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Original Research Article

Bacteriological spectrum of infections in orthopaedic implants and their antibiotic susceptibility pattern

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ABSTRACT

Background: Orthopaedic implant infections are one of the most challenging complications among orthopaedic surgeries which occurs despite the best management practices. The rise of antibiotic-resistant bacteria is set to pose a major challenge in the treatment of these infections.
Aim: The present study is done to identify the risk factors and bacteriological isolates responsible for orthopaedic implant infections and to study their antimicrobial susceptibility patterns.
Materials and Methods: This was a cross-sectional study carried out at a tertiary care hospital in India over eighteen months on patients presenting with the signs and symptoms of infections post-implant surgery. Microbiological samples were collected & processed as per the standard guidelines.
Results: Out of 57 patients with implant infections, 44(77%) had internal fixators & 13 (23%) had prosthesis insertion. 32(56%) patients presented with delayed infection. The most common risk factors were Diabetes, smoking, extensive trauma followed by alcohol consumption. The most common site infected was Tibia. The most common bacteria isolated were S.aureus (28%) followed by Coagulase-negative staphylococci & E.coli (19.2%) each. Among Staphylococci isolates, 59% of the isolates were methicillin-resistant. Among Gram-negative isolates, 56.6% of the isolates were either ESBL or/and AmpC producers and 20% were carbapenemase producers.
Conclusion: Despite best management practices, orthopaedic implant-related infections are often encountered. The high incidence of Multidrug-resistant organisms observed in this study is the cause of concern and underscores the need for better preventative and therapeutic strategies like strict adherence to the antibiotic policy and multidisciplinary approach to reduce the incidence & burden of treatment in these infections.

1. Introduction

Orthopaedic implants are highly susceptible to microbial infections resulting in increased risk of mortality& decreased quality of life leading to high medical costs& economic burden.[1] Orthopaedic implant infections lead to complications such as prolonged hospitalization and possibility of disability following interventions like implant removal and re-implantation along with long-term anti-microbial treatment.[2] Implant-related infections are common despite appropriate surgical antibiotic prophylaxis, well-established aseptic operation theatres, and guidelines for prevention of surgical site infections.

Incidence of Prosthetic joint infections (PJI) is between 0.3% and 1.9% following total hip and knee replacement respectively and goes up to 10% in revision cases.[3,4] The incidence of infection is between 1 to 3% in fractures after open reduction and internal fixation and is up to 50% for some high-risk fractures.[5] Some of the studies conducted in India have reported orthopaedic implant infections ranging

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from 0.7% to 6%.[2,6]

Implant-related infections are classified depending upon the duration of onset of symptoms as early: <2 weeks in fixation implants and<3 months in PJI, delayed: 2-10 weeks in fixation implants and 3-24 months in PJI, and late: >10 weeks in fixation implants and >24 months in PJI.[7,8]

Many international studies have investigated the variables associated with the onset of infections in orthopaedic implantation surgery. Various risk factors play a role in orthopaedic implant infections which include implant location, type of wound, Patient factors (like obesity, diabetes, advanced age, smoking, use of corticosteroids, iron deficiency, etc.), Surgical techniques, extended operative duration, the higher number of operating room personnel, post-operative care & cleanliness, biocompatibility of the material, implant surface properties and design.[1,9] The basic survival mechanism of the microorganisms is the formation and existence within biofilm due to which they resist the anti-microbial action as well as the host immune system.

There has been a change in the spectrum of microorganisms causing orthopaedic implant infections and their antibiotic susceptibility profiles over time as suggested by recent studies. Hence, updated epidemiological data, identification & analysis of the characteristics of pathogen distribution on orthopaedic implant infections may guide in decision-making on surgical options and systemic antimicrobials to the surgeons to improve the cure rate & preventive measures. This study aimed to assess the type of pathogens and risk factors with a focus on their antimicrobial susceptibility in orthopaedic implant infections.

2. Materials and Methods

This cross-sectional study was carried out in the Department of Microbiology, at a tertiary care teaching hospital, in Bangalore India, for a period of 18 months from Dec 2022-May 2024.

The patients admitted to the department of Orthopaedics with the signs and symptoms of infections following prosthesis or implant surgery, confirmed by routine &laboratory investigations were included in the study.

2.1. Inclusion criteria

1. Infection occurring at implant site with the presence of clinical signs of infection like fever, suppuration, local persisting pain, local signs of inflammation, hematoma and delayed wound healing in cases of early infection; joint pain or loosening in delayed infections; presence of sinuses, loosening and sepsis in case of late infections along with elevation of serum acute phase reactants after few weeks after discharge from hospital of all age groups and both sex.
2. Definitive pathogenic bacteria detection of at least one culture positive on surgically obtained tissue
3. Presence of Orthopaedic hardware at the time of presentation.

2.2. Exclusion criteria

1. Patients presenting with implant infections operated elsewhere other than our hospital.
2. The specimens having polymicrobial flora or no definitive pathogenic bacteria identified.
3. Cases lacking relevant medical history.

2.3. Method

The surgical procedures in implant-related infections were categorized as fixation and replacement /arthroplasty procedures. Cases of prosthetic joint infections were defined as per the ICM criteria 2018[10] and fracture-related infections (internal fixation and external fixation) were diagnosed as per the consensus definition for fracture-related infections published in 2018.[11] Isolates from the first positive-culture samples alone were included for patients presenting with recurrent infections. Data on the basic patient information, examination findings, underlying illnesses like diabetes mellitus/ uremia/ chronic osteomyelitis/arthritis/ concurrent urinary tract infection, type of implant, nutritional status, smoking, alcoholism etc were collected.

2.4. Microbiological procedures

Samples included tissues, synovial fluid, pus from the implant site/sinus tract, and implants. According to the IDSA-Infectious Diseases Society of America guidelines,[8] a virulent pathogen in a single specimen of a tissue biopsy or synovial fluid represents causative organism eg: Staphylococcus aureus whereas, at least two culture-positive peri/pre-operative samples were considered significant for less virulent microorganisms like coagulase-negative staphylococci & Cutibacterium acnes. The Vitek 2 (BioMérieux) Identification System was used for aerobic bacterial identification and antibiotic susceptibility testing. Resistant organisms were further tested phenotypically for production of ESBL, Amp C and Carbapenemases among Gram-negative bacteria and Methicillin resistance among Staphylococcus spp according to the current edition of CLSI- M100 guidelines.[12]

2.5. Statistical analysis

Statistical analysis: The data was recorded in an excel sheet and statistical analysis was done with the software SPSS-23 version. Data was calculated as percentages and proportions.

3. Results

A total of 57 patients presented with the signs and symptoms of infections after undergoing implant or prosthesis surgeries which were confirmed by laboratory investigations during the study period. The most commonly affected age group was 30-60 years (61.4%) with male predominance of 42 patients (73.6%). 3.5% of patients belonged to age group of < 30yrs & 35% of patients were > 60yrs of age. The most commonly affected site was Tibia (31.5%) followed by the ankle (21%) and knee (15.8%) as depicted. (Table 1) Considering the type of procedure, 44 (77% with extramedullary in 33% & intramedullary in 44%) patients had insertion of fixators, and 13(23%) had prosthesis insertion (7% Hip & 16% Knee). The most common implants used were intramedullary interlocking nail (65.7%) and dynamic compression plates (11%). A total of 12(21%) patients presented with early acute infection, 32(56%) with delayed infection and 13(23%) presented with late infection (Table 2). The most common risk factors were Diabetes, smoking, extensive trauma followed by alcohol consumption as shown (Table 3).

Table 1: Site affected

Site affected	No	Percentage
Knee	9	15.8
Tibia	18	31.5
Ankle	12	21
Femur	6	10.5
Metatarsals	4	7
Radius/ulna	4	7
Hip	4	7

Table 2: Time of onset

Time of onset	No	Percentage
Early < 2 wks	12	21
Delayed 2-10 wks	32	56
Late >10 wks	13	23

Table 3: Risk factors

Risk factor	No	Percentage
Smoking	28	49
Alcohol	22	38.5
Anemia	19	33.3
Hypertension	9	15.7
Extensive Trauma	27	47.3
Diabetes	30	52.6
Chr.Osteomyelitis	10	17.5
Malignancy	2	3.5
Concurrent UTI	4	7
Uremia	4	7
Albumin <3.4g/dl	11	19.2

The most common pathogens isolated were S.aureus (28%) followed by Coagulase-negative staphylococci (CoNS) & E.coli (19.2% each) as shown (Table 4). Among 27 Gram-positive isolates, 59% of the isolates were methicillin-resistant (MRSA 37 % & MRCoNS-22 %) and 22 % were MSSA, 18.5 % were MSCoNS. Among 30 gram-negative isolates, 17(56.6%) of the isolates were either extended spectrum beta-lactamase (ESBL) or/and AmpC enzyme producers and 6(20%) were carbapenemase producers (Table 5).

4. Discussion

Orthopaedic device-related infections are a major problem in orthopaedics leading to implant failure. Device-related infections are common despite the best sterilization and infection control practices.[2] This study examines the prevalence and the distribution of pathogens, associated risk factors &antimicrobial susceptibility pattern of the pathogens in orthopaedic implant infections thus offering insights for refining the choices of empirical antimicrobial strategies.

The most affected age group was 30-60 years and males were more affected than females similar to the findings of Aditya et al & Boyong et al.[2,13] As men are engaged more in manual labor and physical activity, this could account for orthopaedic infections being more common in males. In women, a high incidence of osteoarthritis was noted. The most common affected sites were the tibia (31.5%) &ankle (21%) followed by the knee, femur, foot, radius, and hip. Fernandes A et al &Aditya et al[2,14] have reported implants in the femur & tibia as most commonly affected followed by the foot, humerus & knee.

Out of 57 cases that were studied, 47% were open fractures with extensive tissue damage which led to infections. This was a major risk factor, and these patients developed an early onset of the infections compared to the late onset infections seen in closed injuries. Other risk factors noticed were smoking, Diabetes, alcohol, malnutrition, hypertension, and anemia. Diabetic patients are more prone to infection due to rapid biofilm formation, impaired neutrophil function or micro-vascular changes influencing wound healing.[15] Smoking is responsible factor for altering the process of wound healing due to nicotine, nitric oxide, and carbon monoxide and increasing the risk of infection. In orthopaedic infections, smoking is reported as an important risk factor in a study by Singh JA et al.[16] Alcoholism and smoking were noted in 49% & 38.5% of patients in the present study respectively compared to 51.87% and 71.25% reported by Angappan et al.[7] In the present study, 17.5% of chronic osteomyelitis developed implant infections which could be due to tissue disruption during implant surgery reactivating the latent foci.[14] Undernutrition showed a predisposition for implant infections in 19% of patients in this study due to altered

Table 4: Organisms isolated & their antibiotic resistance pattern

Antibiotic	E.coli 11(19%)	Klebsiella 6 (11%)	Proteus 8(14%)	Pseudomonas 5(9%)	SA 16(28%)	CoNS 11(19%)
Amikacin	3(27%)	3(50%)	2(25%)	2(40%)	-	-
Amoxicillin/Clavulanic Acid	9(82%)	5(83%)	6(75%)	-	-	-
Ciprofloxacin	8(72%)	3(50%)	7(87%)	3(60%)	9(56%)	6(54%)
Levofloxacin	-	-	-	4(80%)	5(31%)	4(36%)
Ceftriaxone	9(82%)	5(83%)	6(75%)	-	-	-
Colistin	1(9%)	2(33%)	-	0	-	-
Cefuroxime	9(82%)	5(83%)	5(62%)	-	-	-
Cefuroxime Axetil	9(82%)	5(83%)	5(62%)	-	-	-
Ertapenem	6(54%)	4(66%)	4(50%)	-	-	-
Cefepime	5(45%)	3(50%)	4(50%)	2(40%)	-	-
Gentamicin	5(45%)	3(50%)	4(50%)	2(40%)	4(25%)	6(54%)
Tobramycin	3(27%)	3(50%)	2(25%)	2(40%)	-	-
Imipenem	4(36%)	3(50%)	-	2(40%)	-	-
Meropenem	4(36%)	3(50%)	3(38%)	2(40%)	-	-
Cefoperazone/ Sulbactam	5(45%)	3(50%)	6(75%)	2(40%)	-	-
Trimethoprim/ Sulfamethoxazole	5(45%)	3(50%)	4(50%)	-	10(63%)	4(36%)
Tetracycline	9(82%)	4(66%)	5(62%)	2(40%)	6(38%)	5(46%)
Tigecycline	0	0	-	-	-	-
Piperacillin/ Tazobactam	5(45%)	4(66%)	2(25%)	2(40%)	-	-
Aztreonam	6(54%)	3(50%)	5(62%)	3(60%)	-	-
Ceftazidime	9(82%)	5(83%)	6(75%)	3(60%)	-	-
Erythromycin	-	-	-	-	10(63%)	8(73%)
Clindamycin	-	-	-	-	8(50%)	6(54%)
Daptomycin	-	-	-	-	0	0
Linezolid	-	-	-	-	0	0
BenzylPenicillin	-	-	-	-	16(100%	7(64%)
Rifampicin	-	-	-	-	0	2(18%)
Teicoplanin	-	-	-	-	0	0
Vancomycin	-	-	-	-	0	0
Cefoxitin	6(54%)	1(16%)	4(50%)	-	10(63%)	6(54%)
Total	11	6	8	5	16	11

Table 5: Distribution of ESBL, AmpC & Carbapenemase producers

Isolates	No	%
ESBL and AmpC co-producers	2	7
ESBL producers alone	11	37
AmpC producers alone	4	13
Neither ESBL nor AmpC producers	7	23
Cabapenemase producers	6	20

immunity.

The delayed onset of implant-associated infections was noted in 56% of cases whereas early onset & late onset was noticed in 21% & 23% of infections respectively. Early and delayed onset was noted in infections associated with internal fixation and the reason is attributed to the fact that these infections are mostly exogenously acquired and could be related to inadequate infection control practices. Prosthetic joints are susceptible to hematogenous seeding during their entire lifetime hence they are associated with late-onset infection.[17] Similar findings have been reported by Shaziabenazir et al[15] unlike Fernandes et al & Angappan et al[14,18] who reported increased early-onset infections.

The predominant pathogens were S.aureus (28%) followed by Coagulase-negative staphylococci & E.coli (19.2% each). In this study, we found that S. aureus was the common pathogen in patients with infections associated with internal fixation, whereas CoNS was the predominant pathogen in PJI. This could be due to the variations in the interstitial milieu of implants and also for a reason that S. aureus and CoNS have multiple mechanisms for attachment and biofilm formation that could contribute to implant infections.[17] Our findings were consistent with that of Rosteius et al and Boyong et

al[3,19] who reported Staphylococcus aureus as the most common pathogen followed by CoNS. Similarly, Sarangi Samir K et al[20] reported Staphylococcus aureus as the most common aerobic isolate (31.1%) which was followed by Pseudomonas aeruginosa. Aditya et al[2] reported Pseudomonas aeruginosa and Staphylococcus epidermidis being the most common bacteria among orthopaedic implant-related infections. The diversity of pathogens in different orthopaedic infections could be due to the varied characteristics of the implant biomaterial, surrounding microenvironment, adaptation by the pathogen, surgical site, the tissues involved, and individual tissue response. Among Gram-negative bacilli (GNB), Enterobacteriaceae were more predominant, which may be because most of the patients with these isolates had direct trauma leading to an open fracture thereby causing infection.[21] Studies have reported high incidence of Enterobacteriaceae in developing countries.[22]

Antimicrobial susceptibility showed S.aureus strains sensitive to Vancomycin, Teicoplanin, linezolid& Daptomycin similar to the findings by Shakti et al[23] The sensitivity of staphylococcus aureus to azithromycin, and trimethoprim/Sulfamethoxazole was around 62%. Rate of MSRA isolation among Staphylococcus aureus in our study was 62.5%. Boyong et al[13] reported 43.9% MRSA, Latha T et al[24] reported 57.3% of MRSA whereas Aditya et al[2] reported 10% of MRSA isolates among Staph aureus isolates. However, 36.36% MRCoNS were isolated among CoNS in our study unlike Boyong et al & Tsai et al[13,25] who reported significantly higher MRCoNS. These discrepancies may be due to the difference in the capability to adapt to environmental changes among staphylococci. In this study, 40% isolates of Pseudomonas aeruginosa were sensitive to amikacin, Cefipime, carbapenems &Piperacillin+ tazobactam. Among Enterobacteriaceae, decreased susceptibility was noted for amoxiclav, cephalosporins and carbapenem antibiotics. Multidrug-resistant Gram-negative bacteria isolated in our study were 76%. This was very high compared to the incidence of 8% & 6.4% reported by Bernadette et al & Benito et al.[26,27] This high level of resistance may be due to the production of biofilm leading to long-term antimicrobial therapy and prolonged hospital stay. ESBL producers among Gram-negative bacilli were 40% in our study similar to the study conducted on Orthopaedic implant infections by Shakti et al & Fernandes A et al who reported 37% & 32% respectively[14,23] whereas Chandrika et al[28] reported 60% ESBL. ESBL and AmpC co-producers accounted for 7% in the present study whereas, Juan C et al[29] reported less prevalence of ESBL and AmpC co-producers (1.6%) in contrast to a study by Ganesh Perumal et al[30] who reported 44%. Resistance due to Carbapenemase production among GNBs was 20% in this study. Though CRE has not been a major pathogen in orthopaedic infections, an increase in rates is the cause of concern.

5. Conclusion

Diagnosing and managing orthopaedic implant-associated infections remains challenging. This study reports information on the microbial etiology & risk factors associated with Orthopaedic implant infections at our center. The main pathogens were S. aureus, CoNS and E.coli which showed variations in antimicrobial susceptibility. The high incidence of Multidrug-resistant organisms observed in this study is a problem in the field of orthopaedic implant-related infections. These findings inform the need for improved preventative and therapeutic strategies emphasizing strict adherence to antibiotic policies and a multidisciplinary y approach involving orthopaedics and microbiologists to reduce the incidence & treatment burden with orthopaedic implant infections. However, multicenter studies with longer periods are required to validate the above findings.

6. Limitations of the Study

The microbiology of only aerobic culture-positive orthopaedic infections was assessed. Infections caused by fungi and Mycobacterium tuberculosis & anaerobes which are usually culture-negative have not been reported. Molecular characterization of antibiotic resistance for the isolates was not performed in this study which would highlight the mechanism of resistance & prevalent genes responsible for drug resistance. The data represents a single center, hence the results are exposed to the risk of local epidemiologic bias.

7. Ethical Approval

Consent to perform the study was obtained from the Research Ethics Committee of our hospital with form number VIEC/2022/APP/70.

8. Conflict of Interest

None.

9. Source of Funding

None.

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