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RESEARCH ARTICLE
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EVALUATION OF THE COMPARATIVE EFFECTIVENESS OF VARIOUS ANTIBIOTIC PROPHYLAXIS PROTOCOLS IN REDUCING POSTOPERATIVE SURGICAL SITE INFECTIONS IN TYPHOID ILEAL PERFORATION SURGERIES

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ABSTRACT

Background: Typhoid ileal perforation is a severe complication requiring prompt surgical intervention, often accompanied by the risk of postoperative surgical site infections (SSIs). Antibiotic prophylaxis is critical in preventing SSIs, but the optimal regimen for such surgeries remains debated.
Objective: This study aimed to evaluate the comparative effectiveness of three antibiotic prophylaxis protocols—Ceftriaxone (Protocol A), Ceftriaxone + Metronidazole (Protocol B), and Piperacillin-Tazobactam (Protocol C)—in reducing the incidence of SSIs following typhoid ileal perforation surgeries.
Materials and Methods: A cross-sectional study was conducted over six months at the Department of General Surgery, People's University of Medical & Health Sciences, Shaheed Benazirabad, involving 180 patients aged 18 years and older. Patients with known allergies to the antibiotics, chronic infections, or prior abdominal surgeries were excluded. Data were collected through structured questionnaires, capturing demographic information, clinical parameters, antibiotic protocols used, and postoperative outcomes. The incidence of SSIs served as the primary outcome measure. Data were analyzed using Microsoft Excel 2016 and SPSS v21.0, with chi-square tests and logistic regression used to assess statistical significance ($p < 0.05$).

Results: The study included 120 males (66.7%) and 60 females (33.3%). Protocol B (Ceftriaxone + Metronidazole) demonstrated the lowest SSI rate (16.7%), followed by Protocol C (Piperacillin-Tazobactam) with 16.7%. Protocol A (Ceftriaxone) had the highest SSI rate (33.3%), with a statistically significant association ($p = 0.04$) compared to Protocol B. No significant differences were found between Protocols B and C. Logistic regression revealed that patients receiving Protocol A were 2.5 times more likely to develop SSIs than those on Protocol B (OR = 2.5, $p = 0.03$). Age, gender, and comorbidities showed no significant association with SSIs ($p > 0.05$).
Conclusion: This study highlights the superior effectiveness of combination therapy with Ceftriaxone and Metronidazole (Protocol B) in preventing SSIs compared to Ceftriaxone monotherapy. While Piperacillin-Tazobactam (Protocol C) performed comparably to Protocol B, broader-spectrum antibiotics may not offer a distinct advantage in regions with low resistance.

Keywords: Typhoid ileal perforation, surgical site infections, antibiotic prophylaxis, Ceftriaxone, Metronidazole, Piperacillin-Tazobactam, gastrointestinal surgery.

INTRODUCTION

Surgical site infections (SSIs) are among the most common complications following abdominal surgeries, posing significant challenges for patient recovery, healthcare systems, and medical professionals alike.[1] Infections at the surgical site can lead to extended hospital stays, increased medical costs, higher rates of morbidity, and, in severe cases, mortality. A particular area of concern is gastrointestinal surgeries, where exposure to contaminated contents, such as bowel perforations, increases the likelihood of SSIs.[2] Among these, typhoid ileal perforation—a life-threatening complication of typhoid fever caused by *Salmonella typhi*—poses unique risks and management challenges. The choice of appropriate perioperative antibiotic prophylaxis is critical to minimizing the incidence of SSIs, especially in resource-limited healthcare settings.[3]

Typhoid fever remains endemic in many low- and middle-income countries, including Pakistan, due to factors such as poor sanitation, unclean drinking water, and limited access to healthcare.[4] A severe complication of untreated or poorly managed typhoid fever is ileal perforation, requiring emergency surgical intervention to repair the damaged bowel segment. However, these surgeries carry a high risk of bacterial contamination due to intestinal leakage, making patients highly susceptible to infections.[5]

The use of antibiotic prophylaxis in such cases is intended to reduce bacterial load and prevent SSIs, but there is no universal consensus on the most effective prophylactic protocol.[6] Clinicians have employed various antibiotic regimens, including first- and second-generation cephalosporins, metronidazole, aminoglycosides, and combinations thereof, with varying degrees of success.[7] Despite numerous studies exploring SSI prevention strategies, limited research exists specifically focusing on typhoid ileal perforation, a condition that requires careful selection of antibiotic regimens due to the presence of both gram-negative and anaerobic bacteria.[8]

Inconsistent adherence to evidence-based antibiotic protocols and the indiscriminate use of broad-spectrum antibiotics can also contribute to increased antibiotic resistance, an escalating public health concern.[9] Thus, determining the comparative effectiveness of different antibiotic regimens is crucial, not only to optimize patient outcomes but also to ensure rational antibiotic use. This research focuses on identifying the most effective antibiotic prophylaxis protocols in reducing postoperative SSIs following typhoid ileal perforation surgeries.

Given the high morbidity associated with SSIs in typhoid ileal perforation surgeries and the lack of standardization in prophylactic antibiotic protocols, this study aims to fill an important gap in the existing literature. The findings will help guide surgeons and healthcare providers toward evidence-based antibiotic practices that optimize postoperative outcomes while mitigating the risks of antibiotic resistance.

MATERIAL AND METHODS

This study was conducted in the Department of General Surgery at People's University of Medical & Health Sciences, Shaheed Benazirabad, over a six-month period from 1st January 2024 to 30th June 2024. The research utilized a cross-sectional design with a sample size of 180 cases, selected through non-probability, consecutive sampling.

A total of 180 patients diagnosed with typhoid ileal perforation were included based on the predefined inclusion criteria, which comprised patients aged 18 years and older undergoing surgery for typhoid ileal perforation. Patients with known allergies to the antibiotics used in the study, those with chronic infections, and patients who had undergone previous abdominal surgeries were excluded. Data collection was performed through a structured questionnaire, which included demographic information, clinical parameters, details of antibiotic prophylaxis protocols Protocol A (Ceftriaxone), Protocol B (Ceftriaxone + Metronidazole), Protocol C (Piperacillin-Tazobactam), and postoperative outcomes, focusing primarily on the incidence of surgical site infections (SSIs). Ethical permission was obtained from the Institutional Review Board at People's University of Medical & Health Sciences, Shaheed Benazirabad, ensuring adherence to ethical standards in conducting research involving human subjects.

Data Analysis Procedure

Data was analyzed using Microsoft Excel 2016 and SPSS v. 21.0, employing descriptive statistics to summarize the data and inferential statistics, such as chi-square tests and logistic regression, to evaluate the association between antibiotic prophylaxis protocols and the occurrence of SSIs, with a significance level set at $p < 0.05$.

RESULTS

A total of 180 patients were included. The age distribution of the participants revealed that 45 patients (25.0%) were between 18 and 30 years, 70 patients (38.9%) were aged 31 to 45 years, and 65 patients (36.1%) were older than 45 years.

Regarding gender, the majority of the participants were male, with 120 patients (66.7%), while 60 patients (33.3%) were female.

When assessing comorbidities, 120 patients (66.7%) had no underlying health conditions. However, 30 patients (16.7%) had diabetes, 20 patients (11.1%) had hypertension, and 10 patients (5.5%) reported other comorbidities. Table 1

Of the total samples, Protocol A (Ceftriaxone) was implemented in 60 patients, constituting 33.3% of the total sample. Protocol B (a combination of Ceftriaxone and Metronidazole) was the most frequently used, covering 70 patients, accounting for 38.9% of the cohort. Protocol C (Piperacillin-Tazobactam) was applied to 50 patients, representing 27.8% of the cases. **Table 2**

Among the 180 patients, Protocol A (Ceftriaxone) was associated with SSIs in 20 patients (33.3%), while 40 patients (28.6%) did not develop SSIs, making up 33.3% of the total sample. A statistically significant association was found between Protocol A and the occurrence of SSIs ($p = 0.04$).

Protocol B (Ceftriaxone + Metronidazole) resulted in SSIs in 10 patients (16.7%), whereas 60 patients (42.9%) were free of infections, representing 38.9% of the total sample. This protocol showed a lower incidence of SSIs compared to Protocol A but did not demonstrate statistical significance.

For Protocol C (Piperacillin-Tazobactam), SSIs occurred in 10 patients (16.7%), and 40 patients (28.6%) did not develop infections, accounting for 27.8% of the total sample. Although this protocol showed a comparable infection rate to Protocol B, no statistically significant difference was noted. **Table 3**

In this study, the occurrence of surgical site infections (SSIs) in typhoid ileal perforation surgeries was evaluated based on patient demographics. Among the 40 patients who developed SSIs, the age distribution was as follows: 25.0% (10 patients) were aged 18–30 years, 37.5% (15 patients) were aged 31–45 years, 25.0% (10 patients) were aged 46–60 years, and 12.5% (5 patients) were over 60 years. In comparison, the 140 patients who did not develop SSIs were distributed as follows: 25.0%

(35 patients) in the 18–30 age group, 32.1% (45 patients) in both the 31–45 and 46–60 age groups, and 10.7% (15 patients) in those over 60 years. There was no statistically significant difference in SSI incidence based on age, as indicated by a p-value of 0.75.

Regarding gender, 62.5% (25 patients) of those who developed SSIs were male, while 37.5% (15 patients) were female. In the non-SSI group, 71.4% (100 patients) were male, and 28.6% (40 patients) were female. The analysis showed that gender did not significantly influence the incidence of SSIs, with a p-value of 0.21. **Table 4**

In the analysis presented in Table 5, a logistic regression was conducted to evaluate the factors associated with surgical site infections (SSIs) following typhoid ileal perforation surgeries. The results indicated that Protocol A was significantly associated with an increased likelihood of developing SSIs compared to Protocol B, with an odds ratio (OR) of 2.5 (95% CI: 1.1–5.7) and a p-value of 0.03. This finding suggested that patients who received Protocol A were 2.5 times more likely to experience SSIs compared to those treated with Protocol B, and this association was statistically significant.

In contrast, the comparison between Protocol A and Protocol C showed an OR of 1.8 (95% CI: 0.8–4.2) with a p-value of 0.12, indicating no significant difference in the likelihood of SSIs between these two protocols. Similarly, age greater than 45 years was associated with an OR of 1.5 (95% CI: 0.7–3.3) and a p-value of 0.23, which also suggested no significant impact on SSI rates. Gender, specifically being male, yielded an OR of 1.2 (95% CI: 0.6–2.5) and a p-value of 0.35, further supporting the lack of significant associations with SSIs in this cohort. Overall, only the comparison between Protocol A and B reached statistical significance, highlighting the potential effectiveness of different antibiotic prophylaxis protocols in the prevention of SSIs. **Table 5**

Table 1: Demographic Characteristics of Patients (n = 180)

Variable	Categories	Frequency (n)	Percentage (%)
Age (years)	18-30	45	25.0
	31-45	70	38.9
	>45	65	36.1
Gender	Male	120	66.7
	Female	60	33.3
Comorbidities	None	120	66.7
	Diabetes	30	16.7
	Hypertension	20	11.1
	Others	10	5.5

Table 2: Distribution of Patients According to Antibiotic Prophylaxis Protocols (n=180)

Antibiotic Protocols	n	%
Protocol A (Ceftriaxone)	60	33.3
Protocol B (Ceftriaxone + Metronidazole)	70	38.9
Protocol C (Piperacillin-Tazobactam)	50	27.8

Table 3: Incidence of Postoperative Surgical Site Infections (SSIs) According to Antibiotic Protocols (n=180)

Antibiotic Protocol	SSI Occurrence (n=40)	No SSI (n=140)	Total (n=180)	p-value
Protocol A (Ceftriaxone)	20 (33.3%)	40 (28.6%)	60 (33.3%)	0.04*
Protocol B (Ceftriaxone + Metronidazole)	10 (16.7%)	60 (42.9%)	70 (38.9%)	
Protocol C (Piperacillin-Tazobactam)	10 (16.7%)	40 (28.6%)	50 (27.8%)	

*Significant at $p < 0.05$

Table 4: SSI Incidence Based on Demographics (n=180)

Variable	SSI Occurrence (n=40)	No SSI (n=140)	p-value
Age Group (years)			
18–30	10 (25.0%)	35 (25.0%)	0.75
31–45	15 (37.5%)	45 (32.1%)	
46–60	10 (25.0%)	45 (32.1%)	
>60	5 (12.5%)	15 (10.7%)	
Gender			
Male	25 (62.5%)	100 (71.4%)	0.21
Female	15 (37.5%)	40 (28.6%)	

Table 5: Logistic Regression Analysis of Factors Associated with SSI

Variable	Odds Ratio (OR)	95% CI	p-value
Protocol A vs. B	2.5	1.1–5.7	0.03*
Protocol A vs. C	1.8	0.8–4.2	0.12
Age (>45 years)	1.5	0.7–3.3	0.23
Gender (Male)	1.2	0.6–2.5	0.35

*Significant at $p < 0.05$

DISCUSSION

This study evaluated the comparative effectiveness of three antibiotic prophylaxis protocols—Protocol A (Ceftriaxone), Protocol B (Ceftriaxone + Metronidazole), and Protocol C (Piperacillin-Tazobactam)—in preventing postoperative surgical site infections (SSIs) following typhoid ileal perforation surgeries. The study found that Protocol A (Ceftriaxone) had the highest rate of SSIs (33.3%) with a statistically significant association ($p = 0.04$), while Protocols B and C both showed lower infection rates (16.7%) without significant differences between them. This section compares these findings with previous studies to highlight similarities, contradictions, and the implications of antibiotic selection in such surgeries.

Antibiotic Efficacy in Preventing SSIs

The finding that a combination therapy (Protocol B: Ceftriaxone + Metronidazole) was more effective than monotherapy (Protocol A: Ceftriaxone) aligns with previous studies on gastrointestinal surgeries. Studies by Hassan et al. (2020) demonstrated that broad-spectrum coverage, particularly involving anaerobic and Gram-negative pathogens, significantly reduced SSIs in abdominal surgeries.[10] In typhoid-related perforation surgeries, bacteria such as *Salmonella typhi* and intestinal flora play critical roles in infections. The combination of Ceftriaxone (targeting Gram-negative organisms) and Metronidazole (covering anaerobes) offers comprehensive coverage, reducing the risk of infections.
Similarly, Kannan et al. (2021) reported that dual antibiotic therapy reduced SSIs by 40% compared to monotherapy in gastrointestinal surgeries.[11] This aligns with our results showing that Protocol B was more effective than Protocol A. However, our findings deviate from this study in the sense that the difference between Protocol B and Protocol C (Piperacillin-Tazobactam) was not statistically significant, suggesting that both protocols provide effective prophylaxis without a clear advantage of one over the other.

Single-Agent vs. Combination Therapy

Our study found that Ceftriaxone alone (Protocol A) resulted in higher SSIs (33.3%) compared to other protocols, with a statistically significant association ($p = 0.04$). These findings are consistent with those of Kannan et al. (2021), who reported that single-agent prophylaxis, though effective in some clinical settings, often fails to provide sufficient coverage for the polymicrobial environment of gastrointestinal surgeries, leading to increased postoperative infections.[11]

Conversely, other studies have argued that monotherapy with broad-spectrum agents such as Ceftriaxone can still be effective under strict surgical protocols. For instance, a study by Vasu and Sagar et al. (2018) reported a lower SSI rate (22%) with Ceftriaxone alone, highlighting that the success of monotherapy may depend on factors such as intraoperative contamination control, surgical technique, and patient comorbidities.[12] The higher rate of SSIs in our study suggests that these factors may have had varying influences on the outcomes in typhoid ileal perforation surgeries.

Efficacy of Piperacillin-Tazobactam (Protocol C)

Our study did not find a significant difference in the SSI rates between Protocol C (Piperacillin-Tazobactam) and Protocol B (Ceftriaxone + Metronidazole). However, other studies, such as D'Angelica et al. (2023), have reported superior outcomes with Piperacillin-Tazobactam, particularly in surgeries with high contamination risks.[13] Vu's study noted a 10% reduction in SSIs compared to combination therapies due to Piperacillin-Tazobactam's broader spectrum and coverage of multi-drug-resistant organisms. [14]

The lack of a significant difference in our study may reflect regional variations in bacterial resistance patterns, patient populations, or differences in surgical techniques. In resource-limited settings where resistance to extended-spectrum antibiotics like Piperacillin-Tazobactam is lower, combination therapy involving Ceftriaxone and Metronidazole might perform comparably well. This aligns with studies from regions with limited antibiotic resistance, where dual therapy remains a cost-effective and reliable option.

Impact of Age and Comorbidities on SSIs

Our study did not find a statistically significant association between patient age and SSI rates ($p = 0.75$), which contrasts with findings from Ruiz de Gopegui Miguelena et al. (2021) that identified older age as a significant predictor of SSIs in gastrointestinal surgeries.[15] Vu's study highlighted that immunosenescence and delayed wound healing in older adults contribute to higher infection rates, especially in those over 60 years.[14]

The lack of significance in our cohort might reflect a more balanced distribution of postoperative care across age groups or a sample size insufficient to capture subtle age-related differences. Additionally, we observed that 66.7% of our patients had no comorbidities, which may have minimized the potential confounding effects of conditions such as diabetes and hypertension, both of which are commonly linked to increased SSI risk.

Role of Gender in SSI Development

While males constituted a majority of the study population (66.7%), we found no significant association between gender and SSI incidence ($p = 0.21$). This result aligns with findings by Zwicky et al. (2022), which reported no significant gender-based differences in SSIs following abdominal surgeries.[16] However, some studies, including those by Li et al. (2021), have observed slightly higher SSI rates in males, hypothesizing that differences in immune response or lifestyle factors may contribute.[17]

The absence of such a trend in our study suggests that the variability in SSI rates might be more influenced by surgical and antibiotic factors than by demographic characteristics. This reinforces the need for standardized infection control measures irrespective of patient demographics.

Our findings highlight the importance of selecting appropriate antibiotic protocols for typhoid ileal perforation surgeries. Protocol B (Ceftriaxone + Metronidazole) emerged as the most effective option with significantly lower SSI rates than Protocol A (Ceftriaxone). This aligns with prior research emphasizing the need for combination therapies to cover the diverse microbial environment involved in gastrointestinal surgeries.[18] [19]

However, the lack of significant differences between Protocol B and Protocol C (Piperacillin-Tazobactam) raises questions about the added benefit of broader-spectrum antibiotics in regions with

lower resistance patterns. Cost considerations and antibiotic stewardship are crucial when deciding between dual therapy and broader-spectrum agents.

One limitation of our study is the relatively small sample size (n = 180), which may limit the generalizability of the results. Additionally, the study was conducted in a single center, and factors such as regional bacterial resistance patterns, surgical expertise, and postoperative care protocols may have influenced the outcomes.

CONCLUSION

The findings revealed that Protocol B (Ceftriaxone + Metronidazole) was associated with the lowest rate of SSIs, significantly outperforming Protocol A ($p = 0.04$). However, no significant difference in effectiveness was observed between Protocols B and C, suggesting that both are viable options.

These results underscore the importance of combination antibiotic therapy in reducing SSIs in gastrointestinal surgeries, particularly in polymicrobial infections. While broader-spectrum antibiotics like Piperacillin-Tazobactam did not show a distinct advantage over dual therapy, they may still be relevant in specific clinical settings with higher contamination risks. Age, gender, and comorbidities were not significantly associated with SSIs, emphasizing that antibiotic selection and surgical protocols play more critical roles in infection prevention.

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