# Topical Use of Gentamicin in Potentially Contaminated Laparoscopic Cholecystectomy After Bile Spillage During Gall Bladder Retrieval.

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## ABSTRACT

***Objective:*** To observe the effects of topical Gentamycin as a prophylactic measure to control post-operative port site infection after bile spillage during gall bladder retrieval in patients undergoing laparoscopic cholecystectomy.
***Study Design:*** Quasi-experimental study.
***Place and Duration of Study***: Pak-Emirates Military Hospital, Rawalpindi, from Feb to Aug 2019.
***Methodology:*** The study population comprised 80 patients (divided into two groups) diagnosed with cholelithiasis and underwent elective laparoscopic cholecystectomy. Seven surgeries were converted into open cholecystectomies, and bile spillage was recorded in 42 patients who underwent uneventful surgery. These patients were then examined for 30 days to evaluate port site infection.
***Results:*** It was seen that EPSI was more common in patients in the fourth decade of their life even after Gentamicin prophylaxis 6 (14.29%). A deeper analysis of the study showed that EPSI was more common in patients with Class-I obesity and their fourth decade of life. When compared to the gender, we found that the ratio of EPSI was higher in the female population (1:2) as compared to males (1:4).
***Conclusion:*** In our research, topical use of Gentamicin in potentially contaminated laparoscopic cholecystectomy after bile spillage during gall bladder retrieval proved beneficial.

**Keywords:** Bile spillage; Gentamicin; Laparoscopic cholecystectomy; Port site infection.

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## INTRODUCTION

Nosocomial infections or hospital-acquired infections (HAIs) are acquired in hospitals when a person is admitted for reasons other than the infection. One of the important types of nosocomial infections is Surgical site infections (SSIs), defined as a superficial or deep infection to the surgical site within 30 days of a surgical procedure. They are among the most common HAI, followed by catheter-associated urinary tract infections, ventilator-associated pneumonia and gastrointestinal infections.[1] It has been noted that seven out of one hundred patients in developed countries and ten out of a hundred patients in developing countries suffer from hospital-acquired infection, making it a common problem in the third world.[2] Post-operative SSIs can be pretty harmful and a less frequent cause of mortality but a significant source of morbidity. In Pakistan, the incidence of SSI is approximately 8.84% in their patients, while in developed countries like the United States (USA), it is only 1.9%.[3]

There are certain patient-dependent and surgery-related factors that predict the incidence of SSIs. In cholecystitis, the infection develops due to bile stasis, resulting in the contamination of the biliary system and may cause choledocholithiasis. In the community of surgeons, it was believed that bile spillage is a sterile condition, but now it is proven that bile spillage is a cause of surgical site infection.[4] The causes of SSIs are exposure to surgical wounds to microbes from the patient's skin, mucous membranes, or the hospital environment due to improper sterilization techniques.

Laparoscopic cholecystectomy (LC) has replaced the open technique for cholecystectomy worldwide for its benefits over the former. It is less invasive, associated with fewer complications like pain, fewer cosmetics problems, quick recovery, and a shorter hospitalization period, meaning an earlier return to normal daily activities. It is often considered protective against surgical site infections. This has reduced the economic burden on healthcare systems worldwide.[5,6] Conversely, like any other surgical procedure, there are complications associated with LC, most importantly, port site infection (PSI), post-operative abdominal pain, gall bladder perforation and bile spillage. PSI is one of the complications challenging the benefits of

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laparoscopic cholecystectomy, adding to the patient's morbidity and putting the reputation of the institution and surgeon at stake. The bile spillage and gall bladder perforation are accidental but also believed to occur due to the lesser experience of the surgeon.[7,8] It has been observed that bile spillage is so common in training institutes that it is almost documented in half of the patients undergoing laparoscopic cholecystectomy and is associated with SSI.[4]

Surgeons commonly use many improvised remedies as prophylaxis of PSI like irrigation, intraoperative or topical antibiotics. Once SSI is confirmed, wound assessment is very important in making further decisions about the patients' health. For this, Southampton Wound Assessment Scale can be used to evaluate and score the wound.[9] This scale enables surgical wound healing to be graded according to a defined criterion by giving every wound a numerical value and a more objective assessment. This wound grading system is shown in the Table-I.[10]

**Table-I: Southampton wound assessment scale.**

| Grade | Appearance | |
|---|---|---|
| 0 | Normal Healing | |
| I | Normal Healing with Mild Bruising or erythema | |
| | Ia | Some Bruising |
| | Ib | Considerable Bruising |
| | Ic | Mild Erythema |
| II | Erythema Plus Other Signs of Inflammation | |
| | IIa | At One Point |
| | IIb | Around Sutures |
| | IIc | Along Wound |
| | IId | Around Wound |
| III | Clear or Haemoserous Discharge | |
| | IIIa | At One Point Only (≤ 2cm) |
| | IIIb | Along Wound (>2 cm) |
| | IIIc | Large-Volume |
| | IIId | Prolonged (> 3 days) |
| IV | Pus | |
| | Iva | At One Point Only (≤ 2cm) |
| | IVb | Along Wound (>2 cm) |
| V | Deep or severe wound infection with or without tissue breakdown; hematoma requiring aspiration | |

The study aims to document the benefits of using topical antibiotics that can be a very cost-effective and applicable modality in preventing epigastric port site infections (EPSI) after bile spillage during gall bladder retrieval as the epigastric port is used for gall bladder retrieval in our setup. The importance of this study can be emphasized by the fact that there is no data available on this topic in developing countries like Pakistan.

## METHODOLOGY

This was a quasi-experimental study conducted at the Department of General Surgery, Pak-Emirates Military Hospital, Rawalpindi. For this study, after the approval of the Institutional Ethical Committee (Letter no. A/28/EC/43/19 dated 20th November 2019), data was collected from November 2019 to February 2020. A sample of 80 participants was calculated using WHO sample size calculator.[11]

**Inclusion Criteria:** Patients of age 18 to 60 years, who were diagnosed with cholelithiasis on abdominal ultrasonography were included in the study.

**Exclusion Criteria:** Patients suffering from any comorbid disease like diabetes mellitus, hypertension or ischemic heart disease, asthma or any chronic ailment were excluded from the study.

As per the standards, the patients were randomly divided into two groups of 40 individuals each by third-party randomization, and they were sent to two teams of surgeons. The distribution of patients was blinded, and the third person was randomly assigned to each participant. Out of the eighty surgeries carried out by the two teams, seven were converted to open cholecystectomy for complications. Moreover, out of the rest of 73 laparoscopic cholecystectomies, bile spillage was recorded in 42 subjects. Therefore, a total of 42 procedures of elective laparoscopy were followed from admission till the 30th post-operative day.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Mean and the standard deviation was computed for EPSI in both groups and age of the patients. Frequencies and percentages were computed for categorical variables such as gender and BMI.

## RESULTS

Forty-two patients met the inclusion criteria. The mean age of these patients was 42.00 ± 11.13 years (Range: 18-60 years), and most of the participants were from the fourth and sixth decade of their lives (23, 54.76%). 37(69.8%) individuals were females, and 5(9.4%) were males. The mean body mass index (BMI) was 27.06 ± 4.37kg/m2. Patients were examined on the 7th, 15th and 30th post-operative days and SSI were labelled on the clinical evaluation based on any signs like fever, chills, bad smell from wound, pain, and tenderness at the surgical site, pus or drainage, erythema, increase in temperature as compared to the surrounding skin.

24(57.10%) out of these 42 patients had prophylactic Gentamicin used at the port-site while the rest 18 did not get any topical medication. 13 patients (31.00%) out of 18 in the control group developed an infection at the epigastric port site, but none of 24 patients in the prophylactic Gentamicin group suffered from infection shown in Table-II.

**Table-II: Outcome of use of topical Gentamicin versus to antibiotic in contaminated Epigastric Port Site.**

| Complication During Surgery | Outcome n (%) | |
|---|---|---|
| | Epigastric Port Site Infection (EPSI) | Normal |
| Spillage (No Topical Antibiotic Used) | 13 (31.00) | 5 (11.90) |
| Spillage, Gentamicin | - | 24 (57.10) |

The wounds were graded according to the Southampton wound scoring system. According to this scale, the surgical site infection can be classified from grade-I to grade-V, i.e. from mild bruising to deep or severe wound infection. The results of the wound grading were shown in the Figure-1.

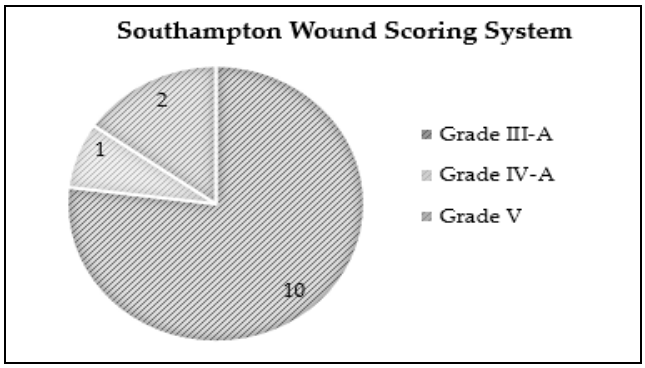


**Figure-1: Occurrence of Surgical site infections (SSI) in study population according to Southampton Wound Scoring System.**

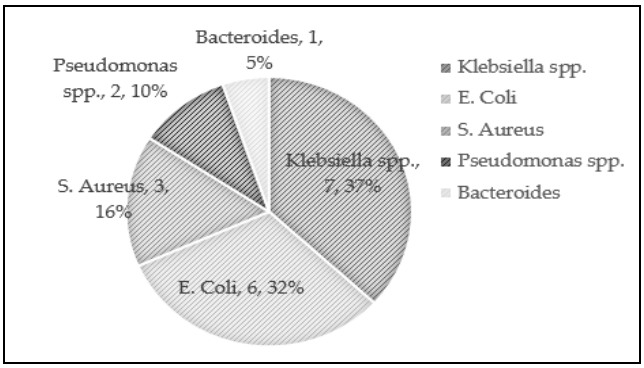


**Figure- 1: Percentage of different bacteria in pus culture.**

Two (15%) patients who were suffering from grade V-SSI were admitted to the hospital, and wound exploration in the operation theatre was done. Pus culture from 13 infected wounds was sent for culture, and sensitivity was done. The result showed Klebsiella spp. was present in 7(37%) samples, E. coli was present in 6(32%), S. Aureus in 3(16%), and Pseudomonas spp. in 2(10%), and Bacteroides were present in one sample. All the organisms were found sensitive to Gentamicin (Figure-2).

It was seen that EPSI was more common in patients in the fourth decade of their life even after Gentamicin prophylaxis, (6, 14.29%). A deeper analysis of the study showed that EPSI was more common in patients with class-I obesity and their fourth decade of life. When compared to the gender, we found that the ratio of EPSI was higher in the female population (1:2) as compared to males (1:4) shown in Table-III.

**Table-III: Evaluation of body mass index (BMI) as a factor effecting Surgical site infections (SSI).**

| Age Groups | BMI Groups | Outcome | | Total |
|---|---|---|---|---|
| | | Normal | EPSI | |
| 20-29 years | Normal Weight | 0 | 1 | 1 |
| | Class I Obesity | 1 | 1 | 2 |
| 30-39 years | Normal Weight | 1 | 1 | 2 |
| | Overweight | 0 | 1 | 1 |
| | Class I Obesity | 0 | 4 | 4 |
| 40-49 years | Normal Weight | 1 | 1 | 2 |
| | Overweight | 0 | 1 | 1 |
| 50-59 years | Normal Weight | 0 | 2 | 2 |
| | Overweight | 0 | 1 | 1 |
| | Class I Obesity | 2 | 0 | 2 |

## DISCUSSION

Laparoscopic cholecystectomy is the gold standard procedure for cholecystectomy. Compared to open cholecystectomy, it is safe, and there are chances of early recovery, but complications cannot be denied in any surgical procedure. Therefore, in laparoscopic cholecystectomy, along with other complications, there are chances of port-site infections, especially after the bile spillage during gall bladder retrieval through the epigastric port site. The topical use of antibiotics can prevent this complication, but it can reduce the hospital stay period and financial burden on the patient.

In Pakistan, the situation is even more serious because organisms develop resistance to many

antibiotic drugs. Although the surgeons take all the measures to prevent PSI, the incidence has not decreased to zero even after that. There is no consensus among the surgeons or guidelines present regarding topical antibiotics for the prevention of surgical site infection.[11]

With time the instruments used in LC have evolved, techniques have improved, and even the port size and the number of ports have reduced, making laparoscopy the gold standard for cholecystectomy. Compared to open cholecystectomy, laparoscopy has the edge of small scars, less pain, quick recovery, early discharge, and early activity. Besides, some serious complications are associated with laparoscopic cholecystectomy, including bile duct injury, bile leaks, bleeding, and bowel injury. In complicated cases, laparoscopic surgery is converted to open surgery if needed. The incidence rate of bile spillage in our study and its association with SSI is comparable to the study conducted by Peponis *et al*,.[4] The main reasons for such complications are on the part of patient selection, surgical inexperience, and the technical constraints inherent to the minimally invasive approach. These complications are unpredictable and can be prevented.

Moreover, the gall bladder perforation (GP) and spillage occur mainly due to inadequate experience of the surgeon, and the incidence of this complication decreases as the surgeon gains experience.[12] This can be related to our setting, a training institute with many surgeons undergoing training or having experience of just a few years. As it is a known fact that cholecystitis is more common in females, the same was found in our study. Warren *et al*,[13] conducted a comprehensive study and found a high prevalence of surgical site infection after laparoscopic cholecystectomy. However, surgical site infections or port site infections can be prevented. Thus, a major risk of morbidity can be reduced, and a hospital stay can be minimized. This will increase the efficacy of laparoscopic procedures.

PSI is caused by microbes from an endogenous source like skin flora, the flora of mucous membranes of viscera, or exogenous flora from contaminated sources present in the sterile surgical field.[14] Peponis *et al*,[4] have proved that bile spillage is a cause of surgical site infection, and it can be categorized under the endogenous source of SSI. They have documented in a study in which a large sample population was screened, and it was found that bile spillage is the source of surgical site infection. In our study, bile spillage was recorded in 42 subjects (54%). Therefore, in our case, potentially contaminated laparoscopic cholecystectomy after bile spillage during gall bladder retrieval has a fair chance of increased SSIs. The organisms like *E. coli, Klebsiella, Pseudomonas, S. Aureus, Salmonella,* and *Bacteroid fragilis* are often found in surgical site infection pus culture and are usually treated with 2nd generation cephalosporins and quinolones.[15]

It can be said that there is no consensus on the use of topical antibiotics for the prevention of surgical site infection, and limited data is available on PubMed regarding the association of bacteria in the gallbladder to the bacterial culture in the wound and risk factors for wound infection must be evaluated.[11] Many studies have been performed to see an association between bacterial culture from bile samples of the gall bladder and the bacterial culture of pus from SSI. In contrast to our study, a recent study conducted in India concluded with the insignificant association of a positive bile culture with the risk of surgical site infections after biliary tract surgery.[16] Though we did not take bile culture and compare it with the pus culture from SSI, we did focus on the prophylactic approach to prevent SSI after the incidence of bile spillage. Our study has also documented a higher incidence of SSI after bile spillage than clean surgery. Another study concluded that in patients with positive bile culture who develop surgical site infections, two-thirds of them are caused by different strains.[16] This means that port-site infections after laparoscopic cholecystectomy can be caused by contamination of both bile and surroundings and a wide range of microbes are responsible for them. Therefore, just using a prophylactic antibiotic against microorganisms present in bile cannot solve our problem.[17]

Surgeons use several modalities to prevent surgical site infections. For example, wound irrigation and skin preparation with antiseptics are also novel ways of preventing surgical site infection after the surgery.[18] A study conducted in Turkey by Sarkut *et al*,[19] also concluded that although surgical site infection is rare after elective laparoscopic cholecystectomy, intravenous antibiotic prophylaxis does not significantly affect the outcome. Moreover, according to them, after LC and bile spillage, we are left with few options like the use of topical antibiotics.

The use of topical Gentamicin is effective in preventing surgical site infections in many surgical procedures other than LC. In a meta-analysis by Lv *et*

*al*,[20] it was found that the use of Gentamicin as a topical prophylactic agent after colorectal surgery has significantly reduced the incidence of SSI. As pus culture had shown that all the organisms in our study samples were found sensitive to Gentamicin, so, it was a drug of choice in our setup. In a Cochrane database review by Heal *et al*,[21] it has been suggested that it is better to use a topical antibiotic as prophylactic to facilitate primary intention by reducing the risk of SSI compared to using no antibiotic. Compared to this study, our results are more specific to bile spillage in LC, which might be responsible for SSI. They have argued in their review that the process of primary healing must not be hampered by microbial contamination, and this risk can be well addressed by using topical antibiotics.

For patients undergoing surgery, the cost of medical procedures and hospital expenses in developing countries is crucial. On the other hand, the rapidly rising trend in antibiotic resistance is becoming a public health concern, especially in developing countries like Pakistan. Compared to other antibiotics, Gentamicin is cost-effective. It is readily available, and due to these reasons, it is the most effective and cheap solution for SSIs in potentially contaminated LC after bile spillage during gall bladder retrieval, as there was a significant relationship found between the clean wound and the use of Gentamicin ($p$<0.05) in our study.

We suggest using topical Gentamicin in patients at increased risk of developing port site infection due to contamination after laparoscopic cholecystectomy, which is an effective and cheaper measure to prevent port site infection.

## CONCLUSION

In our research, topical use of Gentamicin in potentially contaminated laparoscopic cholecystectomy after bile spillage during gall bladder retrieval proved beneficial.

**Conflict of Interest:** None.

**Author's Contribution:** AA:, ZH:, AJ: Conception, design, iterpretation and analysis of data, writing, FR:, TMS:, SI: interpretation and analysis of data, Writing.

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