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Gram negative osteoarticular infections: An observational study over one year

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Background

Osteoarticular infections form an important part of orthopedic & infectious disease practice. Currently, gram negative infections have become increasingly important. Therefore we analyzed the gram negative osteoarticular infections at our institute with respect to the causative organisms, antibiotic susceptibility, treatment used and outcome.

Methodology

This is an observational study at a tertiary care center in Pune, India. 37 consecutive patients of bone and joint infections (which included native joint septic arthritis, periprosthetic joint infections, spine infections and osteomyelitis) from 1st January 2022 to 31st December 2022 were included. There were total 19 gram negative infections, 17 of which were identified by culture and 2 patients where cultures were repeatedly negative and the organism was identified only via 16S RNA sequencing or Multiplex PCR. Antibiotic susceptibility, treatment used and outcome was studied for all patients.

Results

19 samples (16 Gram negative monomicrobial and 3 polymicrobial which also had gram negative organisms) were derived from 9 patients who were male and 10 were female. 10 patients were above the age of 65. There were 8 knee prosthetic joint infections, 5 infective spondylodiscitis, 2 septic arthritis, 2 fracture related implant infections, 1 hip prosthetic joint infection and 1 chronic osteomyelitis. The types of organisms found are shown in Figure 1.

The novel modality of Joint infection Multiplex PCR panel was employed for 1 sample - which detected *Pseudomonas aeruginosa*, while for 2 samples, identification was carried out by 16S RNA sequencing - which detected *Acinetobacter baumanii* in 1 sample and *Achromobacter xylosoxidans* in the other. 7 of the 19 organisms were resistant to 3rd generation cephalosporins, 5 were resistant to Beta-lactam/Beta-lactamase inhibitor (BL-BLIs), 6 were resistant to carbapenems, 8 were resistant to aminoglycosides and 11 were resistant to fluoroquinolones. A detailed susceptibility pattern of all the organisms is shown in Figure 2.

Table 1: Clinical profile including diagnosis, organism, treatment and outcome.

Sr No.	Diagnosis	Organism	Antibiotics	Surgical Intervention	Outcome
1	L5-S1 disc prolapse with large epidural abscess with spondylodiscitis (post injection)	*Pseudomonas aeruginosa*	Inj Ceftazidime 2 g IV tid + Inj Amikacin 1 g IV od for 6 weeks	L5-S1 lumbar decompression + discectomy + fusion	Good
2	Lumbar canal stenosis L3-S1 with grade 1 degenerative spondylolisthesis L4-5 (post op infection)	*Achromobacter denitrificans*	Tab levofloxacin 500 mg od + Tab minocycline 100 mg bid; did not tolerate minocycline so changed to tab co-trimoxazole (800/160) tid and Inj meropenem 1 g iv tid was also given for 15 days	None, implant retained	Good
3	Right knee septic arthritis (post liver transplant, biliary stricture + bacteremia)	*Klebsiella pneumoniae*	Inj ceftazidime-avibactam 2.5 g tid + Inj aztreonam 2 g tid x 6 weeks; multiple courses	Multiple aspirations + joint lavage	Failed
4	Bilateral knee - total knee replacement – periprosthetic joint infection	*Achromobacter denitrificans*	Tab levofloxacin 500 mg od + Tab minocycline 100 mg bid for a long time, still under treatment	None, implants retained	Good
5	Left knee septic arthritis	*Pseudomonas aeruginosa*	Tab ciprofloxacin 500 mg bid for a long time, still under treatment	Joint lavage	Good
6	Left knee - total knee replacement – periprosthetic joint infection	*Achromobacter xylosoxidans*	Tab minocycline 100 mg bid for a long time, still under treatment	None, implant retained	Good
7	Left hip - total hip replacement – periprosthetic joint infection	*Enterobacter aerogenes, Kocuria kristinae*	Tab ciprofloxacin 500 mg bid for a long time, still under treatment	None, implant retained	Good
8	Right knee total knee replacement – periprosthetic joint infection	*MRSA, Klebsiella pneumoniae*	Inj Ceftazidime-avibactam 2.5 g tid + aztreonam 2 g tid + Inj Teicoplanin 400 mg iv od for 3 months	None, implant retained	Lost to follow up
9	TI1 fracture with implants insitu with non healing wound	*Acinetobacter baumanii*	Tab minocycline 100 mg bid x 6 weeks	Implants removed	Good
10	Grade 3 compound fracture of the tibia	*Enterococcus faecalis, Pseudomonas aeruginosa*	Inj ceftazidime + avibactam 2.5 g tid + aztreonam 2 g tid + Inj ampicillin 2 g IV qid for 6 weeks	Implants removed	Good
11	Chronic osteomyelitis of left tibia	*Pseudomonas aerugonisa*	Tab ciprofloxacin 750 mg bid for 6 weeks	None	Good
12	Left knee - total knee replacement – periprosthetic joint infection	*Burkholderia cepacia*	Inj ceftazidime 2 g iv tid + tab minocycline 100 mg bid for a long time	None, implant retained	Lost to follow up
13	Right knee - total knee replacement – periprosthetic joint infection	*Achromobacter xylosoxidans*	Tab minocycline 100 mg bid for a long time	None, implant retained	Lost to follow up
14	Infective spondylodiscitis	*Pseudomonas aeruginosa*	Tab ciprofloxacin 500 mg bid for 8 weeks	Lost to follow up	Lost to follow up
15	L5-S1 discectomy / laminectomy - stabilization (post op infection)	*Pseudomonas aeruginosa*	Tab ciprofloxacin 750 mg bid for a long time	Lost to follow up	Lost to follow up
16	Left knee - total knee replacement – periprosthetic joint infection	*Achromobacter xylosoxidans*	Tab co-trimoxazole (800/160) tid	None, implant retained	Good
17	Spinal fixation (post op infection)	*Klebsiella pneumoniae*	Inj cefazidime-avibactam 2.5 g IV tid + Inj aztreonam 2 g IV tid for 8 weeks	Lost to follow up	Lost to follow up
18	Right knee - total knee replacement – periprosthetic joint infection	*Achromobacter xylosoxidans*	Inj ceftazidime 2 g IV tid for 6 weeks + Tab minocycline 100 mg bid	None, implant retained	Failed
19	Left knee - total knee replacement – periprosthetic joint infection	*Achromobacter xylosoxidans*	Lost to follow up	Lost to follow up	Lost to follow up

OD: Once a day; Bid: Twice a day; Tid: Thrice a day; Qid: Four times a day.

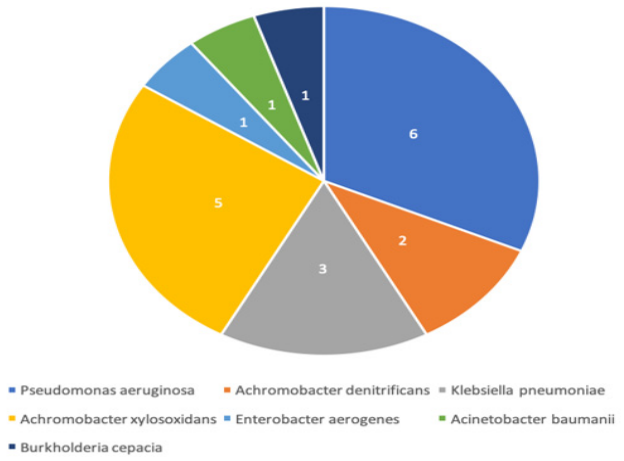

Figure 1: Gram negative osteoarticular infections (n=19).

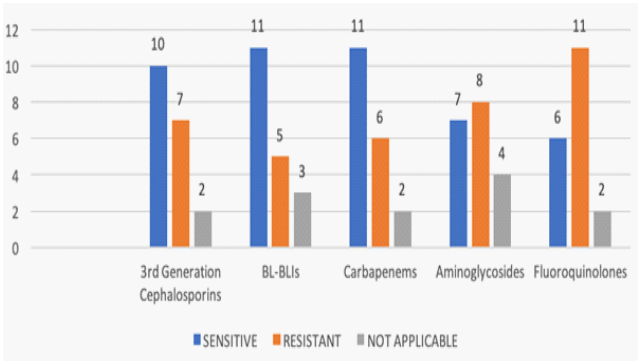

Figure 2: Antibiotic susceptibility patterns of the gram negative organisms (n=19).

Of the 6 carbapenem resistant organisms, 3 were *Klebsiella pneumoniae,* 2 were *Achromobacter xylosoxidans,* and 1 was *Pseudomonas aeruginosa*. Xpert CARBA-R test was performed on 2 of the *Klebsiella pneumoniae* isolates, which revealed presence of NDM+OXA-48 like carbapenemases. Ceftazidime-avibactam + Aztreonam synergy test was performed for 3 of the organisms and it showed positive synergy. The detailed information of the diagnosis, organism, treatment given and outcome is shown in Table 1. 10 of the patients in our study had a good outcome, 2 failed and required re-treatment. 8 patients are still under treatment and 7 were lost to follow up.

Discussion

Osteoarticular infections including septic arthritis, periprosthetic joint infections, osteomyelitis and spinal infections cause significant morbidity and mortality, as well as a burden on healthcare. Often, these infections are nosocomial and caused by Multi-Drug Resistant (MDR) organisms. The presence of foreign bodies like implants and prosthesis add to the challenges due to biofilm formation and the need for removal of the same. Data from the Western World suggests that gram positive organisms like *Staphylococcus aureus* and *coagulase negative Staphylococci* [1,2] are important causes, but as our study reveals, gram negative organisms are equally important causes of osteoarticular infections in India. This poses a significant challenge due to the antimicrobial resistance of these organisms. In our study, the most common causative organism was *Pseudomonas aeruginosa*. 11 organisms in our study were MDR; 6 were carbapenem resistant. Similar results are seen in other studies from India [3]. 3 of the carbapenem resistant organisms were *Klebsiella pneumoniae*, out of which the Xpert CARBA-R test was performed on 2 isolates, where both NDM+OXA-48 like carbapenemases were found. Synergy testing with ceftazidime-avibactam + aztreonam was positive for all the *Klebsiella* isolates. However, this test was not performed for the other carbapenem resistant isolates. The limitations of this study include a small sample size, unavailability of susceptibility data for some isolates and lack of information about the outcome of some of the patients.

It is important to know local epidemiology of antimicrobial resistance, as it helps guide the clinicians in deciding empiric antibiotics while waiting for culture results. In cases where cultures do not grow an organism, multiplex PCRs and 16S RNA sequencing may be used to reveal the causative organisms, but the susceptibility of the same remains unknown. Besides, the true significance of sequencing results is somewhat difficult to ascertain at present. Our study had 2 patients where cultures were repeatedly negative, the organism was discovered via 16S RNA sequencing and antibiotics were chosen based on local epidemiological data.

Conclusion

Contrary to the Western data, Indian data shows a significant proportion of Gram negative organisms in osteoarticular infections. MDR gram negative organisms, especially carbapenem resistant pose an immense challenge in diagnosis and management. This study highlights the need for large scale as well as repeated studies to provide clinicians the guidance that they need.

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