



(RESEARCH ARTICLE)



## The use of triple antibiotic prophylaxis during total knee replacement surgeries in Awka, Nigeria

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### Abstract

**Introduction:** Total knee arthroplasty periprosthetic joint infection (PJI) poses a significant challenge in orthopaedic surgery, often resulting in early failure and associated with high morbidity and mortality rates. Various treatment strategies exist, including debridement, antibiotic therapy, and prosthesis retention, with preventive measures such as antibiotic-impregnated cement and prophylactic antibiotics administration recommended by the American Academy of Orthopaedic Surgeons (AAOS).

**Methodology:** This prospective cohort study was conducted in an orthopaedic hospital in Awka, Southeast Nigeria, spanning seven years (2014-2021). A total of 134 patients who underwent primary and revision knee arthroplasty were included. The hospital's antibiotic prophylaxis protocol for implant surgeries, including arthroplasties, involved a triple combination of ceftriaxone, ciprofloxacin, and metronidazole administered pre-, intra-, and postoperatively for a minimum of 7 days.

**Results:** The study population had a mean age of 63.6 years, predominantly female (77.7%), and of Christian faith (100%). Most participants were of Igbo ethnicity (99.3%), married (90.7%), and engaged in business (37.7%). Severe osteoarthritis was the primary diagnosis in 97.0% of cases, while rheumatoid arthritis accounted for 3.0%. The triple antibiotic prophylaxis regimen resulted in only one case of superficial infection, with no instances of deep infection recorded.

**Conclusion:** Triple antibiotics prophylaxis, comprising ceftriaxone, ciprofloxacin, and metronidazole, demonstrated effectiveness in preventing infections associated with total knee arthroplasty. This regimen maintained surgical site infection prevalence within acceptable limits for clean surgeries, without observable antibiotic resistance in the study population.

**Keywords:** Total knee arthroplasty; Periprosthetic joint infection; Antibiotic prophylaxis; Infection prevention

### 1. Introduction

Total knee arthroplasty periprosthetic joint infection (PJI) is a severe complication in orthopaedic surgery, often leading to early failure. Treatment carries high morbidity and mortality rates, surpassing those of several cancers. Debridement, antibiotic therapy, and prosthesis retention are utilized for specific TKA PJI cases to salvage implants and minimize invasive procedures, though success rates vary widely. Preventive measures include antibiotic-impregnated cement, laminar flow, and timely administration of prophylactic antibiotics, notably cefazolin or cefuroxime, recommended by the American Academy of Orthopaedic Surgeons (AAOS), with consideration of local MRSA incidence. [1,6,20]

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In 1970, the National Nosocomial Infectious Surveillance Survey was launched with the aim of pinpointing factors contributing to postoperative wound infections. This landmark initiative laid the groundwork for the formulation of guidelines aimed at preventing such infections. The culmination of these efforts came to fruition in 1985 with the release of the Center for Disease Control's (CDC) seminal guidelines for the prevention of postoperative wound infections,[2]

A cornerstone of these guidelines was the provision of updated estimations regarding the rates of surgical site infections (SSI) across various surgical contexts. These estimations delineated SSI rates as ranging from 1% to 5% for clean surgeries, 3% to 11% for clean/contaminated procedures, 10% to 17% for contaminated surgeries, and exceeding 27% for procedures classified as dirty. Such delineations provided crucial benchmarks for assessing the risk landscape associated with different surgical scenarios. [3,4]

Recently, the CDC classified incisional surgical site infections (SSIs) into two categories: superficial and deep. According to the CDC, a superficial SSI is defined as an infection occurring within 30 days of the operation, involving only the skin or subcutaneous tissue of the incision, and exhibiting at least one of the following criteria: They are purulent drainage from the superficial incision, positive culture from the superficial incision, clinical symptoms such as pain, tenderness, swelling, redness, or warmth along with an opening of the incision by a surgeon, unless the culture is positive, diagnosis of superficial incisional SSI by the surgeon or attending physician. On the other hand, a deep SSI, according to the CDC, involves the deep soft tissues of the incision and presents with at least one of the following criteria: purulent drainage from the deep incision. Spontaneous dehiscence of the deep incision or opening by the surgeon when the patient exhibits clinical symptoms of infection, including fever, localized pain and/or tenderness, or an abscess. Other evidence of deep infection is found on direct examination, during reoperation, or by histopathologic or radiologic examination. [3,5,6,7,13]

In 2016, the CDC modified the time frame for defining deep SSIs associated with implants from within 1 year of the index surgery to within 90 days. However, the time frame remains within 30 days of the operation if no implant is left. This change aims to provide more precise criteria for identifying deep SSIs and align with clinical practice and research needs.[13][14]

The 2017 guidelines from the U.S. CDC did recommend against the continuation of antibiotics postoperatively after total joint arthroplasty. They did emphasize the judicious use of antibiotics, including the timing and duration of prophylactic antibiotic administration. [5,6,14]

The CDC guidelines recommend that antibiotics should be administered within 60 minutes before incision for most procedures, and the duration of prophylactic antibiotics should not exceed 24 hours after surgery unless there are special circumstances. Prolonged use of antibiotics can increase the risk of antibiotic resistance and other complications. [6, 17,19]

In the meticulous preparation preceding surgery, the timing of interventions emerges as a critical determinant of patient outcomes. Within this framework, the administration of antibiotics assumes pivotal significance, guided by the imperative to commence infusion within sixty minutes of incision initiation or tourniquet application, whichever comes first. This strategic temporal alignment seeks to optimize antibiotic concentrations precisely as the surgical procedure unfolds, thereby bolstering the defence against potential postoperative infections. [1,8,9]

Nevertheless, the pharmacokinetic idiosyncrasies inherent to distinct antibiotic agents introduce nuances in their administration protocols. Vancomycin is given over sixty to one hundred and twenty minutes. This deliberate modulation mitigates the risk of adverse reactions, notably histamine release, which can precipitate hypotension and the potentially severe red man syndrome. [2,10]

Further complexity emerges upon consideration of the differential tissue penetration rates characterizing various antibiotics. While certain agents, such as cefazolin, demonstrate rapid infiltration into bone, synovium, and soft tissue, others traverse a more protracted trajectory. Vancomycin, characterized by its comparatively slower tissue permeation, necessitates early administration to ensure adequate concentrations are attained at the surgical site. [3,11]

The correlation between *Staphylococcus aureus* (*S aureus*) colonization and the risk of periprosthetic joint infection (PJI) is gaining prominence in the orthopaedic literature. Research indicates that patients preparing for orthopaedic surgery exhibit *S aureus* colonization rates akin to those observed in the broader population. Notably, among individuals undergoing total joint arthroplasty (TJA), nearly 20% are carriers of *S aureus*. This prevalence underscores the significance of *S aureus* carriage as a potential predisposing factor for PJI development. [17,18,19,20,21]

This study aims to test the outcome of different antibiotic regimens in a developing country with poor capacity for top-class arthroplasty theatres and the risks of fake and substandard drugs.

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## 2. Methodology

This study was conducted in Princeton Orthopaedic Hospital, Awka, Southeast Nigeria.

It was a prospective cohort study that included other studies conceptualized in an encompassing questionnaire and recorded over a 7-year period.

It included 130 patients who underwent primary and revision knee arthroplasty in Awka, Nigeria, between 2014 and 2021. Our centre has an antibiotic prophylaxis protocol for all implant surgeries, including arthroplasties.

This protocol involves using a triple combination of antibiotics in the pre-, intra-, and postoperative period up to a minimum of seven days after the operation.

The three antibiotics include ceftriaxone 1g, ciprofloxacin 200mg, and metronidazole 500mg.

Ceftriaxone was given one hour before the commencement of surgery, while metronidazole and ciprofloxacin were given in the immediate postoperative period.

Ceftriaxone was given 1g daily, metronidazole was given 500mg 8hourly and ciprofloxacin was given 200mg 12hourly. They were given up to 7days post operation before the discharge of the patient from hospital.

The theatre setting was a normal room closed off from external air and occasionally fumigated.

Surgeries were carried out under aseptic conditions. The surgeon and two assistants used sterile impervious gowns, normal face masks, and caps, and no exhaust head gear.

The skin preparation was done with savlon, spirit and 10% povidone iodine.

Sterile impervious extremity drapes were used for all the patients to drape the knee to be operated on. Povidone-impregnated ioban was used to cover the knee to condone off the skin in the immediate vicinity of the incision.

The knee was implanted with gentamycin-impregnated bone cement. All the surgeries were performed under a pneumatic tourniquet, which was deflated after the wound had been dressed.

All the infected primary knee arthroplasties who presented during this study period were excluded from this study.

One surgeon performed all the one hundred and thirty surgeries.

All the knees were drained after surgery and drains were removed in 48 hours.

The wounds were dressed with povidone iodine-soaked gauze, and the dressings were opened for the first time after 7 days. The patients were discharged on the 8<sup>th</sup> day.

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## 3. Results

The demographic profile of the participants undergoing knee injury treatment is summarized in Table 1. The mean age of the subjects was 63.6 years, with a standard deviation of 9.29 years, ranging from 27 to 87 years. The majority of the participants were females (77.7%), and the predominant religion was Christianity (100%). Most participants belonged to the Igbo tribe (99.3%), and the majority were married (90.7%). In terms of occupation, the highest proportion was engaged in business (37.7%), followed by unemployed individuals (36.9%), civil servants (20.0%), and retired individuals (5.4%).

**Table 1** Demographic Characteristics

Variable	Frequency	Percentage (%)
Mean Age (years)	63.6 ± 9.29	27-87
Gender		
Male	29	22.3
Female	101	77.7
Christian	130	100
Tribe		
Igbo	129	99.3
Others	1	0.7
Marital Status		
Married	118	90.7
Widowed	6	4.6
Single	6	4.6
Occupation		
Business	49	37.7
Unemployed	48	36.9
Civil Servants	26	20.0
Retired	7	5.4

### 3.1. Diagnosis

Severe Osteoarthritis is the most prevalent diagnosis, constituting the majority of cases at 97.0%. This indicates a high prevalence of severe osteoarthritis among patients requiring knee-related medical care. Rheumatoid Arthritis accounts for a smaller proportion of cases at 3.0%. While less common than osteoarthritis, it remains a significant contributor to knee-related diagnoses.

#### 3.1.1. Antibiotics Regimen

Triple antibiotics prophylaxis, involving the use of ceftriaxone, a third generation cephalosporin, ciprofloxacin, a fluoroquinolone, and metronidazole, a nitroimidazole played a crucial role in preventing infections and promoting recovery.

There was one incidence of superficial infection, but no incidence of deep infection was recorded.

**Table 2** Medical details

<b>Patient hypertensive</b>		
No	49	37.0
Yes	81	62.3
<i>Diabetic patient</i>		
No	107	82.3
Yes	23	17.7

**Table 3** Surgery details

<b>Surgery Details</b>		
Knee infection after surgery/ Infection from referred cases		
No	129	99.2
Yes	1	0.77
Deep /organ Space infection	0	0.0
Superficial infection Antibiotics used in Centre of study	1	0.77
Ceftriaxone, Metronidazole, and Ciprofloxacin	130	100

#### 4. Discussion

Prosthetic joint infections, though uncommon, are a significant concern because they can lead to multiple surgeries, difficulty in fully clearing the infection, lifelong disability, significant financial costs, and emotional strain. Treating these infections is complicated and requires both surgical and medical interventions.[1] Patients may need long-term courses of antibiotics. It is worse when these surgeries are carried out in a resource-poor environments where health insurance coverage for arthroplasties is almost non-existent. Therefore, any form of post-arthroplasty infection in this environment becomes disastrous and may eventually lead to severe incapacitation, sepsis and eventual mortality due to a lack of resources to pursue needed salvage procedures. [6,37]

Considering the above, any practising surgeon in this environment would seriously reconsider following the CDC guideline for prophylaxis in his arthroplasty patients.

The Center for Disease Control and Prevention (CDC) classified surgical wound as clean, clean contaminated, contaminated, dirty wo und.[3] They released a new guideline in 2017 regarding the prevention of surgical site infections. One of their recommendations suggests giving patients a single dose of antibiotics before surgery, without any additional doses afterward, including for total joint replacement surgeries. [4,13]

In a developing country like ours, where the burden of malnutrition, fake and substandard drugs and disease burden is high, adhering to a regimen of one antibiotic dose preoperatively and no more may create more problems than it intends to solve.

In the treatment of infections when it has occurred, some scholars have given antibiotics to these patients up to one year. [35] If antibiotics are given so freely for one year after the complication has happened, why not give antibiotic to up to 1 week for prevention rather giving it for prevention.

The American Association of Hip and Knee Surgeons (AAHKS) disagrees with the CDC recommendation also, particularly regarding total joint replacements, as it goes against current international standards of care and lacks sufficient evidence and research. AAHKS still suggests giving antibiotics after surgery and calls for further studies to clarify the best approach.[3,6] Perhaps, the AAHKS may look into this study , despite the small sample size, to conduct a bigger study based on the triple regimen.

With the prevalence of severe osteoarthritis in this environment and the increasing need for knee arthroplasty, waiting for western-type theatres and all the details will leave patients suffering for a long time waiting for surgery. Therefore, many of the arthroplasties done in this environment in theatres without lamina flow devices are done with normal theatre caps, facemasks and gowns. Therefore, pre-, intra-, and post-op antibiotic regimen becomes a decision left for the surgeons practising in this milieu to determine based on clinical findings, and common cultures and sensitivities of antibiotics. My centre protocol was based on successes recorded with antibiotics used for other surgeries like open

reduction and internal fixation and external fixation of open fractures using culture results from minor surgical wounds and presenting infected surgeries.

So, the use of a third-generation cephalosporin like ceftriaxone, which is bactericidal and effective against gram-positive and gram-negative organisms, a quinolone like ciprofloxacin, also a bacteriocidal drug, and metronidazole working against anaerobes was considered an option to cover for any possibility of infection, including hospital-acquired ones.

The reason for the proposed one shot of cefazolin pre-op by CDC was to prevent antibiotics resistance but however, weighing the benefits against the risk, this study clearly shows that for a period of 7years doing primary knee arthroplasty and revision surgery in 134patients with severe osteoarthritis and others with aseptic loosening, only one superficial infection with redness, swelling and serous discharge requiring re-admission in other to have intravenous antibiotics therapy, was diagnosed. Despite the the fact that lamina flow theatre was not used, our finding/prevalence of 0.7% is comparable to what is obtained in any part of the developed world where all the procedures and protocols are followed, and at variance with most of the obtained prevalences in similar environments in Nigeria[23-29]. Single prophylaxis were found to have higher rate of SSIs but dual prophylaxis was found more beneficial.[5] None has tried triple prophylaxis. These patient have been followed up to minimum of 3 years to 10years now without presenting with illnesses resistant to these three medications.

Most surgeons in developing countries follow aseptic procedures meticulously, like in any other part of the world. Infact, some of the cases seen in this environment may never be seen in any of the developed world. The type of deformities seen in patients presenting with severe arthritis in Nigeria may become a spectacle in the western world. The pictures may make it to the museum. These are people who have waited for years to save money for their surgeries, as is the case with many of our patients, and to finally present for surgery with that level of deformity requiring bone grafts and prolonged theatre sessions may be so much risk to take to stop at one dose of pre-operative antibiotics. Despite the fact that some studies have found that subsequent use of post-operative antibiotics after the initial preoperative dose may not give additional benefit.[1,10, 11,14,15,19] However, some other studies have noted that post-operative doses after the initial pre-operative dose have an advantage over preoperative-only doses.[ 3,35,38]

So, if we ignore confounding factors like the expertise of the operating surgeon, the operating time, and patient comorbidities, what made the difference between the prevalence of 0.77% of SSIs in our centre and that of other similar centres operating under almost the same conditions? Could it be due to the triple regimen of antibiotic prophylaxis?

In Ibadan, Nigeria, the work done by Ifesanya and Alonge on open fractures, showed the use of triple antibiotics in the aggressive treatment of open fractures with farm contamination. Their result showed an infection rate of 12.9%, comparable with some centres abroad.[22] Though my study is not about open fractures, looking at the outcome from Ifesanya et al., which kept their infection rate to an acceptable limit, the use of triple antibiotics looked promising, considering the environment where this study was conducted and the late health-seeking behaviour of our people and the use of alternative medicine.[30]

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## 5. Conclusion

Triple antibiotic prophylaxis involving the use of ceftriaxone, a third-generation cephalosporin, ciprofloxacin, a fluoroquinolone, and metronidazole, a nitroimidazole, is very effective in prophylaxis for Total knee arthroplasty. It keeps the prevalence of SSIs within the limit of the generally accepted prevalence for clean surgeries without noticeable antibiotic resistance within the study population.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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