

Comparing Single Dose Versus Multiple Doses Antibiotic Prophylaxis in Preventing Surgical Site Infections Following Open Appendectomy for Uncomplicated Appendicitis

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Abstract

Background: Acute appendicitis is the leading cause of acute surgical abdomen. Studies have shown that a single dose of antibiotics is as effective as multiple doses in preventing surgical site infections (SSI) after appendectomy, with advantages such as cost savings, fewer adverse reactions, and reduced risk of antibiotic resistance. Despite these benefits, multiple doses are still commonly used. This study compared the efficacy of single-dose versus multiple-dose antibiotic prophylaxis in preventing SSI after open appendectomy for uncomplicated appendicitis.

Methodology: A one-year prospective study was conducted at the university of Benin teaching hospital (UBTH), Benin City, involving 62 adult patients with uncomplicated appendicitis. A total of 76 patients were initially recruited, but after histological evaluation, 62 patients were analyzed, 29 received a single dose of antibiotics, and 33 received multiple doses following the exclusion of the negative appendectomies. All patients were given intravenous 1.5 g cefuroxime and 500 mg metronidazole at anesthesia induction, with the multiple-dose group receiving two additional doses. Outcomes assessed included SSI occurrence, cost of antibiotics, and SSI management costs.

Results: SSI rates were similar between groups (3.5% vs. 3.0%), but the cost of multiple-dose regimens was over twice that of single-dose. Side effects were more frequent with multiple doses. Both SSI cases were superficial and associated with higher BMI.

Conclusion: Single-dose antibiotic prophylaxis is equally effective, more economical, and safer than multiple doses.

Keywords: Open Appendectomy; Surgical Antibiotic Prophylaxis; Surgical Site Infection; Uncomplicated Appendicitis.

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How to cite: Brotobor O, Brotobor D, Mukoro JU, Odeyale AR. Comparing Single Dose Versus Multiple Doses Antibiotic Prophylaxis in Preventing Surgical Site Infections Following Open Appendectomy for Uncomplicated Appendicitis. Niger Med J 2025;66(1):187-197. <https://doi.org/10.71480/nmj.v66i1.670>.

Quick Response Code:



Introduction

The vermiform appendix, long regarded as a vestigial organ, is now recognized as an important part of the immune system [1]. It contributes to lymphocyte function and serves as a reservoir for normal gut flora [1-3]. Acute appendicitis, characterized by inflammation of the appendix, is the most common cause of acute surgical abdomen and necessitates appendectomy, one of the most frequently performed surgeries worldwide [4]. The condition has a higher incidence in developed countries and among Caucasians [5]. However, there is a rising prevalence in newly industrialized nations, including urban areas of Sub-Saharan Africa [6,7]. Although the exact incidence in Nigeria remains unclear, appendicitis is the leading cause of surgical emergencies in the country [8,9]. Studies from Northern Nigeria report an incidence of 2.6 per 100,000 person-years [9,10], while other research indicates it accounts for 15-40% of emergency surgeries in most Nigerian centers [11-14].

Acute appendicitis can be classified as uncomplicated or complicated. Uncomplicated cases involve simple inflammation without abscess, gangrene, or perforation, while complicated cases present with one or more of these features [15,16]. Diagnosis is primarily clinical, although imaging and inflammatory markers are used as supplementary tools. Appendectomy remains the gold standard treatment for acute appendicitis [17,18]. However, it is associated with risks, particularly in elderly patients or cases of complicated appendicitis [19]. Common complications include surgical site infections (SSIs), ileus, bleeding, injury to adjacent organs, and adhesive bowel obstruction. SSIs are the most frequent complication, affecting approximately 5-10% of patients undergoing open appendectomy for uncomplicated appendicitis [20]. These infections are more prevalent in complicated cases and open surgical procedures.

Preventing SSIs is a critical goal in appendectomy. Surgical antibiotic prophylaxis (SAP) is a widely recommended strategy involving the perioperative use of antibiotics to minimize microbial load at the surgical site. Proper SAP administration is crucial and includes factors such as the choice of antibiotics, timing, dosing, route of administration, and redosing when necessary [21,22]. The Centers for Disease Control and Prevention (CDC) classifies wounds from uncomplicated appendicitis surgeries as contaminated, indicating potential for microbial contamination during the procedure [21-25]. Guidelines recommend that SAP duration should be limited to the shortest effective period, typically a single dose or no longer than 24 hours postoperatively [26-28]. Despite this, compliance with these principles is poor, and prolonged antibiotic use remains common.

Extended use of antibiotics for SAP carries several risks, including increased financial costs, prolonged hospital stays, antibiotic-related complications, and the development of antibiotic-resistant strains of microbes [28-31]. The emergence of multidrug-resistant organisms is particularly concerning [29]. Additionally, prolonged antibiotic use should not compensate for deficiencies in aseptic techniques, suboptimal theatre or ward conditions, poor surgical techniques, or inadequate perioperative preparation. SAP must be viewed as an adjunct rather than a replacement for these critical practices.

Appropriate timing of SAP administration has been identified as the most important factor in preventing SSIs [32]. However, there is no global consensus on whether a single dose or multiple doses of SAP is more effective for appendectomy. This lack of agreement extends to the Nigerian context, where studies specifically addressing SAP duration and SSI rates in appendectomy for uncomplicated appendicitis are lacking. Research is needed to compare the outcomes of single dose versus extended antibiotic regimens in terms of SSI rates following open appendectomy for uncomplicated appendicitis.

The present study aimed to address this gap by evaluating the effectiveness of a single preoperative dose of antibiotics versus multiple doses administered postoperatively. The research was conducted with the goal of generating evidence-based recommendations. It also evaluates the costs of postoperative prophylaxis, including drug expense, hospital stay, and side effects, while examining the impacts of

infections on hospital stays, wound care costs, and readmission. The hypothesis posits that there is no significant difference in SSI rates between the two approaches. If confirmed, these findings could support the adoption of shorter antibiotic regimens, reducing costs, hospital stays, and the risk of antimicrobial resistance without compromising patient safety.

Globally, appendectomy represents a substantial surgical burden, making appropriate SAP practices essential for optimizing patient outcomes. By examining the impact of SAP duration on SSI rates in a local context, this study seeks to contribute to the broader effort to improve surgical care standards while minimizing unnecessary antibiotic use and its associated complications.

Methodology

This study, conducted in a tertiary hospital in Nigeria's south-south geopolitical zone, examined the use of single versus multiple doses of prophylactic antibiotics in open appendectomy for uncomplicated appendicitis. The University of Benin Teaching Hospital serves patients from major cities in the region. Adult patients diagnosed with acute appendicitis at the emergency room or surgical outpatient clinic were enrolled, provided they met the inclusion criteria and consented to participate. A total of 76 patients were initially recruited, but after histological evaluation, 62 patients were analyzed, 29 received a single dose of antibiotics, and 33 received multiple doses following the exclusion of the negative appendectomies. Group A (single-dose prophylaxis) and Group B (multiple doses, including two additional postoperative doses).

This prospective comparative study spanned 12 months (January to December 2020). Eligible patients included adults (≥ 18 years) with non-gangrenous, non-perforated appendicitis and American Society of Anesthesiologists (ASA) class I or II status. Exclusion criteria included pediatric patients, underweight or overweight individuals, smokers, and those with allergies to study medications. Antibiotics used were Cefuroxime sodium and Metronidazole, chosen for their broad-spectrum efficacy and tolerability. Ethical approval was obtained, and patient confidentiality was ensured throughout.

Operative and Postoperative Protocols

The diagnosis was based on clinical evaluation, supported by blood tests and imaging when necessary. All patients received a single preoperative dose of antibiotics at the induction of anesthesia. The surgical procedure involved a Lanz incision, a muscle-splitting approach, and standardized wound closure techniques. Randomization into groups was achieved using sealed envelopes and patient numbering.

In Group A, no further antibiotics were administered postoperatively, while Group B received additional doses at 8 and 16 hours after the preoperative dose. Postoperative care included pain management, graded oral intake, and monitoring for wound infection. Discharge criteria included absence of SSI, full mobilization, and adequate pain control. Outpatient follow-ups occurred on the 7th, 14th, and 30th days post-surgery to monitor wound healing and detect SSI.

Surgical Site Infection Criteria

SSI diagnosis was based on criteria such as purulent drainage, wound dehiscence, positive microbiological culture, or evidence of an abscess on imaging. SSIs were classified into superficial, deep, or organ/space infections. Recorded variables included wound state, antibiotic cost, days of hospitalization, and SSI rates.

Data Collection and Analysis

Data was collected using structured proformas and analyzed with SPSS version 22. Continuous variables were summarized using means and standard deviations, while categorical data were expressed as

frequencies and percentages. Statistical tests, including t-tests and Chi-square tests, were applied, with significance set at $p \leq 0.05$.

Findings and Implications

This research highlights the effectiveness of standardized antibiotic regimens and operative protocols in preventing SSIs. By comparing single and multiple-dose prophylactic strategies, it seeks to optimize antibiotic use, reducing costs, resistance risks, and complications while ensuring patient safety. The study emphasizes the importance of adherence to surgical guidelines and provides a foundation for larger-scale investigations.

Results

This study randomized 76 patients into two groups to compare the effectiveness of single-dose (Group A) and multiple-dose (Group B) preoperative antibiotic prophylaxis. Fourteen patients (18.4%) were excluded due to negative histological findings for appendicitis, leaving 62 participants for analysis: 29 in Group A and 33 in Group B see Table 1. The sociodemographic parameters of the study participants are also displayed in Table 1. The mean age of all the subjects was 28.4 ± 9.2 years, while those in group A had a mean age of 25.4 ± 7.6 compared to group B 31.1 ± 9.7 with a p-value of 0.103.

Table 1: Sociodemographic parameters of the study population.

Variables	Group A n = 29	Group B n = 33	Total n = 62	Stats	P value
Age (yrs)					
Mean \pm std	25.4 \pm 7.6	31.1 \pm 9.7	28.4 \pm 9.2	t= -2.574	0.013
Range	18 – 52	20 – 52	18 – 52		
Age group (yrs)					
<20	7 (24.1)	0 (0.0)	7 (11.3)		
20 – 29	16 (55.5)	17 (51.5)	33 (53.2)		
30 – 39	5 (17.2)	9 (27.3)	14 (22.6)	Fishers	0.001
40 – 49	00 (0.0)	5 (15.2)	5 (8.1)		
\geq 50	1 (3.4)	2 (6.1)	3 (4.8)		
Gender					
Male	15 (51.7)	15 (45.5)	30 (48.4)	$\chi^2 = 0.243$	0.622
Female	14 (48.3)	18 (54.5)	32 (51.6)		
Occupation					
Professional					
Skilled	1 (3.4)	5 (15.2)	6 (9.7)		
Unskilled	11 (37.9)	15 (45.5)	26 (41.9)	Fishers	0.206
Unemployed	17 (58.6)	13 (39.3)	30 (48.4)		
Educational status					
Primary	0 (0.0)	2 (6.1)	2 (6.1)		
Secondary	9 (31.0)	10 (30.3)	19 (30.6)	Fishers'	0.401
Tertiary	20 (69.0)	21 (63.6)	41 (66.1)		
Residence					
Within Benin	27 (93.1)	31 (93.9)	58 (93.5)	Fishers'	0.258
Outside Benin	2 (6.9)	2 (6.1)	4 (6.5)		

The clinical presentation of the study participants is presented in Table 2. There was no significant difference in the clinical presentation of both study groups. Right iliac fossa pain (100%), anorexia (87.1%), and Nausea and vomiting (79.0%) were the most common symptoms while tenderness (100%) and rebound tenderness (95.2%) were the most common signs.

Table 2: Clinical presentation of study participants

Variables	Group A n = 29	Group B n = 33	Total n = 62	Stats	P value
Symptoms					
Periumbilical/Epigastric pain	18 (62.1)	15 (45.5)	33 (53.2)	$\chi^2 = 1.711$	0.191
Right iliac fossa pain	29 (100.0)	33 (100.0)	62 (100.0)	NA	NA
Anorexia	26 (89.7)	28 (84.8)	54 (87.1)	Fishers	0.713
Nausea/Vomiting	23 (79.3)	26 (78.8)	49 (79.0)	$\chi^2 = 0.003$	0.960
Fever	7 (24.1)	13 (39.4)	20 (32.3)	$\chi^2 = 1.644$	0.200
Signs					
Tenderness	29 (100.0)	33 (100.0)	62 (100.0)	NA	NA
Rebound tenderness	27 (93.1)	32 (97.0)	59 (95.2)	Fishers'	0.595

The analysis of time of antibiotic use to skin incision, duration of surgery, and duration of admission in both groups is shown in Table 3. There was no significant difference between the two groups.

Table 3: Analysis of time of Antibiotic use to skin incision, duration of surgery, and duration of admission.

Variables	Group A n=29		Group B N=33		Total N=62		P value
	Mean \pm SD	Range	Mean \pm SD	Range	Mean \pm SD	Range	
Time interval between antibiotics administration to skin incision (Min)	8.7 \pm 2.1	5 – 13	8.6 \pm 2.2	6 – 14	8.6 \pm 2.1	5 - 14	0.843
Duration of surgery (Min)	52.5 \pm 14.5	32 – 84	54.1 \pm 9.6	36– 70	53.3 \pm 12.0	32 - 84	0.603
Duration of admission (days)	2.1 \pm 0.3	2 - 3	2.1 \pm 0.3	2 – 3	2.1 \pm 0.3	2 – 3	0.537

The incidence of side effects from SAP was higher in Group B (12.1%) than in Group A (6.9%), but the difference was not statistically significant ($p = 0.676$). The frequency of the symptoms in group B compared to group A subjects were nausea 4 (12.1%) vs 2 (6.90%), metallic taste 2 (6.06%) vs 1 (3.45%), and vomiting 1 (3.03%) vs 0 (0.0%), most likely from metronidazole. See Figure 1.

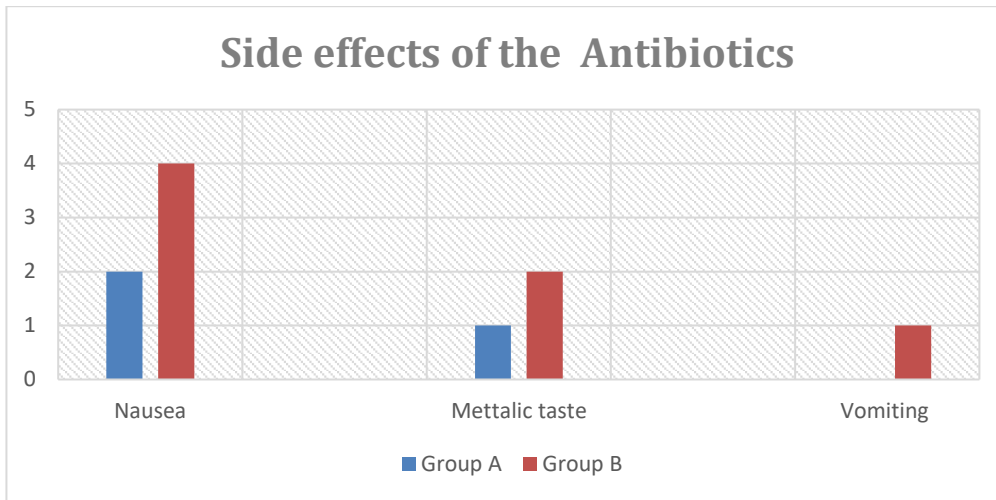


Figure I: Frequency of side effects of the prophylactic antibiotics used in the Study Groups.

Postoperative wound infection rates were identical, with one superficial incisional surgical site infection (SSI) in each group (3.5% in Group A and 3.0% in Group B); the difference was not statistically significant. These infections were diagnosed within the first week of post-surgery. Coagulase-negative staphylococcus and Staphylococcus aureus were isolated from patients in Groups A and B, respectively. Costs associated with wound dressings for these SSIs were higher in Group A (₦12,000 vs. ₦7,500 in Group B), but overall costs of wound care for the two cases were similar (₦29,280 vs. ₦30,180). Neither patient required readmission or antibiotics for SSI management.

Peritoneal swabs from all surgeries showed no bacterial growth after 24 hours of incubation. The study reported a negative appendectomy rate of 18.4%, higher among females (23.8%) than males (11.8%), although the difference was not statistically significant.

The mean body mass index (BMI) and weight range were similar between groups. Group A had a BMI of 22.6 ± 1.4 kg/m² (range 20.2–24.5), and Group B had a BMI of 23.1 ± 1.0 kg/m² (range 20.5–24.9), with no significant difference ($p = 0.136$). The subjects with SSI had a BMI ≥ 24.5 (see Table 4). Both groups had comparable total white blood cell (WBC) counts, but Group B exhibited a significantly higher mean neutrophil percentage (74.7% vs. 68.0%, $p = 0.024$). Absolute neutrophil counts were not significantly different. Relative neutrophilia was significantly more common in Group B ($p = 0.008$), but rates of leucocytosis were similar across groups, affecting only 25.8% of patients.

Ultrasound scans were performed on 71% of participants but were diagnostic in only 15.9% of cases. Surgical parameters, including the time between antibiotic administration and incision (8.6 ± 2.1 minutes), duration of surgery (53.3 ± 12 minutes), and length of hospital stay (2.1 ± 0.3 days), were comparable between groups see Table 3. Most surgeries were performed by senior registrars, with no significant difference in distribution between groups.

Table 4: Association between BMI and SSI among study participants

BMI category	No SSI n =60	SSI n = 2	Total	Stats	P value
19.5 – 20.4	3 (5.0)	0 (0.0)	3 (4.8)		
20.5 – 21.4	6 (10.0)	0 (0.0)	6 (9.7)		
21.5 – 22.4	13 (21.7)	0 (0.0)	13 (21.0)	Fishers	0.005
22.5 – 23.4	20 (33.3)	0 (0.0)	20 (32.3)		
23.5 – 24.4	16 (26.7)	0 (0.0)	16 (25.8)		
≥24.5	2 (3.3)	2 (100.0)	4 (6.5)		

Discussion

This study evaluated the effectiveness of single versus multiple-dose prophylactic antibiotics in preventing surgical site infections (SSIs) after open appendectomy for uncomplicated appendicitis. The mean age of participants was 28.4 ± 9.2 years, with group A (single-dose) averaging 25.4 ± 7.6 years and group B (multiple-dose) 31.1 ± 9.7 years. These findings align with a previous report by Nwashilli et al. where the mean age was also 28.4 years [33], but they differed slightly from studies in Zaria [9] and other locations [34], which reported younger mean ages [8]. Most cases occurred in the third decade of life, consistent with global trends for appendicitis, although pediatric cases were excluded. There was a slight female predominance (male-to-female ratio of 1:1.1), which contrasts with the traditionally reported male predominance in appendicitis. Similar findings of female predominance were noted in studies by Nwashilli et al, Duduyemi [35], and Ali et al. in Nigeria [36], while others reported a male majority. The reasons for this gender variation remain unclear [37].

The duration of surgery, time from antibiotic administration to incision, and hospital stay were similar between the two groups. The mean surgery duration in this study was consistent with Hussain et al. [38], but slightly longer than Khalifani et al. [39], likely due to differences in operating surgeon cadres. The average hospital stay was shorter (2 ± 0.3 days) compared to Nwashilli et al. (3.6 ± 1.94 days), where complicated appendicitis cases were included. Other studies found no significant difference in hospital stay between single-dose and multiple-dose groups, emphasizing the efficacy of single-dose prophylaxis [38,40].

The overall SSI rate in this study was low (3.3%), with no significant difference between group A (3.5%) and group B (3.0%). Both infections were superficial and managed with local wound care without additional antibiotic therapy. This rate is comparable to other studies, such as Nwashilli et al. (2.8%) and Hussain et al. (4.5%), and aligns with findings from studies in Hong Kong, Pakistan, and Iran, where SSI rates ranged from 1.32% to 9.1%. [34]. Importantly, these studies consistently showed no advantage of prolonged postoperative antibiotic use in reducing SSI rates. Prolonged antibiotic use, however, increased the risk of side effects and cost of treatment.

Side effects were observed in 6.9% of group A and 12.1% of group B, though the difference was not statistically significant. Nausea, metallic taste, and vomiting were the most common side effects, aligning with findings from another study [41]. More severe complications like neuropathy were rare and typically associated with prolonged antibiotic use. Body mass index (BMI) was a significant factor in SSI

occurrence. All patients had normal BMI (18.5–24.9 kg/m²), but both cases of SSI occurred in individuals with BMI \geq 24.5 kg/m², suggesting a higher BMI predisposition to infection. Thapa et al. similarly reported a higher mean BMI in patients with SSI [42]. The low overall SSI rate in this study could be attributed to the exclusion of high-risk groups such as diabetics and smokers.

Microbial cultures from SSI cases identified *Staphylococcus aureus* and coagulase-negative *Staphylococcus* as causative agents. These findings are consistent with previous studies by Salim et al., who reported *Staphylococcus aureus* as the most common pathogen in postoperative wound infections, along with *Pseudomonas* and *Escherichia coli* [43]. The low number of infections in this study limited the diversity of microbial isolates. Cost analysis revealed that single-dose prophylaxis was significantly cheaper than multiple doses, with mean costs of wound dressing and antibiotics in group A being 5,282.1 \pm 1,949.8 Naira compared to 8,701.8 \pm 1,044.5 Naira in group B. Patients with SSI incurred even higher costs due to additional wound care, antibiotics, and other expenses, with a mean total cost of 29,730 \pm 636.4 Naira compared to 13,020 \pm 3,818.4 Naira for those without SSI. This economic burden highlights the importance of effective prophylaxis to prevent SSIs. The study observed variations in SSI rates between different studies, even with similar antibiotic regimens, suggesting that SSI prevention depends on multiple factors beyond antibiotic prophylaxis, such as surgical technique, patient selection, and hospital protocols [5,44-46].

Conclusion

In conclusion, single-dose and multiple-dose preoperative antibiotic regimens showed comparable effectiveness in preventing postoperative wound infections and minimizing adverse events. Both regimens demonstrated low rates of SSI and similar cost implications. Despite differences in neutrophilia percentages and rates of neutrophilia, clinical outcomes remained consistent between the groups. The findings support the use of single-dose antibiotic prophylaxis as an effective and potentially cost-efficient alternative to multiple-dose regimens in appendectomy patients. The study also demonstrated that a single-dose preoperative antibiotic regimen is as effective as multiple doses in preventing SSIs following open appendectomy for uncomplicated appendicitis. Prolonged antibiotic use offers no additional benefit, increases the risk of side effects, and significantly raises treatment costs. These findings support the adoption of single-dose prophylaxis as a cost-effective and safe approach in similar clinical settings.

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