobic bacteria has been reported in 25–50% of patients cultured.[10] E. coli, Klebsiella, Pseudomonas and Staphylococcus are established in 75.85% of bacteriologic findings.[11,7] Bacteroides fragilis is the single most commonly isolated anaerobe.[10]

At present the use of prophylactic antibiotics in elective cholecystectomy is controversial.[12] Morbidity studies have confirmed that infective complications are most commonly due to organisms that have been cultured from the bile.[6] As it may not be possible to diagnose which patients have bactibilia by routine investigation, it is advisable to use prophylactic antibiotics to reduce the incidence of wound infection.[12–15]

Good surgical techniques and judicious use of prophylactic antibiotics seem to two major a positive bile culture and subsequent wound infection.[16] Secondly antibiotic therapy did not sterilize bile, but merely altered biliary bacteriology.[17] Major complications are usually related to technical pitfalls.[18]

Many studies also tried to demonstrate the relationship of various risk factors and possibility of bactibilia and concluded that in patients with no risk factors (56.9%) the incidence of a positive bacteriology was low and they should receive no antibiotic prophylaxis.

Patients with one risk factor had a 36% incidence of positive bacteriology and minimal pre-operative prophylaxis is recommended. Patients with two or more risk factors had a 77.6% incidence of positive bacteriology and full peri-operative prophylaxis is recommended.[19] The important risk factors identified are diabetes mellitus, colic episodes within 30 days before surgery[7] and patients who are elderly[19].

Antibiotic prophylaxis in elective surgery continues to be administered haphazardly.[20] Surgeons use different prophylactic antibiotic regimens to minimize post operative infectious complications. Ampicillin in combination with sulbactam, Aminoglycoside, Amikacin, Cefalexin, Ceftriaxone, Ofloxacin and Pefloxacin are recommended in premedication by various randomized trials.[11,21] Appropriate use of prophylactic antibiotics, as identified by culture and sensitivity patterns prevalent in that community, will help reduce post operative infective complication.[3]

The purpose of this study was to enable the surgeons in being rational and cost effective in prescribing prophylactic antibiotics in elective cholecystectomy and to define an antibiotic policy for patients of calculus cholecystitis undergoing elective cholecystectomy.

factors for lower incidence of septic complications after biliary tract surgery.[13] In contrast, many studies demonstrate that antibiotic prophylaxis is justified only in high risk patients[14] and in all other patients, antibiotic prophylaxis does not seem to affect the incidence of postoperative infective complications[14,15] and no correlation exists between

MATERIAL AND METHODS

This descriptive case-series study was carried out at Combined Military Hospital, Rawalpindi, which is a tertiary care hospital. The duration of the study was 21 months to gather a larger sample size of 150 cases of calculus cholecystitis undergoing elective Open or Laparoscopic cholecystectomy and a convenient (non-probability) sampling technique was used.

Research and ethics committee of the Combined Military Hospital, Rawalpindi permitted the study. Written informed consent was taken from all patients recruited in the study. A total number of 150 patients undergoing elective cholecystectomy, diagnosed to have calculus cholecystitis on ultrasonography, were included in the study and were admitted to the hospital.

Cases of acute cholecystitis and cholangitis, perforated gall bladder, empyema, choledocolethiasis and Calculus cholecystitis, diagnosed on the basis of history, physical examination, leukocytosis and ultrasonography were excluded from the study.

The patients were kept nil per orally for eight hours before surgery and prophylactic antibiotic was given after the induction of anaesthesia. Five ml of bile was aspirated from the intact gall bladders of the patients with a sterile disposable syringe and sent for bacteriological examination in Armed Forces Institute of Pathology. All the information regarding isolated bacteria and their sensitivities to various antibiotics were recorded on a *pro forma*.

Data was analysed using SPSS-11. Mean and standard deviation were calculated for quantitative variables like age, height and weight. Frequencies and percentages were calculated for categorical variables like gender, isolated bacteria and effective antibiotics.

RESULTS

A total of 150 cases were studied. There were 52 (34.7%) males and 98 (65.3%) females in the study group (male to female ratio 1:1.8) The mean age of the patients in the study group was 44.56±13.84 years. Mean height was 157.14±12.09 cm. Mean weight was 73.24±11.25 kg.

There was growth of bacteria in 57 (38%) of the cases but no growth was seen in 93 (62%). Types of growths are shown in table-1.

Pseudomonas aeruginosa was most commonly sensitive to Piperacillin-Tazobactum combination followed by Ipenem. Antibiotic sensitivity pattern against cultured organisms is shown in table-2.

The most effective antibiotic, against all the grown bacteria, was Imipenem. Overall antibiotic sensitivity against cultured organisms is shown in table-3.

Table-1: Growth frequencies of organisms in bile cultures (n=150)

Parameters	Frequency	Percentage
Growth of organisms	57	38.0
No growth	93	62.0
Pseudomonas aeruginosa	23	15.3
E. coli	14	9.3
Klebsiella pneumonia	12	8.0
Enterobacter agglomerans	6	4.0
Citrobacter freundii	6	4.0

Table-2: Antibiotic sensitivity pattern against the organisms cultured

Organisms Cultured	Antibiotic Tested	n	Sensitive Cases (%)
Pseudomonas aeruginosa	Piperacillin Tazobactum Combination	23	18 (78.3)
	Imipenem	23	15 (65.2)
	Amikacin	23	13 (56.5)
	Ceftazidime	23	12 (52.2)
	Cefoperazone Sulbectum Combination	23	11 (47.8)
	Enoxacin	23	8 (34.8)
	Gentamycin	23	4 (17.4)
E. coli	Imipenem	14	12 (85.7)
	Piperacillin Tazobactum Combination	14	12 (85.7)
	Amikacin	14	10 (71.4)
	Gentamycin	14	6 (42.9)
	Cefoperazone Sulbectum Combination	14	5 (35.7)
	Enoxacin	14	3 (21.4)
	Sparfloxacin	14	3 (21.4)
Klebsiella Pneumoniae	Imipenem	12	9 (75)
	Piperacillin Tazobactum Combination	12	8 (66.7)
	Cefoperazone Sulbectum Combination	12	4 (33.3)
	Sparfloxacin	12	2 (16.7)
	Gentamycin	12	1 (8.3)
	Enoxacin	12	1 (8.3)
	Amikacin	12	0 (0)
Enterobacter agglumerans	Imipenem	6	4 (66.7))
	Amikacin	6	3 (20)
	Enoxacin	6	3 (50)
	Gentamycin	6	3 (50)
	Piperacillin Tazobactum Combination	6	2 (50)
	Ciprofloxacin	6	2 (33.3)
	Sparfloxacin	6	1 (16.7)
Citrobacter ferrundii	Imipenem	6	5 (83.3)
	Piperacillin Tazobactum Combination	6	2 (33.3)
	Cefoperazone Sulbectum Combination	6	2 (33.3)
	Amikacin	6	1 (16.7)
	Enoxacin	6	1 (16.7)
	Gentamycin	6	0 (0)
	Sparfloxacin	6	0(0)

Table-3: Overall antibiotic sensitivity against all organisms cultured (n=57)

Antibiotics	Sensitive	Percentage of sensitivity
Imipenem	44	77.2
Piperacillin tazobactum ombination	36	63.2
Amikacin	24	42.1
Cefoperazone sulbectum combination	19	33.3
Gentamycin	17	29.8
Enoxacin	16	28.1
Ceftazidime	15	26.3
Ciprofloxacin	10	17.5
Sparfloxacin	10	17.5
Augmentin	8	14
Cotrimoxazole	8	14
Xonef	7	12.4
Meropenem	5	8.8
Vancomycin	4	7.0
Cefpirome	3	5.3
Ofloxacin	3	5.3
Teicoplanin	3	5.3
Ampicillin	2	3.5
Ceftriaxone	2	3.5
Doxycycline	2	3.5
Piperacillin	2	3.5
Tetracycline	2	3.5
Amoxycillin	1	1.8
Chloramphenicol	1	1.8
Cefotaxime	1	1.8
Minocyclin	1	1.8
Ceftizoxime	1	1.8

DISCUSSION

Acute and chronic cholecystitis is one of the commonest diseases of gastrointestinal tract and cholecystectomy is a commonly performed surgical procedure having a low morbidity and mortality rate. There is still risk of infective complications ranging from superficial surgical site infection to life threatening gram negative septicaemia. In this study an effort has been made to understand the bacteriological patterns of bile in patients undergoing surgery for calculus cholecystitis and to know sensitivity of various drugs effective against those microorganisms and to define an ideal antibiotic for prophylaxis in elective cholecystectomy.

Western figures in various studies showed that cholelithiasis is more common in females than in males[1] and a higher prevalence of gallstones has been observed in women in all age groups.[22] The Grepco study[23] found a female-to-male ratio of 2.9 between the ages of 30–39 years; the ratio narrowed to 1.6 between the ages of 40–49 years and 1.2 between the ages of 50–59 years. It was the same in our study where there were 52 (34.7%, n=150) males and 98 (65.3%) females in the study group (male to female ratio 1:1.8).

Age is a major risk factor for the gallstones. Gallstones are exceedingly rare in children except in the presence of haemolytic states. Many western studies have shown the age of 40 years appearing to represent the cut-off between relatively low and high rates of cholecystectomies. This observation was validated in the Sirmione study[24] in which the incidence between the ages of 40 and 69 years was four times higher than that in younger subjects. Ballal *et al* and Patnaik *et al* demonstrated cholelithiasis to be more common in the age group of 40–49.[1,2] In our study, the mean age of the patients was 44.56 years in consonance with various regional and international studies.

Obesity is a well established risk factor for the development of cholesterol gallstones, presumably due to enhanced cholesterol synthesis

and secretion.[25] The risk is particularly high in women[26], in those with morbid obesity[27], and in younger age groups in which a threefold increase in risk has been reported[24]. In our study the mean weight of the patients in the study group was 73.24 Kg (BMI=23.30).

Obesity was not a risk factor for gall stone disease as per results of our study. Our population in general is not obese. According to World Health Organisation statistics 2002, the average BMI of Pakistani male is 23.7 and that of female is 24.5. There may be gender or racial factors in our setup which predispose to gallstones other than obesity. These aspects, however, need further evaluation by performing prospective studies on a larger sample.

There was growth of bacteria in 38% of the cases. Csendes *et al* in his study described rates of positive bile cultures ranging from 22–46%.[28] Chang *et al* concluded in their study that positive rate of bile culture was 25% for uncomplicated gall bladder stones.[3] Delikaris *et al* demonstrated twenty-six per cent of the bile cultures to be positive.[29] Reiss *et al* concluded that the general incidence of positive bile cultures was 27%[30] while Den Hoed *et al* demonstrated it to be positive in 22%[31]. According to Sattar *et al*, out of 100, 36 patients had positive bile culture.[21] In our study, the positive culture rate is in comparison to various regional and international studies.

Chang *et al*, in their study observed that for gallstone diseases, the most common organisms cultured were Gram negative bacteria (74%), in which *Escherichia coli* (36%) and *Klebsiella* (15%) were most commonly found, followed by Gram positive (15%) bacteria such as *Enterococcus* (6%), *Staphylococcus* (3%) and *Streptococcus* (2%). *Bacteroides* (5%) and *Clostridium* (3%) were occasionally found anaerobes (9%).[3] Petakovic *et al* studying bacteriological patterns of bile in Croatia found that *E. coli*, *Klebsiella* and *Staphylococcus* were established in 75.85% of bacteriologic findings in their study, and all the rest in 24.15% which included *Citrobacter, Serratia, Enterobacter, Proteus* and *Pseudomonas*.[11]

Similar findings concluding *E. coli* as the major isolate were also noted by Tocchi *et al*[7], Ballal *et al*[1], Reiss *et al*[30], Den Hoed[31] *et al* and Lorenz *et al*[32] in their studies. *E. coli* followed by *Klebsiella* were also the most commonly cultured organisms in study conducted by Sattar *et al* but he also noticed *Pseudomonas* to be present in 16.66% of the organisms cultured.[21] In our study, out of the total 57 positive cultures, *Pseudomonas aeruginosa* was the most common organism, present in 23 cases (40%). *E. coli* was the second most common organism, growing in 14 cases (24.5%). *Klebsiella* was present in 12 (21%) of the cases, *Enterobacter agglumerans* in 6 (10.5%) and *Citrobacter freundii* in 6 (10.5%) of the cases. The reason of this changed pattern is uncertain but may be attributable to regional differences of commonly occurring pathogenic bacteria and to the abuse of antibiotics. This regional changed pathogenic pattern, to some extent, is also demonstrated by the study of Sattar *et al* conducted at Jinnah Postgraduate Medical Centre, Karachi.[21]

Chang *et al*, on the basis of culture sensitivity pattern in their study suggested Ampicillin in combination with Sulbactam and Aminoglycoside for empirical therapy.[3] Similar suggestions were made is the study by Lorenz *et al* documenting Amoxicillin plus Beta-lactamase inhibitors or Quinolones to be suitable antibiotics for the prophylaxis of biliary infections.[32] Petakovic *et al* suggested Amikacin, Cefalexin, Ceftriaxone, Ofloxacin and Pefloxacin in premedication for Cholecystectomy.[11] Lu *et al* described Imipenem and Aztreonam as the most effective antibiotic against various Billiary pathogens having sensitivity of 77.8% and 66.7% respectively.[33] Reiss *et al* found Gentamycin showing the highest sensitivity rate (91%).[30] Sattar *et al* concluded that most of the biliary organisms in their study were highly sensitive to the 2nd generation Cephalosporins and Quinolones.[21] In our study, the most effective antibiotic, against all the grown bacteria, was Imipenem (77.2%).

The second most effective antibiotic was Piperacillin-Tazobactum combination (63.2%). Amikacin was third most effective antibiotic (42.1%). Consensus about a single best antibiotic effective against most of biliary pathogens has yet not developed as evident from various regional and international studies cited above.

This disparity may be due to regional differences in pathogenic organisms and various drug regimens prevalent in different communities. In our study, *Pseudomonas* was the most commonly cultured organism, sensitive mostly to Piperacillin-Tazobactum combination followed by Imipenem, so these two agents should be considered for prophylaxis while performing cholecystectomy.

CONCLUSIONS

In our study *Pseudomonas* was cultured in most of the cases followed by *E coli* and *Klebsiella.* Due to this changed pattern, Imipenem, Piperacillin-Tazobactum combination and Amikacin turned out to be the most effective antibiotics against these organisms

RECOMENDATIONS

We recommend the use of Imipenem and Piperacillin-Tazobactum combination as first-line drugs for prophylaxis while performing cholecystectomy, especially in high risk cases.

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