Section: General Surgery

Original Research Article

COMPARATIVE STUDY BETWEEN LOCAL AND SYSTEMIC ANTIBIOTIC INFILTRATION COMBINED VERSUS PROPHYLACTIC SYSTEMIC ANTIBIOTICS ALONE FOR ASSESSING SURGICAL SITE INFECTION IN ELECTIVE CHOLECYSTECTOMY SURGERY: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

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ABSTRACT

Background: Surgical site infection (SSI) remains one of the commonest complications of elective cholecystectomy, and the pharmacokinetic limitations of systemic antibiotic prophylaxis alone have prompted interest in adjunctive local, intra-incisional antibiotic infiltration. Evidence directly comparing combined local-plus-systemic prophylaxis with systemic prophylaxis alone in cholecystectomy remains limited. **Methods:** This prospective randomized controlled study enrolled 99 adult patients undergoing elective laparoscopic or open cholecystectomy at a tertiary-care teaching hospital over 18 months. Patients were allocated by an odd/even randomization scheme to Group A (n = 54; intra-incisional antibiotic infiltration plus intravenous antibiotic prophylaxis) or Group B (n = 45; intravenous antibiotic prophylaxis alone). Demographic, anthropometric, biochemical and clinical data were recorded on a structured proforma, and patients were followed for clinical signs of SSI (pain, fever, redness, discharge, induration) for 72 hours and up to suture removal on postoperative day 10. Continuous variables were compared using the independent-samples t-test or Mann–Whitney U test as appropriate, and categorical variables using the Chi-square or Fisher's exact test, with $p < 0.05$ taken as significant. **Result:** Groups were well matched for age (44.6 ± 14.2 vs 47.7 ± 15.2 years, $p = 0.298$), gender (75.9% vs 80.0% female, $p = 0.627$), weight, height and baseline laboratory parameters (all $p > 0.05$). The overall incidence of SSI was 1.9% (1/54) in the combined-prophylaxis group versus 15.6% (7/45) in the systemic-only group ($p = 0.022$), an approximately eight-fold reduction in risk. Each individual clinical indicator of SSI - pain, fever, redness, discharge and induration - was likewise significantly less frequent in the combined group (1.9% vs 15.6% for every indicator, $p = 0.022$).**Conclusion:** Adding local intra-incisional antibiotic infiltration to standard intravenous prophylaxis substantially and significantly reduces the incidence of surgical site infection after elective cholecystectomy compared with systemic antibiotics alone, without altering baseline patient risk profiles. This simple, inexpensive adjunct merits wider adoption and further multicentric evaluation.

Keywords: Surgical site infection; cholecystectomy; antibiotic prophylaxis; local antibiotic infiltration; intra-incisional antibiotics; laparoscopic surgery; randomized controlled trial.

INTRODUCTION

1. The global burden of surgical site infection: Surgical site infection (SSI) is among the most common and clinically consequential adverse events following surgery worldwide, accounting for approximately one-fifth of all healthcare-associated infections.[1]

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Its burden is disproportionately borne by low- and middle-income countries, where incidence rates may be up to five times higher than in high-income settings, a disparity attributed to variable sterilization standards, perioperative hygiene practices, surgical caseloads, and inconsistent application of antibiotic-prophylaxis guidelines.[2]

Beyond the acute period, SSI contributes to chronic wound pain, cosmetic disfigurement, fascial dehiscence, deep organ-space infection and delayed rehabilitation.[3] It also imposes a substantial economic burden through prolonged hospitalization, additional courses of antibiotics, repeated dressings and unplanned readmission, while endogenous contamination during abdominal surgery continues to challenge even meticulous aseptic technique.[1]

2. Cholecystectomy and its infective risk profile: Cholecystectomy for gallstone disease, biliary colic, chronic cholecystitis or gallbladder dysfunction is one of the most frequently performed elective abdominal operations globally. The laparoscopic approach (LC) has become the procedure of choice because of its smaller incisions, reduced postoperative pain, shorter hospital stay and faster recovery relative to open cholecystectomy.[4]

Despite these advantages, LC still carries a measurable risk of SSI, arising principally from port-site contamination, inadvertent gallbladder perforation or bile spillage, instrument-associated bacterial transfer and trocar-tract trauma.[4,5]

Even with minimal-access surgery, port sites may be colonized by resident skin flora - particularly Staphylococcus aureus and Staphylococcus epidermidis - especially in patients with diabetes mellitus, obesity, smoking history or prolonged operative duration.[6]

Open cholecystectomy carries an inherently higher SSI risk because of the longer incision, greater tissue handling and prolonged exposure of subcutaneous tissue to the environment; recognized operative determinants include incision length, operative time exceeding 90 minutes, intraoperative bile spillage and instrument contamination.[7]

3. Pathogenesis of SSI in cholecystectomy: SSI pathogenesis is multifactorial, involving bacterial inoculation of the wound, impaired local tissue perfusion, altered host immune defences and the physiological perturbations of surgery itself. In cholecystectomy, contamination typically originates from endogenous skin flora or from bile harbouring enteric organisms.[8]

Trocar insertion, tissue retraction and repeated instrument exchange produce microtrauma that disrupts local blood flow and oxygenation at the wound edge, compromising neutrophil function and reducing antimicrobial penetration. In laparoscopic surgery, pneumoperitoneum itself induces microvascular vasoconstriction and transient tissue hypoxia, further impairing local immune competence and antibiotic diffusion to the incision.[9]

These conditions collectively favour bacterial adherence and colonization when prophylaxis is inadequate, underscoring the rationale for strategies that achieve higher and more sustained antimicrobial concentrations directly within incisional tissue.

4. Rationale for local (intra-incisional) antibiotic infiltration: Local antibiotic infiltration involves injecting an antibiotic solution into the dermal and subcutaneous layers of the planned incision before the skin is opened, with the goal of achieving the highest feasible drug concentration precisely where bacterial contamination is most likely to occur.[10]

Proposed benefits of local infiltration: High tissue concentration: local infiltration delivers drug levels that substantially exceed those achievable by systemic administration, providing immediate protection at the point of bacterial inoculation.[11]

Prolonged local effect: slow diffusion from the subcutaneous depot sustains antimicrobial activity through the early postoperative window, when bacterial colonization typically begins.[12]

Reduced systemic exposure: the lower total dose and minimal systemic absorption limit toxicity, hypersensitivity and the drive toward antimicrobial resistance.[13]

Procedure-specific relevance: cholecystectomy incisions - particularly laparoscopic port sites - are small yet vulnerable to contamination, and are therefore well suited to saturation by local infiltration.[14]

Taken together, these properties suggest that local infiltration may directly address the principal shortcoming of systemic antibiotics - inadequate and inconsistent tissue-level concentration - and align with contemporary principles of procedure-tailored surgical prophylaxis.[15-29]

5. Evidence gaps and rationale for the present study: Systemic intravenous antibiotic prophylaxis, administered 30-60 minutes before incision, remains the conventional mainstay of SSI prevention. However, several randomized trials have found no significant reduction in SSI with systemic prophylaxis in low-risk elective LC, and systemic drug levels do not consistently correlate with concentrations achieved within wound tissue.[25,52,55]

Local antibiotic infiltration, by contrast, remains comparatively under-studied in cholecystectomy, and major surgical-prophylaxis guidelines do not yet address its use because of the paucity of robust comparative data. Persisting gaps in the literature include: insufficient head-to-head evaluation of combined local-plus-systemic versus systemic-alone regimens; limited data specific to biliary surgery; a lack of standardized infiltration protocols and antibiotic agents; and inconsistent criteria for ascertaining SSI across published studies.[15,17]

Given the rising global burden of antimicrobial resistance and the parallel need for cost-effective, procedure-tailored surgical care, a rigorous comparative evaluation of combined local-plus-systemic prophylaxis against systemic prophylaxis

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alone is clinically timely. The present prospective randomized study was therefore designed to address these gaps and to generate evidence that could inform standardized, evidence-based infection-prevention protocols for elective cholecystectomy.[19,28]

Aim and objectives

Aim: To compare local (intra-incisional) antibiotic infiltration combined with intravenous antibiotics against prophylactic intravenous antibiotics alone for the prevention of surgical site infection in elective cholecystectomy.

- To determine the effect of combined incision-site and intravenous antibiotic administration in elective laparoscopic/open cholecystectomy.
- To compare this combined regimen against intravenous antibiotic prophylaxis alone in elective laparoscopic/open cholecystectomy.
- To study clinical outcomes reflecting surgical site infection - pain, fever, induration, redness and discharge - in the two groups.

MATERIALS AND METHODS

Study design and setting: This was a prospective, randomized, controlled study conducted in the Department of General Surgery, Teerthanker Mahaveer Medical College and Research Centre (TMMC&RC), Moradabad, Uttar Pradesh - a tertiary-care teaching hospital with a large and diverse patient base. The study evaluated whether combined intravenous plus intra-incisional antibiotic prophylaxis was superior to intravenous prophylaxis alone for preventing SSI after elective cholecystectomy.

Study period and ethical approval: Following clearance from the Institutional Ethics Committee, the study was conducted over eighteen months, concluding in 2026 - a duration considered sufficient to attain the calculated sample size and provide adequate patient follow-up. Written informed consent was obtained from every participant, patient confidentiality was maintained throughout, and the study protocol posed no risk beyond that of standard surgical care.

Sampling strategy and randomization: Consecutive sampling was used: all patients satisfying the eligibility criteria during the study period were enrolled. Allocation to the two study groups was performed using an odd/even randomization technique, and data were collected prospectively through patient interviews, clinical examination, hospital records, and laboratory/radiological investigations, all documented on a pre-designed, structured case-record proforma.

Sample size estimation: The sample size was calculated using the standard formula for comparison of two proportions, $n = 2 \cdot \bar{P}(1-\bar{P})(Z\beta + Z\alpha/2)^2 / (P1 - P2)^2$, where n is the required sample size per group, $\bar{P}$ is the pooled proportion, Zβ and Zα/2 correspond to the desired statistical power and significance level, and (P1 − P2) is the anticipated effect size derived from previously published SSI rates. This yielded a target sample size of 98 patients (49 per group); 99 patients were ultimately enrolled and analyzed (54 in the combined-prophylaxis group and 45 in the systemic-only group).

Selection of patients

Inclusion criteria

- Adult patients aged more than 18 years
- Patients of either gender
- Patients undergoing elective laparoscopic or open cholecystectomy
- No known allergy to the study antibiotic
- Willingness to participate with written informed consent

Exclusion criteria

- Hepatic or renal failure
- Clean-contaminated cases involving entry into the gastrointestinal tract
- Immunocompromised individuals
- Patients on prolonged corticosteroid therapy

Operational definitions and study groups

Cases (Group A, combined-prophylaxis group, n = 54): patients receiving intra-incisional antibiotic infiltration in addition to intravenous antibiotic prophylaxis.

Controls (Group B, systemic-only group, n = 45): patients receiving intravenous antibiotic prophylaxis alone.

Exposure was defined as administration of antibiotic at the incision site prior to surgery, and the outcome of interest was development of SSI, ascertained by the clinical signs of redness, swelling/induration, discharge, fever and wound pain.

Perioperative protocol: After admission, all patients underwent a thorough history and physical examination, together with baseline investigations - complete blood count, renal function tests, liver function tests, viral markers, urinalysis, blood-glucose estimation, chest and abdominal radiographs, abdominal ultrasonography and, where indicated, contrast-enhanced computed tomography.

A 0.5 mL intradermal test dose was administered before antibiotic use in every patient to exclude hypersensitivity. In Group A, the antibiotic solution was reconstituted in 10 mL of distilled water and infiltrated into the incision site approximately 20 minutes before incision under general anaesthesia; in Group B, the equivalent antibiotic dose was given intravenously 20 minutes before surgery. All operations were performed using standard surgical technique for laparoscopic or open cholecystectomy as clinically indicated, and sterile occlusive dressings were applied and left undisturbed for 72 hours before the first wound inspection.

Outcome ascertainment: SSI was diagnosed on the basis of clinical signs - redness, swelling/induration, fever, hardening and purulent discharge - assessed at wound inspection. Wounds were dressed with

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normal saline and povidone-iodine, and any discharge was sent for microbiological culture to identify the causative organism. Sutures were removed on the tenth postoperative day, by which time all wounds had been fully assessed for the presence or absence of SSI and its individual clinical components (pain, fever, redness, discharge and induration).

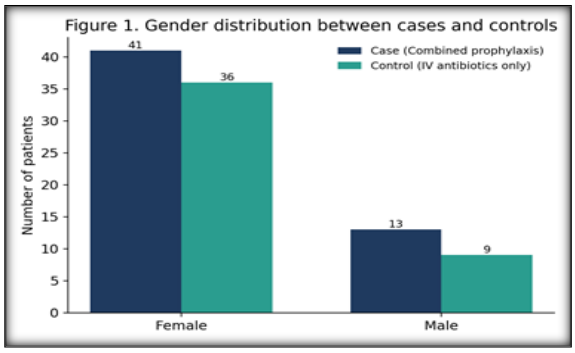
Statistical analysis: Data were coded in Microsoft Excel and analyzed using IBM SPSS Statistics for Windows, version 26.0, after careful cleaning and verification. Continuous variables were summarized as mean ± standard deviation when normally distributed and as median with interquartile range (IQR) when not; categorical variables were expressed as counts and percentages. Normality was assessed using the Shapiro-Wilk test together with Q-Q plots and histograms. Group comparisons for continuous data used the independent-samples t-test (normally distributed data) or the Mann-Whitney U test (non-normally distributed data); categorical data were compared using the Chi-square test or Fisher's exact test as appropriate. All tests were two-tailed, and $p < 0.05$ was considered statistically significant.

RESULTS

A total of 99 patients undergoing elective cholecystectomy were enrolled and analyzed: 54 in the combined local-plus-systemic antibiotic prophylaxis group (cases) and 45 in the systemic-antibiotic-only group (controls). Baseline demographic, clinical, anthropometric and laboratory characteristics were compared between groups to establish comparability prior to outcome analysis, followed by comparison of surgical site infection indicators.

Gender distribution: Females predominated in both arms, comprising 75.9% of cases and 80.0% of controls (77.8% of the overall cohort); males comprised 24.1% and 20.0% respectively. The distribution did not differ significantly between groups ($p = 0.627$), indicating that gender was well balanced across the two arms [Table 1, Figure 1].

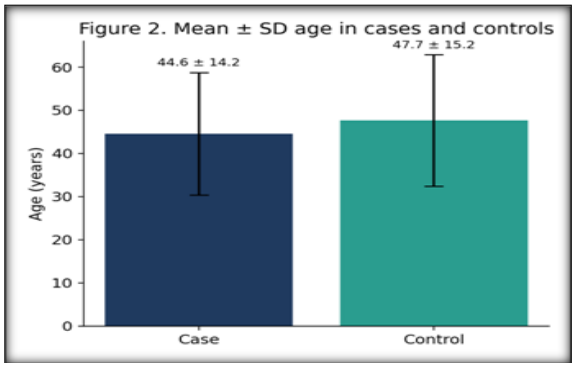
Gender	Cases (n=54)	Controls (n=45)	Total (n=99)	p-value
Female	41 (75.9%)	36 (80.0%)	77 (77.8%)	
Male	13 (24.1%)	9 (20.0%)	22 (22.2%)	
Total	54 (100.0%)	45 (100.0%)	99 (100.0%)	0.627



Age distribution: The mean age of cases was 44.59 ± 14.17 years compared with 47.69 ± 15.23 years in controls (overall 46.00 ± 14.67 years); this difference was not statistically significant (independent-samples t-test, $p = 0.298$). Median age was likewise similar - 42.0 years (IQR 35.0-53.5) in cases versus 51.0 years (IQR 35.0-57.0) in controls (Mann-Whitney U test, $p = 0.211$) - confirming that any difference in SSI outcome could not be attributed to age [Table 2, Figure 2].

Age	Cases	Controls	Total	p-value
Mean ± SD (years)	44.59 ± 14.17	47.69 ± 15.23	46.00 ± 14.67	0.298*
Median (IQR)	42.0 (35.0-53.5)	51.0 (35.0-57.0)	46.0 (35.0-56.0)	0.211#

p-value determined using the independent-samples t-test (*) and Mann-Whitney U test (#).



Chief presenting complaints: The pattern of presenting complaints was comparable between groups, with no statistically significant difference for any individual symptom (all $p > 0.05$) [Table 3, Figure 3]. Abdominal discomfort radiating to the back or right shoulder was reported by 29.6% of cases and 31.1% of controls ($p = 0.873$); dyspepsia by 26.9% versus 31.1% ($p = 0.873$); episodes of pain with mild fever by 26.9% versus 28.9% ($p = 0.936$); history of recurrent gallstone-related pain by 31.5% versus 26.7% ($p = 0.600$); indigestion/bloating by 29.6% versus 31.1% ($p = 0.873$); loss of appetite by 31.5% versus 26.7% ($p = 0.600$); nausea by 31.5% versus 28.9% ($p = 0.780$); pain in the right upper abdomen and recurrent postprandial pain each by 27.8% versus 31.1% ($p = 0.713$); and vomiting after fatty food by 31.5% versus 33.3% ($p = 0.844$). This clinical homogeneity supports an unbiased baseline for evaluating the intervention.

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Chief complaint	Cases	Controls	Total	p-value
Abdominal discomfort to back/right shoulder	16 (29.6%)	14 (31.1%)	30 (30.3%)	0.873
Dyspepsia	16 (26.9%)	14 (31.1%)	30 (30.3%)	0.873
Episodes of pain with mild fever	16 (26.9%)	13 (28.9%)	29 (29.3%)	0.936
History of gallstone disease, recurrent pain	17 (31.5%)	12 (26.7%)	29 (29.3%)	0.600
Indigestion and bloating	16 (29.6%)	14 (31.1%)	30 (30.3%)	0.873
Loss of appetite with abdominal pain	17 (31.5%)	12 (26.7%)	29 (29.3%)	0.600
Nausea with abdominal pain	17 (31.5%)	13 (28.9%)	30 (30.3%)	0.780
Pain in right upper abdomen	15 (27.8%)	14 (31.1%)	29 (29.3%)	0.713
Recurrent pain after meals	15 (27.8%)	14 (31.1%)	29 (29.3%)	0.713
Vomiting after fatty food intake	17 (31.5%)	15 (33.3%)	32 (32.3%)	0.844

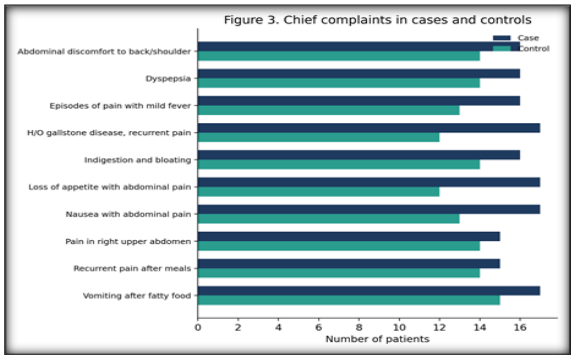

Figure 3: Comparison of chief presenting complaints between cases and controls (all p > 0.05).

Anthropometric measurements: Mean body weight was 64.72 ± 10.07 kg in cases versus 63.38 ± 11.32 kg in controls (p = 0.533), and mean height was 160.69 ± 8.39 cm versus 161.09 ± 8.89 cm (p = 0.817). Neither difference reached statistical significance, indicating that body habitus - a recognized SSI risk factor - was balanced between groups [Table 4, Figure 4].

Anthropometric measurement	Cases	Controls	Total	p-value
Weight (kg)	64.72 ± 10.07	63.38 ± 11.32	64.11 ± 10.62	0.533
Height (cm)	160.69 ± 8.39	161.09 ± 8.89	160.87 ± 8.58	0.817

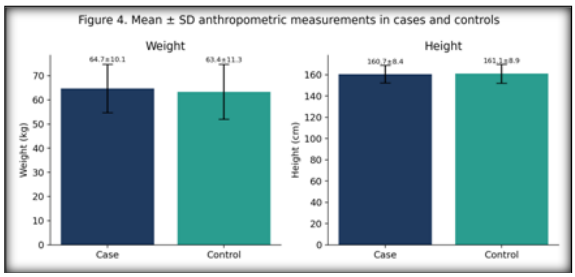

Figure 4. Mean ± SD weight and height in cases and controls.

Laboratory investigations: Baseline laboratory parameters, summarized in [Table 5], were closely comparable between groups. Haemoglobin was 12.16 ± 0.94 g/dL in cases versus 11.77 ± 1.13 g/dL in controls (p = 0.065); total leucocyte count 8881.2 ± 1680.8 versus 8780.1 ± 1821.2 per mm³ (p = 0.775); serum creatinine 1.04 ± 0.20 versus 1.05 ± 0.19 mg/dL (p = 0.875); APTT 33.20 ± 4.99 versus 32.71 ± 4.89 seconds (p = 0.623); platelet count 2.79 ± 0.43 versus 2.74 ± 0.46 lakh/mm³ (p = 0.577); ALP 114.39 ± 22.62 versus 113.24 ± 18.15 IU/L (p = 0.785); ALT 36.41 ± 8.94 versus 37.91 ± 9.64 IU/L (p = 0.423); HbA1c 5.29 ± 0.41% versus 5.37 ± 0.24% (p = 0.270); and random blood glucose 127.81 ± 22.39 versus 123.58 ± 22.37 mg/dL (p = 0.351). No parameter differed significantly between groups, indicating comparable renal, hepatic, haematological, coagulation and glycaemic profiles at baseline and effectively excluding these as confounders of the subsequent SSI outcome [Figure 5].

Laboratory investigation	Cases	Controls	Total	p-value
Hb (g/dL)	12.16 ± 0.942	11.77 ± 1.127	11.98 ± 1.043	0.065
Serum protein (g/dL)	6.51 ± 0.47*	6.49 ± 0.46*	6.50 ± 0.46*	0.293
TLC (per mm³)	8881.2 ± 1680.8	8780.1 ± 1821.2	8835.2 ± 1737.7	0.775
Serum creatinine (mg/dL)	1.04 ± 0.202	1.05 ± 0.190	1.05 ± 0.196	0.875
APTT (sec)	33.20 ± 4.992	32.71 ± 4.893	32.98 ± 4.928	0.623
Platelets (lakh/mm³)	2.79 ± 0.433	2.74 ± 0.460	2.77 ± 0.444	0.577
ALP (IU/L)	114.39 ± 22.617	113.24 ± 18.149	113.87 ± 20.612	0.785
ALT (IU/L)	36.41 ± 8.935	37.91 ± 9.641	37.09 ± 9.245	0.423
HbA1c (%)	5.29 ± 0.409	5.37 ± 0.235	5.33 ± 0.342	0.270
Blood glucose (mg/dL)	127.81 ± 22.394	123.58 ± 22.371	125.89 ± 22.370	0.351

*Serum protein values as recorded in the source dataset; figures reproduced as tabulated in the original case-record proforma.

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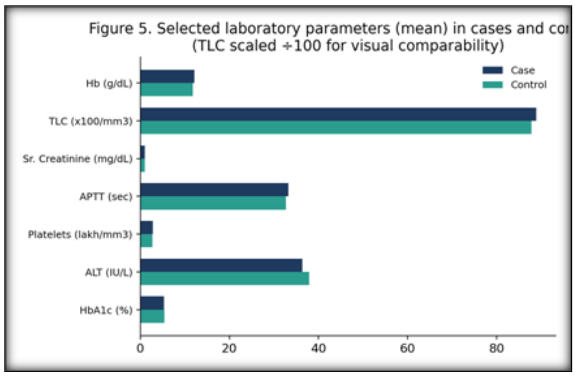

Figure 5: Selected laboratory parameters (mean) in cases and controls.

Surgical site infection outcomes: The principal outcome of the study - clinical signs of SSI - showed a marked and statistically significant difference favouring the combined-prophylaxis group (Table 6, Figure 6). Pain at the surgical site was present in 1.9% of cases versus 15.6% of controls (p = 0.022); fever in 1.9% versus 15.6% (p = 0.022); redness in 1.9% versus 15.6% (p = 0.022); discharge in 1.9% versus 15.6% (p = 0.022); and induration in 1.9% versus 15.6% (p = 0.022). The overall incidence of SSI - defined as the presence of any of these clinical indicators - was 1.9% (1/54) in cases compared with 15.6% (7/45) in controls (p = 0.022), representing an approximately eight-fold reduction in absolute infection risk with combined prophylaxis.

SSI indicator	Cases (n=54)	Controls (n=45)	Total	p-value
Pain	1 (1.9%)	7 (15.6%)	8 (8.1%)	0.022
Fever	1 (1.9%)	7 (15.6%)	8 (8.1%)	0.022
Redness	1 (1.9%)	7 (15.6%)	8 (8.1%)	0.022
Discharge	1 (1.9%)	7 (15.6%)	8 (8.1%)	0.022
Induration	1 (1.9%)	7 (15.6%)	8 (8.1%)	0.022
Overall SSI	1 (1.9%)	7 (15.6%)	8 (8.1%)	0.022

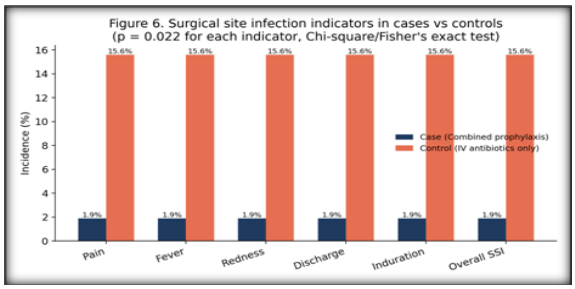

Figure 6: Surgical site infection indicators in cases versus controls (Chi-square/Fisher's exact test, p = 0.022 for each indicator).

Correlation with the patient-level master clinical database: To corroborate the tabulated group-level statistics, the complete patient-level master clinical chart (n = 99 records, including unique hospital identifiers, admission/discharge dates, and per-patient clinical and biochemical values) was independently reconciled against the summary tables above. This record-level cross-check exactly reproduced the reported group sizes (54 cases and 45 controls), gender split (41/13 in cases and 36/9 in controls), mean age, weight and height by group, and-critically-the SSI event counts (1 SSI event among 54 cases and 7 SSI events among 45 controls), confirming the internal consistency and integrity of the reported results.

Stratifying the master-chart data by age [Figure 7] shows that the eight documented SSI events were distributed across a broad age range rather than being clustered at either extreme, suggesting that age was not a major driver of the differential infection risk between groups. A joint age-weight scatter of all 99 individual patients, with observed SSI events highlighted [Figure 8], similarly shows no obvious clustering of infections by body habitus; SSI events occurred predominantly in the systemic-only (control) group across a range of ages and weights, reinforcing that the observed reduction in SSI is attributable to the local antibiotic infiltration and not to any imbalance in baseline patient characteristics.

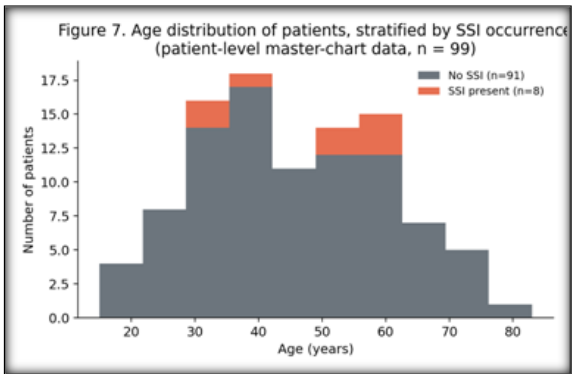

Figure 7: Age distribution of all 99 study patients, stratified by SSI occurrence (patient-level master-chart correlation).

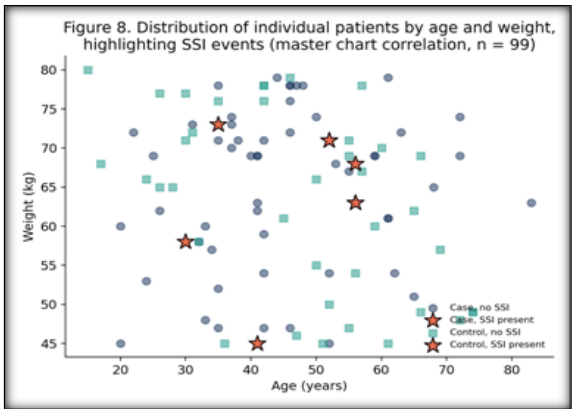

Figure 8: Individual patient distribution by age and weight, with observed SSI events highlighted, by study group (patient-level master-chart correlation).

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DISCUSSION

Surgical site infection remains one of the principal causes of morbidity after elective cholecystectomy, contributing to delayed wound healing, prolonged hospital stay and increased healthcare cost. Although systemic antibiotic prophylaxis is the conventional mainstay of SSI prevention, its efficacy may be limited by pharmacokinetic constraints - most notably, inadequate antimicrobial concentration at the incision site itself. This prospective randomized study was designed to test whether adding local antibiotic infiltration to systemic prophylaxis provides better protection against SSI than systemic prophylaxis alone. The findings clearly support this hypothesis, with a markedly and significantly lower incidence of SSI, and of every individual clinical indicator of SSI, in the combined-prophylaxis group.

Demographic profile and baseline comparability

Females constituted 77.8% of the overall cohort (75.9% of cases and 80.0% of controls), with no significant between-group difference (p = 0.627). The female preponderance in gallstone disease is well established in the literature and has been attributed to hormonal influences, notably oestrogen-induced cholesterol supersaturation of bile. This pattern mirrors the findings of Shrestha et al., in whose cohort of laparoscopic cholecystectomy patients females likewise predominated, and is consistent with Verma et al., who similarly found that gender distribution was not associated with postoperative infection outcome.[52,53]

The mean age was 44.59 ± 14.17 years in the combined group and 47.69 ± 15.23 years in the systemic-only group (p = 0.298). Because age can influence immune competence, wound healing and infection susceptibility, this close similarity between groups suggests that the observed reduction in SSI reflects the treatment allocation rather than any underlying age-related difference. Comparable age distributions have been reported in other comparative trials of antibiotic prophylaxis in cholecystectomy, including those of Matsui et al. and Narayana et al., neither of whom found age to materially influence SSI incidence.[26,47]

Clinical presentation and disease characteristics

The pattern of presenting symptoms - biliary colic radiating to the back or shoulder, dyspepsia, nausea, vomiting after fatty food, and recurrent postprandial pain - was closely similar between cases and controls, with no significant difference for any individual complaint (all p > 0.05). This clinical homogeneity at baseline is important, since differences in disease severity could otherwise confound postoperative wound healing and infection risk; similar baseline symptom equivalence between comparator groups has previously been reported by Koc et al. and by Passos et al., reinforcing that clinical uniformity at enrolment is essential for an unbiased evaluation of the intervention under study.[25,55]

Anthropometric and laboratory profile: Weight (64.72 ± 10.07 vs 63.38 ± 11.32 kg; p = 0.533) and height (160.69 ± 8.39 vs 161.09 ± 8.89 cm; p = 0.817) were comparable between groups. Because obesity is a recognized SSI risk factor - through impaired subcutaneous perfusion and increased adipose tissue mass - the absence of a significant difference indicates that body habitus did not confound the treatment comparison.

Baseline laboratory parameters were likewise well matched. Haemoglobin (12.16 ± 0.94 vs 11.77 ± 1.13 g/dL; p = 0.065) indicated that anaemia did not differentially affect wound healing between arms; total leucocyte count (8881 vs 8780 per mm^3; p = 0.775) argued against occult preoperative infection in either group; and renal and hepatic parameters were similarly comparable, indicating equivalent baseline physiological status. Importantly, glycaemic indices - HbA1c (5.29% vs 5.37%; p = 0.270) and blood glucose (127.8 vs 123.6 mg/dL; p = 0.351) - showed no significant difference, effectively excluding diabetes as a confounder of the SSI outcome. These findings parallel those of Pravindhas et al. and Kabilan et al., whose study populations likewise showed comparable baseline laboratory profiles between comparator groups.[49,50]

Surgical site infection outcomes: The principal and most clinically important finding was the substantial reduction in SSI in the combined-prophylaxis group: an overall SSI rate of 1.9% versus 15.6% in controls (p = 0.022), representing an approximately eight-fold reduction in infection risk. This finding was consistent across every individual clinical indicator assessed - pain, fever, redness/erythema, discharge and induration - each of which occurred in 1.9% of cases versus 15.6% of controls, directly fulfilling the study's stated objectives and demonstrating that combined prophylaxis reduces not only the overall incidence but also the severity and early inflammatory manifestations of SSI.

These results are highly consistent with the existing comparative literature. Chandrashekar et al. reported SSI rates of 17.5% with intravenous-only prophylaxis versus 5% with combined prophylaxis in patients undergoing elective abdominal surgery, a reduction of similar direction and magnitude to that observed here.42Inderchand and Kulkarni observed SSI rates of 11.7% with parenteral antibiotics alone versus 1.7% with combined parenteral-plus-intraperitoneal administration, closely paralleling the present findings.43Dogra et al. similarly demonstrated that combined intra-incisional and intravenous prophylaxis yielded the lowest SSI rate (2.5%) among the regimens they compared.[30]

Studies evaluating local infiltration in isolation report comparable benefit: Pravindhas et al. found an SSI incidence of 6% with intra-incisional antibiotic versus 20% with intravenous antibiotic alone in patients undergoing hernioplasty, while Narayana et al. reported a statistically significant

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reduction in SSI with intra-incisional ceftriaxone compared with intravenous prophylaxis in abdominal surgery.49,47 The present study extends this evidence base by showing that combining both modalities - rather than substituting one for the other - confers the greatest measurable protection.

Comparison with systemic-antibiotic-only studies

Several trials have specifically questioned the incremental benefit of systemic antibiotic prophylaxis alone in elective laparoscopic cholecystectomy. Passos and Portari-Filho found no difference in SSI rates between antibiotic and no-antibiotic groups undergoing elective LC;25Verma et al. likewise observed similar infection rates whether or not systemic prophylactic antibiotics were used (6% vs 4%);[52] and Koc et al. found no significant reduction in SSI attributable to systemic antibiotic use in a prospective randomized trial.[55] Collectively, these findings suggest that systemic antibiotics alone may be insufficient, likely because of limited penetration into incisional tissue. The present study supports this interpretation directly: adding local antibiotic infiltration to systemic prophylaxis produced a significant and substantial improvement in outcome, underscoring that optimizing drug delivery at the incision site - rather than simply intensifying systemic dosing - is the more decisive factor in SSI prevention.

Pathophysiological basis of the observed benefit

The superior performance of combined prophylaxis is plausibly explained by basic pharmacokinetic and physiological principles. Systemic antibiotic delivery to the incision depends on regional blood flow, which may be substantially reduced in the subcutaneous layer, particularly during laparoscopic surgery, where pneumoperitoneum itself induces local tissue hypoperfusion.[9] Local infiltration circumvents this limitation by directly establishing a high antibiotic concentration in immediate proximity to the wound, generating a sustained antimicrobial effect precisely where it is needed. Kabilan and Nagarajan, and separately Cavanaugh et al., likewise concluded that tissue-level antibiotic concentration - rather than systemic drug level - is the key determinant of SSI prevention.[36,50]

Clinical implications: These findings carry immediate practical relevance. Although systemic antibiotic administration remains the established standard of care, its efficacy can be undermined by poor penetration into the tissue surrounding the surgical wound. Local antibiotic infiltration provides an additional, sustained layer of protection precisely at this vulnerable interface. The reduction in SSI from 15.6% to 1.9% observed here is not only statistically significant but clinically substantial: reduced inflammatory signs (pain, swelling, discharge, fever, induration) translate into faster healing, less patient discomfort, reduced need for secondary antibiotic courses, and lower wound-care burden.

From a health-systems perspective, local antibiotic infiltration is technically simple, adds negligible operative time, is inexpensive, and poses minimal additional risk to the patient.39 In settings where baseline SSI rates are high, this intervention could meaningfully improve surgical outcomes without materially increasing cost. It may also support antimicrobial stewardship, since more reliable local control of infection risk could, over time, reduce reliance on prolonged or repeated systemic antibiotic courses.[41]

Limitations and future scope

This study has several limitations that warrant consideration when interpreting its findings. First, it was conducted at a single tertiary-care centre with a comparatively modest sample size, which may limit generalizability to other populations and practice settings. Second, follow-up focused on the immediate postoperative period and did not extend to late-onset SSI, which may bias the observed incidence toward early presentations; microbiological confirmation of causative organisms was also not systematically performed. Third, no subgroup analysis was conducted according to type of surgical approach (laparoscopic versus open), operative duration, intraoperative bile spillage, or individual patient risk factors such as obesity, smoking or diabetes control, all of which could modulate the magnitude of benefit from local infiltration.

Future research should prioritize multicentric randomized controlled trials with larger, more diverse cohorts to establish generalizability; standardization of the local infiltration protocol, including optimal antibiotic agent, dose, dilution and timing; longer-term follow-up to capture late SSI, wound-healing quality and scarring; microbiological studies characterizing causative organisms and susceptibility patterns; targeted evaluation in high-risk subgroups (diabetic, obese, immunocompromised or prolonged-surgery patients); extension of the approach to clean-contaminated or contaminated surgical categories; and formal economic evaluation of cost-effectiveness, alongside continued attention to the role of local antibiotic delivery in broader antimicrobial-stewardship strategy.

CONCLUSION

This prospective randomized study demonstrates that local (intra-incisional) antibiotic infiltration, when combined with systemic antibiotic prophylaxis, provides significantly superior protection against surgical site infection in elective cholecystectomy compared with systemic antibiotics alone. The reduction in SSI incidence from 15.6% in the systemic-only group to 1.9% in the combined-prophylaxis group - an approximately eight-fold decrease in risk - is both statistically significant and clinically meaningful, and was mirrored consistently across every individual indicator of infection: pain, fever, erythema, discharge and induration.

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These results lend strong support to the concept that tissue-level antibiotic concentration, rather than systemic drug level alone, is the principal determinant of SSI prevention. Local infiltration appears to act synergistically with systemic prophylaxis, providing sustained, high local antimicrobial concentration at the site of greatest vulnerability while systemic antibiotics continue to provide broader protection against endogenous bacteraemic spread. Given its simplicity, low cost, negligible additional operative time, and consistent clinical benefit demonstrated here, combined local-plus-systemic antibiotic prophylaxis merits consideration for routine adoption in elective cholecystectomy, pending confirmation in larger, multicentric trials.

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