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Analysis of Microbiological Profile, Antibiogram Pattern and Clinical Outcome in Patients with Suspected Osteomyelitis, in a Tertiary Care Hospital

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ABSTRACT

Osteomyelitis is defined as an inflammation of the bone caused by an infecting organism. Osteomyelitis can be classified as acute, subacute, or chronic, depending on the duration of symptoms. The mechanism of infection can be exogenous or hematogenous. Exogenous osteomyelitis is caused by open fractures, surgery (iatrogenic), or contiguous spread from infected local tissue. To isolate and identify the bacteria causing osteomyelitis in patients attending orthopaedic outpatient department in Calcutta National Medical College, a tertiary care hospital. To study the antibiogram sensitivity and resistance pattern of the bacteria isolated. The present study was a Prospective, Descriptive study. This Study was conducted from 12 months at Department of Orthopaedics, Calcutta National Medical College. In our study, 4 (8.0%) patients had osteomyelitis in Distal tibia, 4 (8.0%) patients had Metacarpal, 3 (6.0%) patients had lesion in Post op both bone forearm, 3 (6.0%) patients had Post op intercondylar fracture humerus, 4 (8.0%) patients had Post op shaft femur, 3 (6.0%) patients had Post op shaft tibia, 6 (12.0%) patients had lesion in Shaft tibia. We demonstrated the microbiological profile, antibiogram pattern and clinical outcome in patients with suspected osteomyelitis, in a tertiary care hospital. The causative organism in chronic osteomyelitis was found to be related to the aetiology of the infection. Majority of haematogenous chronic osteomyelitis involved a solitary Gram-positive organism, most commonly *Staphylococcus aureus*. Incidence of Gram-negative infections were found to be higher than previously reported. Specially in post-traumatic and post-operative infections, *Pseudomonas aeruginosa* were commonly isolated. Resistance to broad spectrum Penicillin, third generation Cephalosporins and even Fluoroquinolones were higher than previously reported. Proper identification of the causative organism and antibiogram sensitivity testing plays a pivotal role in controlling the infection. With my study, we would be able to make a table of most appropriate antibiotics for suspected organisms according to the disease aetiology and it would help in starting the empirical therapy while the culture report arrives.

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Key Words
Osteomyelitis, antibiotic resistance, microbiological profile

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INTRODUCTION

Osteomyelitis is defined as an inflammation of the bone caused by an infecting organism. Osteomyelitis can be classified as acute, subacute, or chronic, depending on the duration of symptoms. The mechanism of infection can be exogenous or hematogenous. Exogenous osteomyelitis is caused by open fractures, surgery (iatrogenic), or contiguous spread from infected local tissue. Chronic osteomyelitis is defined clinically as bone infection with clinical signs persisting for more than 10 days or the relapse of a previously treated or untreated osteomyelitis and bone infection was defined as at least two bone cultures with the same organism growth, or one positive bone culture combined with the intraoperative finding of purulence, acute inflammation on histologic examination consistent with infection, or a sinus tract communicating to the bone. Currently, morbidity and mortality from osteomyelitis are relatively low because of modern treatment methods, including the use of antibiotics and aggressive surgical treatment. But the treatment of chronic osteomyelitis remains a challenge because of the rapid development of antimicrobial resistance and expression of virulence factors8. Pus culture yields the causative organism and this may help in selecting the proper preoperative antibiotics. Therefore, the purpose of this study is to isolate the organisms responsible for osteomyelitis in a tertiary care hospital and to describe their antibiogram profile. Antibiotics have served as the corner stone of modern medicine. Emergence of antimicrobial resistance is a worldwide public health problem and a threat to mankind[1]. In India, the burden of infectious disease is highest among the world and recent reports showed the inappropriate and irrational use of antimicrobial agents against the diseases led to increase in the development of antimicrobial resistance (AMR)[2]. Besides poor financial conditions, inadequate infrastructure, high burden of disease and unregulated sales of cheap antibiotics have amplified the crisis of AMR in India[3,4].

Bacterial infections are a frequent cause of hospitalization and particularly healthcare associated infections are more common in critical care settings.[5] Globally the emergence of antimicrobial resistance and limited availability of treatment options present an increasing challenge for the management of bacterial infections worldwide. Rate of healthcare associated infections range from 5-30% among ICU patients. The increased risk of infection is associated with severity of patient illness, length of exposure to invasive devices and procedures, increased patient contact with healthcare personnel and length of stay in hospital. Over the past 15-20 years, infection control practices and new antimicrobial development have primarily targeted control and treatment of infections caused by gram-positive organisms[6,7]. Recently the incidence of infections caused by gram-negative bacteria in ICU has risen and the lack of available treatment options against some multi-drug-resistant (MDR) strains is alarming. Infections caused by MDR gram-negative organisms are associated with high morbidity and mortality[8]. Hence, careful adherence to infection control and infection treatment guidelines helps to improve patient outcome and reduce hospital cost.

MATERIALS AND METHODS

Study design: Prospective, Descriptive study.

Place of study: Department of Orthopaedics, Calcutta National Medical College.

Period of study: 12 months

Study population: Patients visiting Orthopaedics outpatient and inpatient department in Calcutta National Medical College with suspected osteomyelitis.

Sample size: 50

Inclusion criteria:

- **Age:** 18-60 years
- Both sexes
- Clinically and radiologically (by digital X-ray, CT scan and MRI) diagnosed with suspected osteomyelitis

Exclusion criteria:

- Patients with other bony abnormalities
- Patients with acute osteomyelitis

RESULTS

In our study, 3 (6.0%) patients had *Acinetobacter* sp., 4 (8.0%) patients had *Enterobacter cloacae*, 4 (8.0%) patients had *Escherichia coli*, 5 (10.0%) patients had *Klebsiella pneumoniae*, 11 (22.0%) patients had *Pesudomonas aeruginosa*, 8 (16.0%) patients had *Staphylococcus auerus* (MRSA) and 6 (12.0%) patients had *Staphylococcus aureus* (Table 1).

Among the isolates, 31 (62.0%) patients had Resistance and 9 (18.0%) patients had Sensitivity to Amoxicillin-Clavulanic acid. Among the isolates, 30 (60.0%) patients were resistant to and 15 (30.0%) patients were sensitive to in Cefuroxime. Among the isolates, 33 (66.0%) patients were resistant to and 12 (24.0%) patients were sensitive to in Cefoxitin. Among the isolates, 10 (20.0%) patients were resistant to and 20 (40.0%) patients were sensitive to in Cotrimoxazole. Among the isolates, 30 6.0%) patients were resistant to and 15 (30.0%) patients were sensitive to in Ciprofloxacin. Among the isolates, 23 (46.0%) patients were resistant to and 17 (34.0%) patients were

Table 1: Distribution of organism isolated

Organism Isolated	Frequency	Percentage
Acinetobacter sp.	3	6.0
Enterobacter cloacae	4	8.0
Escherichia coli	4	8.0
Klebsiella pneumoniae	5	10.0
Morgagnella morgagni	2	4.0
Pesudomonas aeruginosa	11	22.0
Proteus mirabilis	1	2.0
Proteus penneri	1	2.0
Proteus vulgaris	1	2.0
Serratia marcescens	2	4.0
Staphylococcus auerus (MRSA)	8	16.0
Staphylococcus aureus	6	12.0
Staphylococcus hemolyticus	2	4.0
Total	50	100.0

sensitive to in Levofloxacin. Among the isolates, 10 (20.0%) patients were resistant to and 13 (26.0%) patients were sensitive to in Clindamycin. Among the isolates, 15 (30.0%) patients were resistant to and 6 (12.0%) patients were sensitive to Erythromycin. Among the isolates, 11 (22.0%) patients were resistant to and 25 (50.0%) patients were sensitive to Amikacin. Among the isolates, 16 (32.0%) patients were resistant to and 28 (56.0%) patients were sensitive to Gentamicin. Among the isolates, 4 (8.0%) patients were sensitive to Azithromycin. Among the isolates, 13 (26.0%) patients were resistant to and 16 (32.0%) patients were sensitive to Tetracycline. Among the isolates, 2 (4.0%) patients were resistant to and 18 (36.0%) patients were sensitive to Linezolid. Among the isolates, 2 (4.0%) patients were resistant to and 19 (38.0%) patients were sensitive to Vancomycin. Among the isolates, 8 (16.0%) patients were resistant to and 28 (56.0%) patients were sensitive to Meropenem. Among the isolates, 9 (18.0%) patients were resistant to and 23 (46.0%) patients were sensitive to Piperacillin/Tazobactam. Among the isolates, 1 (2.0%) patient were resistant to and 5 (10.0%) patients were sensitive to Colistin (Table 2).

Table 2: Distribution of all parameters

		Frequency	Percentage
Amoxicillin-Clavulanic acid	No	10	20.0
	Resistant	31	62.0
	Sensitive	9	18.0
	Total	50	100.0
Cefuroxime	No	5	10.0
	Resistant	30	60.0
	Sensitive	15	30.0
	Total	50	100.0
Cefoxitin	No	5	10.0
	Resistant	33	66.0
	Sensitive	12	24.0
	Total	50	100.0
Cotrimoxazole	No	20	40.0
	Resistant	10	20.0
	Sensitive	20	40.0
	Total	50	100.0
Levofloxacin	No	10	20.0
	Resistant	23	46.0
	Sensitive	17	34.0
	Total	50	100.0
Clindamycin	No	27	54.0
	Resistant	10	20.0
	Sensitive	13	26.0
	Total	50	100.0
Erythromycin	No	29	58.0
	Resistant	15	30.0
	Sensitive	6	12.0
	Total	50	100.0
Amikacin	No	14	28.0
	Resistant	11	22.0
	Sensitive	25	50.0
	Total	50	100.0
Gentamicin	No	6	12.0
	Resistant	16	32.0
	Sensitive	28	56.0
	Total	50	100.0
Azithromycin	No	46	92.0
	Sensitive	4	8.0
	Total	50	100.0
Tetracycline	No	21	42.0
	Resistant	13	26.0
	Sensitive	16	32.0
	Total	50	100.0
Linezolid	No	30	60.0
	Resistant	2	4.0
	Sensitive	18	36.0
	Total	50	100.0
Vancomycin	No	29	58.0
	Resistant	2	4.0
	Sensitive	19	38.0
	Total	50	100.0
Meropenem	No	14	28.0
	Resistant	8	16.0
	Sensitive	28	56.0
	Total	50	100.0
Piperacillin/Tazobactam	No	18	36.0
	Resistant	9	18.0
	Sensitive	23	46.0
	Total	50	100.0
Colistin	No	44	88.0
	Resistant	1	2.0
	Sensitive	5	10.0
	Total	50	100.0

DISCUSSION

The present study was a Prospective, Descriptive study. This study was conducted 12 months at Department of Orthopaedics, Calcutta National Medical College. 50 patients were included in this study. The aim of this study was to identify the organisms causing chronic osteomyelitis in a tertiary care setting. We also studied the anti-microbial resistance and sensitivity patterns. We correlated the origin of the infection with the varied pathogen profile. Though it was a small study population, a wide variety of organisms with a wide range of antibiotic sensitivities were found. This emphasises the importance of identifying the offending bacteria by pus and tissue culture and thereafter tailoring the antimicrobial therapy according to sensitivity pattern. Often, when a patient comes with features of suspected osteomyelitis, there is a duration required between the clinical diagnosis and laboratory confirmation of the pus/tissue sample. Usually, it takes around 48 hrs to get the culture sensitivity report to arrive. As a result, the administration of proper antibiotic gets delayed. My study would come to the rescue as, by identifying the antibiogram pattern and antimicrobial resistance, we will be able to guess the most appropriate empirical antibiotic by clinically judging the disease aetiology and start the therapy as soon as the sample is obtained.

Khatun *et al*.[9] showed that bacterial infections are often found to cause morbidity and mortality around the globe. Indiscriminate use of antibiotic for

treatment of such infections is reported to cause selective pressure and increase in drug resistance. Emergence of antimicrobial resistance is a growing concern for people of all age having bacterial infections.

Masyeni *et al*.[10] observed that antimicrobial resistance (AMR) is emerging global health problem worldwide. Resistant bacteria generate higher morbidity and mortality rates. Lack of awareness of AMR includes self-antibiotic prescription, lack of access to get the bacteria and antibiograms data were leading factors for AMR development.

Our study showed that, most of the patients were Resistant to Amoxicillin-Clavulanic acid [31(62.0%)]. (Z = 4.2697). And a greater number of patients were Resistant to Cefuroxime [30 (60.0%)]. A greater number of patients were also Resistant to Cefoxitin [33 (66.0%)]. Therefore, it can be said that bacteria are already resistant to most commonly prescribed broad-spectrum gram-positive antimicrobials such as Penicillin and third generation Cephalosporins.

Aminu and Yahaya[11] observed that Microbial contamination of fomites such as currency notes is of public health concern as contaminated materials might act as vehicle for the transmission of pathogenic and drug resistant organisms. Antibiotic susceptibility testing was done using disc diffusion method to detect the presence of resistant isolates including multidrug resistant organisms (MDR) and methicillin resistant *Staphylococcus aureus* (MRSA). The results of the study revealed that 84.7% of currencies were contaminated with pathogenic organisms. Bacteria isolated from currencies circulating in hospital were more resistant to antibiotics than non-hospital source isolates ($p<0.05$).

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In our study, 14 cultures showed the growth of *Staphylococcus aureus*, out of which 8 (57%) were MRSA. This rising rate of MRSA may be addressed to the overenthusiastic use of empirical antibiotics without appropriate culture report.

Sheehy *et al*.[12] found *Staphylococcus aureus* to be the most commonly isolated pathogen among a wide range of organisms, which included Gram-negative bacilli, anaerobes and coagulase negative staphylococci.

We also found that, *Pseudomonas aeruginosa* was the most common isolated organism in our study (11 or 22%). Second most common isolated organism was MRSA (8 or 16%).

In our study, out of 50 patients, most of the patients were 21-30 years of age [13 (26.0%)], the mean Age of patients was [35.9200±14.5516].

We found that, male population [31 (62.0%)] was higher than the female population [19(38.0%)].

Anning *et al*.[13] showed that the emergence and upsurge of Multiple Antibiotic Resistant (MDR) Enterobacteriaceae in the environment is a cause of concern as this can result in an outbreak and spread to healthcare settings. MDR Enterobacteriaceae have been associated with high morbidity and mortality due to delay in selecting and delivering active therapy in time. The study was conducted to investigate the level of contamination of raw meat and Ghanaian coins in circulation at Cape Coast Metropolis.

Goh *et al*.[14] diabetic foot infection is a worldwide health problem is commonly encountered in daily practice. This study was conducted to identify the microbiological profile and antibiotic sensitivity patterns of causative agents identified from diabetic foot infections (DFIs). In addition, the assessment included probable risk factors contributing to infection of ulcers that harbour multidrug-resistant organisms (MDROs) and their outcomes.

We observed that, a greater number of patients had Resistance to Levofloxacin [23 (46.0%)]. A lesser number of patients had Resistance to Clindamycin [10 (20.0%)]. In our study, lower number of patients were resistant to Amikacin [11 (22.0%)].

Aminu and Yahaya[11] observed that Microbial contamination of fomites such as currency notes is of public health concern as contaminated materials might act as vehicle for the transmission of pathogenic and drug resistant organisms. Ciprofloxacin had the greatest activity (40-100%) against the isolates. The study revealed that Currency notes circulating in hospital are highly contaminated with potentially pathogenic bacteria including drug resistant healthcare associated pathogens, MRSA and MDR organisms.

In our study, a greater number of patients had Resistance to Ciprofloxacin [30 (60.0%)]. And a smaller number of patients had Resistance to Cotrimoxazole [10 (20.0%)].

We found that, lower number of patients were Sensitive to Azithromycin [4 (8.0%)]. Lower number of patients also had Resistance to Tetracycline [13 (26.0%)]. Lower number of patients had Resistance to Linezolid, Vancomycin [2 (4.0%)].

Vijayakumar *et al*.[15] found that osteomyelitis has been continuing as the most important cause of morbidity among patients with bone infections. Constant change in the trend of organisms involved and resistance pattern has made management of osteomyelitis cases difficult. Antibiotic sensitivity testing of gram-positive organisms showed hundred percent sensitivity to vancomycin and gram-negative bacteria showed highest sensitivity to Cefoperazone+Sulbactam, Piperacillin+Tazobactam, Meropenem and Imipenem. Osteomyelitis caused by methicillin resistant *staphylococcus aureus* and carbapenem resistance gram negative bacteria is a serious concern. Since multidrug resistant strains have emerged in osteomyelitis cases, emphasis should be given for hygiene and targeted antimicrobial therapy.

Gysin *et al*.[16] observed that bacterial superinfections associated with COVID-19 are common in ventilated ICU patients and impact morbidity and lethality. *Pseudomonas aeruginosa* (46%) and Enterobacterales (36%) comprised the two largest etiologic groups. Drug resistance in *P. aeruginosa* isolates was high for piperacillin/tazobactam (65.6%), cefepime (56.3%), ceftazidime (46.9%) and meropenem (50.0%). Enterobacterales isolates showed slightly lower levels of resistance to piperacillin/tazobactam (32%), ceftriaxone (32%) and ceftazidime (36%).

Lang *et al*.[17] showed that empiric antibiotic therapy for suspected vertebral osteomyelitis (VO) should be initiated immediately in severely ill patients and might be necessary for culture-negative VO. Significantly higher rates of resistances were seen in the HAVO cohort for mono-therapies with meropenem (36.4%), piperacillin–tazobactam (31.8%), ceftriaxone (27.3%) and co-amoxiclav (31.8%). The broadest antimicrobial coverage was achieved with either a combination of piperacillin–tazobactam + vancomycin (CAVO: 100.0%; HAVO: 90.9%) or meropenem + vancomycin (CAVO: 100.0%; HAVO: 95.5%). Healthcare association is common in VO.

It was found in our study that; a greater number of patients were Sensitive to Meropenem [28 (56.0%)]. Higher number of patients had Sensitivity towards Piperacillin/Tazobactam [23 (46.0%)].

CONCLUSION

We demonstrated the microbiological profile, antibiogram pattern and clinical outcome in patients with suspected osteomyelitis, in a tertiary care hospital. The causative organism in chronic osteomyelitis was found to be related to the aetiology of the infection. Majority of haematogenous chronic osteomyelitis involved a solitary Gram-positive organism, most commonly *Staphylococcus aureus*. Incidence of Gram-negative infections were found to be higher than previously reported. Specially in post-traumatic and post-operative infections, *Pseudomonas aeruginosa* were commonly isolated. Resistance to broad spectrum Penicillin, third generation Cephalosporins and even Fluoroquinolones were higher than previously reported. Proper identification of the causative organism and antibiogram sensitivity testing plays a pivotal role in controlling the infection. With my study, we would be able to make a table of most appropriate antibiotics for suspected organisms according to the disease aetiology and it would help in starting the empirical therapy while the culture report arrives.

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