Research Article

Open Access

Prevalence and antibiogram study of bacterial isolates in infection after fracture fixation at a tertiary hospital

Abstract

Background: Current treatment protocols for Infection After Fracture Fixation (IAFF) prescribes Vancomycin and Meropenem. This study assesses the appropriateness of empirical antibiotic regimens in the treatment of IAFF and the feasibility of reserving Vancomycin and Carbapenem antibiotics for selected cases. To achieve this aim, we determined the causative bacteria and antibiogram of orthopaedic implant infections and susceptibility to commonly used antibiotics at our institution.

Methods: A retrospective cross-sectional descriptive study of patients who were treated for IAFF between June 2016 and February 2020. The outcome measures include microscopy, culture, and sensitivity (MCS) of samples obtained intraoperatively under sterile conditions.

Results: 178 cases were collected with 65 cases excluded based on the exclusion criteria resulting in 113 cases and 136 cultures. Of the 113 cases investigated in the study, 58% (*n*=66) were males and 42% (*n*=47) were females with ages ranging from 12 to 90 years with a mean age of 41 years. 26 cultured no bacteria (77% culture-positive rate). Forty six percent (46%) of patients cultured a single organism, 54% were mixed bacterial cultures of which 37% tested positive for two organisms and 17% more than two organisms. 110 cultures were included in the antibiogram analysis. The most frequently cultured bacteria was Staphylococcus aureus 29% (n=32), followed by Enterobacter spp. 16 (*n*=16), Acinetobacter Baumannii Complex 9% (*n*=10), Pseudomonas aeruginosa 7% (*n*=8), Proteus 7% (8) and Klebsiella 7% (*n*=8). Bacteriological cultures revealed a Gram-Negative predominance (60%) including Enterobacter, Pseudomonas, Proteus and Acinetobacter. Among the Gram-Positive bacterial isolates recovered (40%), S. aureus was the most common, with only 4 Methicillin-resistant Staphylococcus Aureus (MRSA) cultures.

Sensitivity testing of the Gram-Positive bacteria revealed 84% sensitivity to Cloxacillin, with the remaining 16% sensitive to Vancomycin. Staphylococcus aureus infections were commonly methicillin sensitive. Of the Gram-Negative bacteria, 68% were sensitive to Cefepime. All Gram Negatives were resistant to Penicillin, Ampicillin, Co-Amoxiclav and Cloxacillin.

Conclusions: The results of this study show that IAFF may be safely treated at our institution with a combination of Cloxacillin and Cefepime, adjusting antibiotic cover once culture results are available.

Keywords: infection after fracture fixation, fracture related infection, antibiogram, empirical treatment, implant infection

Volume 14 Issue 2 - 2022

Ivan Landman,[1] Stefne Nolte,[1] Tanita Botha,[2] Jaco Viljoen[1]
[1]Department of Orthopaedic Surgery, University of Pretoria, South Africa
[2]Department of Statistics, Faculty of Natural and Agricultural Sciences, University of Pretoria, South Africa

Correspondence: Dr Jaco Viljoen, MBChB, MMed Orth (UP), Department of Orthopaedic Surgery, University of Pretoria, Steve Biko Academic Hospital, South Africa, Level 7, Bridge A, Steve Biko Academic Hospital University of Pretoria,
Email drjjgviljoen@gmail.com

Received: December 24, 2021 | **Published:** March 02, 2022

Introduction

Infection after fracture fixation (IAFF) is a feared and devastating complication with significant morbidity and, in some instances, mortality.[1,2] This frequently encountered complication poses a unique challenge where both fracture union and control of sepsis are the ultimate goals.[3,4]

The current treatment protocol prescribes Vancomycin and Meropenem to cover respectively Methicillin-resistant Staphylococcus aureus (MRSA) and Cephalosporin resistant Gram-Negative microbes with the addition of Rifampicin to prevent biofilm formation.[3,5–8] Much of the current treatment protocols for IAFF has been extrapolated from research on prosthetic joint infections (PJI) and data focusing on IAFF is scarce.[9–16]

Due to an emerging trend in the sensitivity of Gram-Negative bacteria to a 4th generation cephalosporin at our institution Steve Biko Academic Hospital (SBAH), we propose altering our institutional empirical antibiotic protocol by replacing the Carbapenems with a 4th generation cephalosporin. With this new protocol, we intend to reserve the Carbapenems and Vancomycin thereby limiting antibiotic resistance. We propose the hypothesis that IAFF may be treated safely with a less aggressive antibiotic choice, reserving the Carbapenems and Vancomycin for selected cases. It is difficult to substantiate such a claim due to the limited research on the microbiology of IAFF. The purpose of this cross-sectional descriptive study is to determine the most appropriate empirical antibiotic regime by identifying the common microbes and their antibiotic sensitivity.

Materials and methods

Microscopy, culture, and sensitivity results of all patients who underwent debridement for IAFF at SBAH from June 2016 to February 2020 were included in the study. The sampling frame consisted of the theatre register as well as patient records, X-rays and microbiology results on LabTrack kept at SBAH. The theatre record book of SBAH was used to identify patients that underwent debridement of septic wounds. The patient's name, hospital number, and the date of the procedure were recorded.

The patient file was requested from records and examined for the indication for debridement, the date of the original injury and original fixation. X-ray records were accessed via the Pax system to cross-reference to the patient file. LabTract was used to trace the MC&S results of the qualifying

Results

A total number of 178 cases were collected with 65 cases excluded based on the exclusion criteria resulting in 113 cases and 136 cultures. From the 113 cases investigated in the study, 58% (*n*=66) were males and 42% (*n*=47) were females with ages ranging from 12 to 90 years with a mean age of 41 years (Table 1). Thirteen patients sustained open fractures and the remaining 100 patients closed injuries. Upper limb injuries accounted for 22% (n=25) of the cases and 78% (n=88) was due to injuries of the lower limbs. Details of anatomical distribution are listed in Table 2.

Table 1 Age and Sex

***n*=113**	
Mean Age (years)	41 years (12-90)
Sex (% male)	58% (66)

Table 2 Anatomical distribution

Upper limb 22% (n=25)	
Clavicle	2
Humerus	10
Forearm	12
Lower limb 78% (n88)	
Femur	32
Patella	5
Tibia	20
Foot and Ankle	31

Of the total 113 patients, 26 cultured no bacteria (77% culture-positive rate). Forty six percent (46%) of patients cultured a single organism, 54% were mixed bacterial cultures of which 37% accounted for two organisms and 17% more than two organisms, resulting in 110 cultures being included in the antibiogram analysis.

The most frequently cultured bacteria was Staphylococcus aureus 29% (*n*=32), followed by Enterobacter spp. 14.5% (*n*=16), Acinetobacter Baumannii complex 9% (*n*=10), Pseudomonas aeruginosa 7% (*n*=8), Proteus 7% (8), and Klebsiella 7% (*n*=8). Table 3 depicts bacterial cultures from intraoperative samples in patients with IAFF.

Bacteriological cultures revealed a 60% (*n*=66) Gram-Negative predominance including Enterobacter, Pseudomonas, Proteus, and Acinetobacter. Among the Gram-Positive bacterial isolates recovered (*n*=44), S. aureus was the most common (*n*=32), with only 4 MRSA cultures. Sensitivity testing of the Gram-Positive bacteria revealed an 84% sensitivity to Cloxacillin, with the remaining 16% sensitive to Vancomycin. Staphylococcus aureus infections were commonly Methicillin-sensitive, with only 4 of the 32 S. aureus cultures being MRSA. The susceptibility of the bacterial isolates to commonly used antibiotic regimes are demonstrated in Table 4. Of the Gram-Negative bacteria, 68% were sensitive to Cefepime. All Gram-Negatives were resistant to Penicillin, Ampicillin, Co-Amoxiclav, and Cloxacillin. The susceptibility of isolates to tested antibiotics are detailed in Table 5.

Table 3 Bacterial cultures from intraoperative samples in patients with IAFF

	Total n=110
Staphylococci	
Staphylococcus aureus	32
Staphylococcus epidermidis	1
Streptococci	
Streptococcus group a	3
Streptococcus group b	1
Enterococci	
Enterococcus faecalis	4
Enterococcus faecium	2
Enterobacterales	
Proteus mirabilis	7
Proteus vulgaris	1
Enterobacter cloacae complex	16
Burkholderia Cepacia	1
Klebsiella pneumoniae	6
Klebsiella oxytoca	2
Serratia marcescens	6
Escherichia coli	4
Morganella morganii subsp morganii	2
Non-fermenting Gram-Negative bacilli	
Pseudomonas aeruginosa	8
Acinetobacter baumannii	10
Sphingomonadales	
Sphingomonas paucimobilis	2
Burkholderiales	
Achromobacter denitrificans	1
Alcaligenes faecalis subsp faecalis	1

Table 4 Susceptibility of bacterial isolates to commonly used antibiotic regimes

Antibiotic regimen	**Patients tested (*n*)**	**Cover *n* (%)**
Cloxacillin	32	28 (88%)
Vancomycin	4	4 (100%)
Penicillin + Ampicillin	29	4 (14%)
Ceftazidime	31	14(45%)
Amoxicillin-Clavulanic acid	28	5(18%)
Piperacillin-Tazobactam	30	15(50%)
Cefepime	47	32(68%)
Cloxacillin + Cefepime	79	60 (76%)

Table 5 Susceptibility of isolates to tested antibiotics

Antibiotic regimen	Number of Gram-Positive isolates tested (*n* = 44)	Susceptible Gram-Positive isolates. n, (%)	Number of Gram-Negative isolates tested (*n* = 66)	Susceptible Gram-Negative isolates. n, (%)
Amoxicillin-clavulanic	-	-	28	5 (18%)
Penicillin/Ampicillin	29	4 (14%)		
Cloxacillin	32	28 (88%)	1	0 (0%)
Vancomycin	5	5 (100%)	1	0 (0%)
Ceftazidime	-	-	31	14 (45%)
Cefepime	-	-	47	32 (68%)
Piperacillin/Tazobactam	-	-	30	15 (50%)
Ertapenem	-	-	13	12 (92%)
Imipenem	-	-	18	10 (56%)
Meropenem	-	-	-	-

Discussion

Infection after fracture fixation is a major cause of morbidity in trauma patients and an accurate microbiological and susceptibility profile of causative organisms in a given hospital is important to determine appropriate empirical antibiotic therapy.[17–19]

Negative cultures

Positive cultures were obtained in 75% of the studied patients, comparing well with the review by Venter et al.[13] and Pincher et al.[20] in which 79% and 81% had positive cultures respectively. This is noticeably lower than in comparable studies by Zimmeli et al.[9] 89%, Tuon et al.[17] 93%, and Khosravi et al.[21] 93.9%.[9,17,21] We postulate that our lower positive culture rate may be due to the lack of routinely extended cultures, lack of sonification of explanted hardware, and routine administration of intraoperative prophylactic antibiotics at our institution.[22–24]

Gram stain

In the current study we demonstrated a Gram-Negative predominance as is common in developing countries, particularly *Enterobacteriacea, P. aeruginosa, and Acinetobacter baumannii*,[17,25,26] this corresponds well with the study by Tuon et al.[17] In contrast, Venter et al.[13] demonstrated a 60% Gram-Positive predominance. This may be attributed to the fact that the study by Venter et al.[13] included all patients with chronic osteomyelitis and not only patients with IAFF.

Staphylococcus aureus

Staphylococcus aureus was the most frequent culture in our study and agreed with the study by Arciola et al.,[11] Toun et al.[17] and Khosravi et al.[21] which reported Staphylococci as the most prevalent organism.[11,17,21] We demonstrated an MRSA rate of 3.6% that is significantly lower than in studies by Tuon et al.[17] who reported a rate of 12% and Venter et al.[21] demonstrating an MRSA rate of 15%. This finding supports our hypothesis that Vancomycin may be reserved for culture-proven resistant infections at our institution.

Sensitivity

The antimicrobial susceptibility test further revealed that:

i. Gram-Positive cultures were sensitive to Cloxacillin in 84% of cultures with the remaining 16% resistant to Cloxacillin (4 MRSA, 1 Staph epi, 2 Enterococcus faecium). All the cultures resistant to Cloxacillin were sensitive to Vancomycin.

ii. Of the Gram-Negative cultures, 70% were sensitive to Cefepime and the remaining resistant bacteria were all sensitive to the Carbapenems. Additionally, all the Gram-Negative bacteria were resistant to Penicillin, Ampicillin, Amoxicillin-Clavulanic acid, and Cloxacillin.

Changing empirical therapy

There is no generally accepted consensus on how resistance data should be applied to treatment decisions about empirical antibiotic regimens.[27] The decision to alter empirical antimicrobial regime is a complicated one, and cannot be made based on one single parameter. Considerations include cost, consequences of failed treatment, the correlation between laboratory resistance and clinical response, and overuse of reserve agents.[28,29]

In addition, there is no universally accepted resistance threshold at which to change empirical antibiotic therapy, neither can a universal threshold be applied to all diseases. As an example, the World Health Organisation (WHO) recommend an arbitrary resistance threshold of 5% for treating gonorrhoea.[30] In the treatment of Malaria, the WHO recommends a change in first-line therapy when an arbitrary figure of 25% of patients treated relapse.[31]

The decision to change empirical antibiotic regimes should be made by a multidisciplinary team taking into consideration the severity of the condition and the potential consequences of ineffective treatment.[19,27,32] It is, therefore, reasonable to accept relatively high rates of resistance to first-line agents in the management of non-life-threatening infections in otherwise healthy patients.

Conclusion

The results of this study suggest that Cloxacillin and Cefepime may safely be used as empirical treatment for IAFF in healthy hosts at our institution.

Contribution

This study contributes to the existing literature on the management of IAFF and antibiotic stewardship, reserving the Carbapenems and Vancomycin for selected resistant cases.

Limitations

The limitations of this study are typical of a retrospective study where the strength of the study is dependent on the quality of the medical records. A retrospective study design was chosen to utilise the vast amount of available data and to avoid the high cost associated with a prospective study. The sample size was small but similar to other studies focused on IAFF. The study was performed at a single tertiary centre treating complex trauma and limb reconstruction cases. This may limit the external validity of the study when applied to smaller centres. The high rate of negative cultures may predispose the study to bias.

Ethics statement

The authors declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the Second World Conference on Research Integrity in Singapore, 2010. Before commencement of the study, ethical approval was obtained from the following ethical review board: University of Pretoria MMed committee, as well as the University of Pretoria Faculty of Health Sciences Ethics Committee; Ethics reference number: 524/2019. Patients' records were anonymised by allocating a study number to each patient. Ethical principles as outlined by the World Medical Association Declaration of Helsinki were adhered to.

For this study formal consent was not required.

Funding sources

No funding was received for this study.

Declaration

The authors declare authorship of this article and that they have followed sound scientific research practice. This research is original and does not transgress plagiarism policies.

Author contributions

IL: Data capture, data analysis, draft preparation, manuscript preparation

SN: Data capture, manuscript revision

TB: Statistical Analysis

JV: Study conceptualisation, data capture, data analysis, manuscript revision.

Ackowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

1. Campoccia D, Montanaro L, Arciola CR. The significance of infection related to orthopedic devices and issues of antibiotic resistance. *Biomaterials.* 2006;27(11):2331–2339.
2. Trampuz A, Zimmerli W. Diagnosis and treatment of infections associated with fracture-fixation devices. *Injury.* 2006;37 Suppl 2:S59–S66.
3. Jiang N, Wang BW, Chai YM, et al. Chinese expert consensus on diagnosis and treatment of infection after fracture fixation. *Injury.* 2019;50(11):1952–1958.
4. Fang C, Wong TM, To KK, et al. Infection after fracture osteosynthesis - Part II. *J Orthop Surg (Hong Kong)*. 2017;25(1):2309499017692714.
5. Wouthuyzen-Bakker M, Tornero E, Morata L, et al. Moxifloxacin plus rifampin as an alternative for levofloxacin plus rifampin in the treatment of a prosthetic joint infection with Staphylococcus aureus. I*nt J Antimicrob Agents*. 2018;51(1):38–42.
6. Moran E, Masters S, Berendt AR, et al. Guiding empirical antibiotic therapy in orthopaedics: The microbiology of prosthetic joint infection managed by debridement, irrigation and prosthesis retention. *J Infect.* 2007;55(1):1–7.
7. Marais L, Ferreira N, Aldous C, et al. The management of chronic osteomyelitis: Part II – Principles of post-infective reconstruction and antibiotic therapy. *SA Orthopaedic Journal*. 2014;13(3):32–39.
8. McNally M, Nagarajah K. Osteomyelitis. *Orthopaedics and Trauma*. 2010;24:416–429.
9. Zimmerli W, Ochsner PE. Management of infection associated with prosthetic joints. *Infection.* 2003;31(2):99–108.
10. Holleyman RJ, Baker P, Charlett A, et al. Microorganisms responsible for periprosthetic knee infections in England and Wales. *Knee Surg Sports Traumatol Arthrosc.* 2016;24(10):3080–3087.
11. Arciola CR, An YH, Campoccia D, et al. Etiology of implant orthopedic infections: a survey on 1027 clinical isolates. *Int J Artif Organs.* 2005;28(11):1091–1100.
12. Marais L, Ferreira N, Aldous C, et al. The management of chronic osteomyelitis: Part I - Diagnostic work-up and surgical principles. *South African Orthopaedic Journal*. 2014;13:42.
13. Venter RG, Tanwar YS, Grey JP, et al. The management of chronic osteomyelitis in adults: outcomes of an integrated approach. *SA Orthopaedic Journal.* 2021;20(1):33–38.
14. Metsemakers WJ, Kuehl R, Moriarty TF, et al. Infection after fracture fixation: Current surgical and microbiological concepts. *Injury.* 2018;49(3):511–522.
15. Aggarwal VK, Bakhshi H, Ecker NU, et al. Organism profile in periprosthetic joint infection: pathogens differ at two arthroplasty infection referral centers in Europe and in the United States*. J Knee Surg.* 2014;27(5):399–406.
16. Puetzler J, Zalavras C, Moriarty TF, et al. Clinical practice in prevention of fracture-related infection: An international survey among 1197 orthopaedic trauma surgeons. *Injury.* 2019;50(6):1208–1215.
17. Tuon FF, Cieslinski J, Ono AFM, et al. Microbiological profile and susceptibility pattern of surgical site infections related to orthopaedic trauma. *Int Orthop*. 2019;43(6):1309–1313.
18. Vemu L, Sudhaharan S, Mamidi N, et al. Need for appropriate specimen for microbiology diagnosis of chronic osteomyelitis. *J Lab Physicians*. 2018;10(1):21–25.
19. Bonnevialle P. Operative treatment of early infection after internal fixation of limb fractures (exclusive of severe open fractures). *Orthop Traumatol Surg Res.* 2017;103(1S):S67–S73.
20. Pincher B, Fenton C, Jeyapalan R, et al. A systematic review of the single-stage treatment of chronic osteomyelitis. *J Orthop Surg Res.* 2019;14(1):393.
21. Khosravi A, Ahmadi F, Salmanzade S, et al. Study of Bacteria Isolated from Orthopedic Implant Infections and their Antimicrobial Susceptibility Pattern*. Research Journal of Microbiology.* 2009;4(4):158–163.
22. Yano MH, Klautau GB, da Silva CB, et al. Improved diagnosis of infection associated with osteosynthesis by use of sonication of fracture fixation implants. *J Clin Microbiol.* 2014;52(12):4176–4182.
23. Al-Mayahi M, Cian A, Lipsky BA, et al. Administration of antibiotic agents before intraoperative sampling in orthopedic infections alters culture results. *J Infect.* 2015;71(5):518–525.

24. Boxma H, Broekhuizen T, Patka P, et al. Randomised controlled trial of single-dose antibiotic prophylaxis in surgical treatment of closed fractures: the Dutch Trauma Trial. *Lancet.* 1996;347(9009):1133–1137.

25. Toledo PV, Arend LN, Pilonetto M, et al. Working Group in Healthcare Associated I. Surveillance programme for multidrug-resistant bacteria in healthcare-associated infections: an urban perspective in South Brazil. *J Hosp Infect.* 2012;80(4):351–353.

26. Oliveira PR, Carvalho VC, da Silva Felix C, et al. The incidence and microbiological profile of surgical site infections following internal fixation of closed and open fractures. *Rev Bras Ortop.* 2016;51(4):396–369.

27. The Alliance for the Prudent Use of Antibiotics. April 2003. Framework for Use of Antimicrobial Resistance Surveillance in the Development of Standard Treatment Guidelines. Under Subcontract with the Rational Pharmaceutical Management Plus Program at the Management Sciences for Health, Arlington, VA, USA. 2003.

28. WHO. World Health Organization. Antimicrobial resistance: global report on surveillance. 2014.

29. WHO. World Health Organization. Global antimicrobial resistance and use surveillance system (GLASS) report 2021. 2021.

30. Tapsall JW, Limnios EA, Murphy D, et al. Analysis of trends in antimicrobial resistance in Neisseria gonorrhoeae isolated in Australia, 1997 2006. *J Antimicrob Chemother.* 2008;61(1):150–515.

31. WHO. World Health Organization. Division of Control of Tropical, Diseases

32. Antimalarial drug policies: data requirements, treatment of uncomplicated malaria and management of malaria in pregnancy, report of an informal consultation, Geneva, 14-18 March 1994. Geneva: World Health Organization; 1994.

33. Bauer S, Bouldouyre MA, Oufella A, et al. Impact of a multidisciplinary staff meeting on the quality of antibiotherapy prescription for bone and joint infections in orthopedic surgery. *Med Mal Infect*. 2012;42(12):603–607.