Original Article

DOI: 10.7860/JCDR/2023/62082.17785

Microbiology Section

Microbiological Profile of Osteomyelitis and Antibiotic Resistance Pattern of Bacterial Isolates with Special Reference to MDR Strains at a Tertiary Care Hospital, Kanpur, Uttar Pradesh, India

ROHAN NIGAM[1], SUNEET KUMAR YADAV[2], R SUJATHA[3], DEEPAK SAMEER BIND[4], NASHRA AFAQ[5]

ABSTRACT

Introduction: Osteomyelitis is an inflammatory process that affects bone due to the contiguous infection, direct inoculation, or haematogenous spread of microorganisms. It is an infectious disease that is difficult to diagnose and treatment is complex because of its heterogeneity, pathophysiology, clinical presentation and management.

Aim: To determine microbiological profile osteomyelitis and antibiotic resistance pattern of bacterial isolates with special reference to Multidrug Resistance (MDR) strains.

Materials and Methods: A cross-sectional study was conducted in the Department of Microbiology and Department of Orthopedics Rama Medical College Hospital and Research Centre Kanpur, Uttar Pradesh, India. A total of 100 samples from osteomyelitis cases were aerobically cultured and isolates from culture positives were identified by standard procedures. Antimicrobial Susceptibility Testing (AST) was done following Clinical and Laboratory Standards Institute (CLSI) guidelines. Staphylococcal isolates were screened for methicillin resistance and Gram negative bacilli were screened for MDR production.

Results: Out of 100 samples, 76% were culture positive and 24% were culture negative. Males were more affected than females. Staphylococcal spp. (47.3%) was predominant, *E. coli* (14.4%) and *Klebsiell*a spp. (11.8%), *Pseudomonas* spp. (9.2%), *Proteus* spp. (5.2%), Coagulase-Negative Staphylococci (CoNS) (3.9%). Among the MDR strains, Methicillin Resistant *Staphylococcus aureus* (MRSA) was 44.4%. All the MDR Staphylococcal isolates were 100% sensitive for linezolid. Among the MDR Gram negative bacilli were Extended Spectrum Beta Lactamases (ESBL) (50%), AmpC (17.6%) and Metallo Beta Lactamase (MBL) (14.7%) and they were 100% sensitive for polymixin B and colistin.

Conclusion: The microbiological profile of osteomyelitis in the present study showed high prevalence of MRSA44% as the commonest agent, sensitive only to linezolid. *E. coli* ESBL (50%) and MBL-14.7% were sensitive only to colistin and polymixin B, therefore proper infection control practices and antibiotic policy has to be followed to reduce the incidence of MDR strains.

Keywords: Extended Spectrum beta lactamase, Metalobetalactamases, Methicillin resistant *Staphylococcus aureus*, Multidrug resistance

INTRODUCTION

The word “osteomyelitis” is derived from the ancient Greek words *osteo* (meaning bone) and *muelinos* (meaning marrow) and simply means an infection of medullar portion of the bone [1]. The term osteomyelitis was first used by the French surgeon Edouard Chassaignac in 1852, who defined the disease as an inflammatory process accompanied by bone destruction and is caused by an infecting microorganism [2]. Osteomyelitis is an inflammatory process that affects bone due to the contiguous infection, direct inoculation, or haematogenous spread of microorganisms [3]. Current interest in this condition has increased due to recent changes in the epidemiology, pathogenesis, diagnosis, treatment, and prognosis of the disease [4,5].

However, it is not a single entity; this disease is differentiated according to the aetiology, pathogenesis, and degree of bone involvement, as well as age and the immune condition of the patient [6]. The reported incidence has increased due to co-morbidities such as diabetes mellitus, peripheral vascular disease, trauma and surgery [7]. After an open fracture, the incidence of osteomyelitis can range from 2-16% depending on the type of injury and the treatment administered [8]. It can involve different structures such as the bone marrow, cortex, periosteum, and parts of the surrounding soft tissues, or remain localised [9]. Osteomyelitis mostly affects the growing ends of long bones and it is more common in the lower extremity at metaphysis of femur and proximal end of tibia [10].

Various microorganisms can reach to bone through blood and cause inflammation in bone tissue; rarely soft tissue infection may lead to bone damage. Microorganism reach to the metaphysis of bone through blood flow from skin wound, upper respiratory tract infection, periodontitis and any other infectious region. Bone metaphysic is a region full of blood vessels and slow blood stream which can spread the infection. Direct trauma to bone may cause osteomyelitis [11].

The two most widely used classification systems for osteomyelitis are by Waldvogel FA et al., and Cierny G et al., [12,13]. Under the Waldvogel system, osteomyelitis is first described according to duration, either acute or chronic. Second, the disease is classified according to source of infection, as haematogenous when it originates from a bacteremia or as contiguous focus when it originates from an infection in a nearby tissue. A final category of the classification is vascular insufficiency [14]. The Cierny-Mader osteomyelitis classification combines both anatomic factors (medullar, superficial, localised, or diffuse osteomyelitis) and physiological classes (healthy host, systemic and/or local compromise, and treatment worse than the disease) [15,16]. This classification applies best to long and large bones and it is not very useful for the digits, small bones, or the skull [17-19].

Diagnosis of this condition mainly depends on strong clinical suspicion in non healing ulcer especially in diabetic patient, radiological findings of translucency of bone with patchy sclerosis and adjacent periosteal bone reaction. Magnetic Resonance Imaging (MRI) and blood culture along with deeper bone biopsy or culture and pus culture are mainstay in management protocol of these patients [20]. The bacteria most commonly causing chronic osteomyelitis are *Staphylococcus aureus,* Coagulase negative *Staphylococcus, Pseudomonas* spp., *E. coli, Proteus* spp., *Klebsiella* spp., *Enterococcus* spp., *Enterobacter* spp. and anaerobes like *Peptostreptococcus* spp., *Bacteroides* spp., *Clostridium* spp. Rarely *Salmonella* spp. and *Actinomycetes* [21], *Staphylococcus aureus* constitutes 50-75% cases of chronic osteomyelitis. In most of the cases infection is monomicrobial, infection with multiple organisms are usually seen in diabetes mellitus patients with ulcer in foot [22].

Osteomyelitis is an ongoing problem due to emergence of MDR strains among bacterial pathogens. Beta lactamases are the most evolving mechanism of antibiotic resistance among the family Enterobacteriaceae due to the selective pressure imposed by inappropriate use of third generation cephalosporins, most often encountered in Intensive Care Unit (ICU) settings [23]. ESBL and AmpC enzymes are the most common known beta lactamases. Carbapenems represented a great advance for the treatment of serious bacterial infections caused by beta lactam resistant bacteria [24]. But extensive and unnecessary use of the carbapenems facilitated the emergence of carbapenem resistant bacteria which produced carbapenem hydrolysing enzyme MBL, so called because they contain metal ion that works as a co-factor for enzymatic activity [25]. MRSA is prevalent worldwide and are an important cause of nosocomial infection, resulting in increased morbidity and mortality in the hospital settings worldwide [26].

The study was therefore undertaken to determine the microbiological profile of these cases of osteomyelitis and also to ascertain the antibiotic resistance pattern of these isolates and to find out the MDR strains at a tertiary care centre. It will go a long way in helping the clinician in deciding upon the treatment regime for these patients. The data generated by these studies will also help in formulating hospital antibiotic policies.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the Department of Microbiology and Department of Orthopaedics Rama Medical College Hospital and Research Centre, Kanpur, Uttar Pradesh, India, from January 2020 to December 2020. Samples from outpatients and inpatients admitted to the orthopedic ward suspected to have osteomyelitis was collected after obtaining consent from patients. Ethical clearance was taken from the Institutional Ethical Committee (IEC) reference number (MEC/Reg.N./ECR/872/Inst/2016).

Sample Size: $n=4PQ/L^2$ Where, P=Prevalence, Q=100-p, L=Allowable error, If the allowable error is 10% SS (n)=4×57×43/100

Sample Size n=9804/100=98.04

So, in order to cover up the lost to follow-up, drop-out rate and non response rate the sample size taken in our research study was 100 [27].

Inclusion criteria: Clinically, diagnosed cases of osteomyelitis belonging to all age group and both sexes were included in the study whose samples like pus, pus swabs, sequestrum of bone, and synovial fluid, collected under aseptic precautions, was included and processed for culture and sensitivity.

Exclusion criteria: Patients with malignant and benign tumours, cysts, non infected, non unions, old trauma, and osteomyelitis patients on antibiotic therapy were excluded from the study.

Sample collection and preliminary identification by biochemical tests: All clinical specimens, sequestrum/excised tissue/pus samples received from orthopaedic outpatient and inpatient department were collected in a sterile container. Then the preliminary identification was done by standard procedures (Gram staining and Biochemical Tests). The culture isolates were identified by Gram stain morphology, colony characters and biochemical reactions [28].

Antimicrobial susceptibility test: Antibiotic susceptibility pattern was done on Mueller Hinton Agar by Kirby-Bauer disc diffusion method as recommended by CLSI. The plates were then incubated at 37°C for 18-24 hours. The zones of complete growth of inhibition around each of the disc were measured by using a scale. The interpretation of zone size into sensitive, intermediate or resistance was based on the standard zone size interpretant chart as per CLSI guidelines (2020) [29]. The control strains used were *E. coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853.

STATISTICAL ANALYSIS

The data was entered in Microsoft excel and results were expressed in terms of frequency and percentage.

RESULTS

In the present study, out of 100 samples, there were 76% cases reported for the culture positive and culture negative cases 24%. Tibia was the most common bone involved in osteomyelitis (49%) [Table/Fig-1] and commonest predisposing factor was seen in trauma 48 (48%) cases, followed by postoperative infections 20 (20%), orthopaedic implants 18 (18%), Implant/Diabetes mellitus 8 (8%) and least for Trauma/Diabetes mellitus 2 (2%) [Table/Fig-2]. Out of 100 samples, male were 72% and females were 28%. Staphylococcal spp. (47.4%) was predominant, *E. coli* (14.4%) and *Klebsiell*a spp. (11.8%), *Pseudomonas* spp. (9.2%), *Proteus* spp.(5.2%), CoNS (4.0%) [Table/Fig-3]. Out of 34 organisms isolated, most effective drug of Gram negative bacilli was colistin, followed by polymyxin B 100 (%), tigycyclin, meropenem, imipenem, and piperacillin/tazobactum [Table/Fig-4]. Among the MDR-Gram negative bacilli were ESBL (50%), AmpC (17.6) and

Bone involved	N (%)
Tibia	49 (49)
Femur	34 (34)
Fibula	4 (4)
Ulna	3 (3)
Radius	2 (2)
Metacarpal	2 (2)
Metatarsal	2 (2)
Humerus	2 (2)
Calcaneus	2 (2)
Total	100

[Table/Fig-1]: Showing bones involved in osteomyelitis.

Predisposing factor	N (%)
Trauma	48 (48)
Orthopaedic implants	18 (18)
Postoperative infection	20 (20)
Implant/Diabetes mellitus	8 (8)
Postoperative infection/Diabetes mellitus	4 (4)
Trauma/Diabetes mellitus	2 (2)
Total	**100**

[Table/Fig-2]: Showing predisposing factors for osteomyelitis.

Organisms	No. of organisms	Percentage (%)
Staphylococcus aureus	36	47.4
Staphylococcus lugdenensis	3	4.0
CoNS	3	4.0
Escherichia coli	11	14.4
Klebsiella spp.	9	11.8
Pseudomonas spp.	7	9.2
Proteus spp.	4	5.2
Acinetobacter baumanni	3	4.0
Total	76	100

[Table/Fig-3]: Showing various organisms isolated.

Antibiotics	*E. coli* (11)	*Klebsiella* spp. (9)	*Pseudomonas* spp. (7)	*Proteus* spp. (4)	*Acinetobacter* spp. (3)
Amoxyclav	1 (9%)	0	0	2 (50%)	0
Gentamicin	7 (63.6%)	5 (55.5%)	4 (57.2%)	3 (75%)	1 (33.3%)
Amikacin	8 (72.7%)	5 (55.5%)	4 (57.1%)	3 (75%)	1 (33.3%)
Ciprofloxacin	2 (18.2%)	0	1 (14.2%)	1 (25%)	0
Cotrimoxazole	2 (18.2%)	0	0	3 (75%)	0
Cefoxitin	3 (27.3%)	0	0	3 (75%)	0
Piperacillin	1 (9%)	0 (0%0	4 (57.2%)	4 (100%)	0
Piperacillin/ Tazobactum	4 (36.4%)	0	7 (100%)	4 (100%)	0
Ceftazidime	5 (45.4%)	0	4 (57.2%)	2 (50%)	0
Aztreonem	4 (36.4%)	2 (18.2%)	5 (71.4%)	2 (50%)	0
Ceftriaxone	1 (9%)	0	3 (42.8%)	2 (50%)	0
Cefotaxime	1 (9%)	0	1 (14.2%)	2 (50%)	0
Cefepime	2 (18.25)	0	0	2 (50%)	0
Meropenem	11 (100%)	9 (100%)	4 (57.2%)	3 (75%)	3 (100%)
Imipenem	11 (100%)	9 (100%)	4 (57.2%)	3 (75%)	3 (100%)
Colistin	11 (100%)	9 (100%)	6 (85.7%)	4 (100%)	3 (100%)
Polymyxin B	11 (100%)	9 (100%)	6 (85.7%)	4 (100%)	3 (100%)
Tigecycline	11 (100%)	8 (88.8%)	0	2 (50%)	3 (100%)

[Table/Fig-4]: Antibiotic sensitivity pattern of Gram negative bacilli.

Organisms	No. of isolates	ESBL producers no. (%)
E. coli	11	5 (45.4)
Klebsiella spp.	9	7 (77.7)
Acinatobacter spp.	3	3 (100)
Pseudomonas spp.	7	1 (14.2)
Proteus spp.	4	1 (25)
Total	34	17 (50)

[Table/Fig-5]: Showing Extended Spectrum β Lactamases (ESBL) producers.

Organism	No. of isolates	MBL producers no. (%)
E. coli	11	0
Klebsiella spp.	9	0
Acinatobacter spp.	3	0
Pseudomonas spp.	7	4 (57.1%)
Proteus spp.	4	1 (25%)
Total	34	5 (14.7%)

[Table/Fig-6]: Showing Metallo β Lactamases (MBL producers).

MBL (14.7%) and they were 100% sensitive for polymixin B and colistin [Table/Fig-5-7]. Out of 42 organisms isolated, most effective drug of GPC was vancomycin, teicoplanin, followed by gentamicin, amikacin, erythromycin, clindamycin and ciprofloxacin [Table/Fig-8].

MRSA was found to be 44.4%. All the MDR Staphylococcal isolates were 100% sensitive for linezolid [Table/Fig-9].

Oragnism	No. of isolates	AmpC producers No. (%)
E.coli	11	0
Klebsiella spp.	9	0
Acinetobacter spp.	3	1 (33.3)
Pseudomonas spp.	7	4 (57.1)
Proteus spp.	4	1 (25)
Total	34	6 (17.6)

[Table/Fig-7]: Showing AmpC producers.

Antibiotics	*S. aureus* (36)	*S. lugdenensis* (3)	CONS (3)
Penicillin	0	0	0
Ampicillin	1 (2.7%)	0	0
Gentamicin	34 (94.4%)	3 (100%)	3 (100%)
Amikacin	31 (86.1%)	0	3 (100%)
Ciprofloxacin	6 (16.6%)	0	0
Erythromycin	20 (55.5%)	0	1 (33.3%)
Clindamycin	20 (55.5%)	0	1 (33.3%)
Cotrimoxazole	14 (38.8%)	1 (33.3%)	0
Oxacillin	16 (44.4%)	0	1 (33.3%)
Cefoxitin	16 (44.4%)	0	1 (33.3%)
Linezolid	35 (97.2%)	3 (100%)	3 (100%)
Vancomycin	36 (100%)	3 (100%)	3 (100%)
Teicoplanin	36 (100%)	3 (100%)	3 (100%)

[Table/Fig-8]: Antibiotic sensitivity pattern of Gram positive isolates.

Antibiotics	MRSA (20)	MSSA (16)
Penicillin	0	0
Ampicillin	0	1 (6.2%)
Gentamicin	19 (95%)	15 (93.7%)
Amikacin	16 (80%)	15 (93.7%)
Ciprofloxacin	4 (20%)	2 (12.5%)
Erythromycin	11 (55%)	9 (56.2%)
Clindamycin	11 (55%)	9 (56.2%)
Cotrimoxazole	8 (50%)	6 (37.5%)
Oxacillin	0	16 (100%)
Cefoxitin	0	16 (100%)
Linezolid	19 (95%)	16 (100%)
Vancomycin	20 (100%)	16 (100%)
Teicoplanin	20 (100%)	16 (100%)

[Table/Fig-9]: Antibiotic sensitivity pattern of MRSA, MSSA.

DISCUSSION

Osteomyelitis is an inflammatory process that affects the bone due to the contiguous infection, direct inoculation, or haematogenous spread of microorganisms [1]. It is an infectious disease that is difficult to diagnose, and treatment is complex because of its heterogeneity, pathophysiology, clinical presentation, and management.

In the present study, an attempt was made to know the microbiological profile of osteomyelitis and their antibiotic sensitivity pattern. The results for culture positive was observed to be 76% and 24% were culture negative. This study was parallel to the study performed by the other authors where the culture positive results was found to be 86% and 89% whereas culture negative was observed to be 14% and 11%, respectively [30,31]. There was the another study performed by Shah RV and Sanghavi RV and Khatoon R et al., results of their study were also in correlation to the present study where the culture positive reported was 64% and 84% and the culture negative observed was 36% and 16% [32,33]. In the study by Padmini B and Deepa S reported the rate of culture positive to be 87% and the culture negative was observed

to be 13% [34]. Several predisposing factors associated with osteomyelitis in the present study is comparable with the studies done by various studies [Table/Fig-10] [30-33,35].

In the present study, the commonest bone affected in osteomyelitis was Tibia, followed by femur, which was in accordance with the studies done by other workers [Table/Fig-11] [30,33,35].

In the present study, total of 76 organisms were isolated. The predominant organisms isolated were *S. aureus* followed by *E. coli*, which was in accordance with other studies [Table/Fig-12] [30-33,35].

Study series	Publication year	Trauma (%)	Orthopaedic implants (%)	Postoperative infections (%)	Diabetes (%)
Suguneswari G et al., [35]	2013	53.0	4	26	17
Wadekar MD et al., [30]	2014	44	21	23	12
Singh A et al., [31]	2016	48	28	21	-
Shah RV and Sanghavi RV [32]	2017	76	21	40	13
Khatoon R et al., [33]	2017	57	30	34	04
Present study	2023	48	18	20	14

[Table/Fig-10]: Comparison of predisposing factors [30-33,35].

Bone involved	Suguneswari G et al., [35] (2013)	Wadekar MD et al., [30] (2014)	Khatoon R et al., [33] (2017)	Present study (2023)
Tibia	58	23	55	**49**
Femur	31	48	51	**34**
Fibula	-	1	01	**4**
Ulna	2	4	02	**3**
Radius	1	3	02	**2**
Metacarpal	2	4	03	**2**
Metatarsal	1	3	05	**2**
Humerus	3	9	03	**2**
Calcaneus	2	-	03	**2**
Malleolli	-	3	-	-
Patella	-	2	-	-

[Table/Fig-11]: Comparison of different bones affected in osteomyelitis with other workers studies [30,33,34].

Antibiotic sensitivity was carried out for 100 isolates by Kirby-Bauer disc diffusion method. Of 42 Gram positive isolates, were 100% sensitive to vancomycin to linezolid and teicoplanin. Among 34 Gram negative isolates were 100% sensitive to meropenem, imipenem and polymixin B and colistin. Similar sensitivity was reported by Khatoon R et al., [33]. AST pattern of GPC and GNB of present study and other studies is shown in [Table/Fig-13] [30,32,33].

In the present study, it was observed that the rate of MRSA was found to be (44.4%), ESBL (50%), AmpC (17.6%) and MBL (14.7%). This study was in support with the study performed by Khatoon R et al., where the rate of MRSA was (43.1%), ESBL (51.6%) and AmpC (24.2%) and MBL(14.5%) [33]. In the current study, MRSA isolated was observed to be 16 (44.44%) which was in accordance with the study by Khatoon R et al., [33]. There were another study also performed by the other author where the rate of MRSA isolated was observed to be 52% [31] and the study by Padmini B and Deepa S also supported present study where the rate of MRSA was observed to be 66% [34]. There was a study by Suguneswari G et al., which was in contrast with the current study where the MRSA isolates was observed to be 23% [35].

Clinical symptoms of osteomyelitis can be non specific and difficult to recognise. Signs and symptoms change depending on the category of infection, organism and anatomical location of the disease. From the present study, it was quite clear that drug resistance bacteria along with MRSA strains are becoming alarming because of their increased resistance towards antibiotics-like amikacin, netilmycin, and to a lesser extent to vancomycin and linezolid that leaves the clinicians with less choice to use the appropriate drug for treatment of chronic osteomyelitis. It is high time to emphasise on surveillance to monitor change in aetiology and to follow one health policy to impede the menace created by MDR bacteria.

Limitation(s)

The drawback of the present research study was the small sample size. More insights about the microbiological profile of osteomyelitis and its antibiotic resistance pattern would have been generated

Study series	Publication year	*S. aureus* (%)	*S. lugdenensis* (%)	*S. epidermidis* (%)	CoNS (%)	*E. coli* (%)	*Klebsiella* spp. (%)	*Acinetobacter* spp (%)	*P. mirabilis* (%)	*P. aeruginosa* (%)
Suguneswari G et al., [35]	2013	53.8	-	13.9	-	-	5.82	6.97	9.30	10.6
Wadekar MD et al., [30]	2104	33	-	-	13.0	12	14	-	3	17
Singh A et al., [31]	2016	53	-	-	5.0	7	9	-	2	2
Shah RV and Sanghavi RV [32]	2017	60.6	-	-	-	4.04	13.1	6.06	-	13.1
Khatoon R et al., [33]	2017	34.2	-	-	14.2	19	12.5	-	5.0	18.3
Present study	**2023**	**47.4**	**4**	**-**	**4**	**14.4**	**11.8**	**4**	**5.2**	**9.2**

[Table/Fig-12]: Comparison of organisms isolated by various workers studies [30-33,35].

Publication year	Study	Antibiotic sensitivity GPC isolates	Antibiotic sensitivity GNB isolates	Place
2014	Wadekar MD et al., [30]	Amikacin, Linezolid, Vacomycin	Amikacin, Imipenem	Mysore medical college (Karnataka)
2017	Shah RV and Sanghavi RV [32]	Linezolid, Vancomycin	Piperacillin/tazobactum and Ceftazidime	Shri MP SHAH G Medical College (Gujarat)
2017	Khatoon R et al., [33]	Vancomycin, Linezolid, Teicoplanin	Imipenem, Colistin	Integral University Lucknow (UP)
2023	Present study	Vancomycin, Linezolid, Teicoplanin	Meropenem, Imipenem Colistin, Polymysin B	RMCH&RC Kanpur (UP)

[Table/Fig-13]: Comparision of Antibiotic Susceptibility Pattern of (GPC, GNB) with other workers [30,32,33].

by a large sample size. Also, the present work was self-supported so there was a lack of financial help because of which the gene responsible for MDR could not be targeted.

CONCLUSION(S)

Isolation of causative organism and performance of antibiotic sensitivity studies are critical in the selection of antimicrobial agents. Therefore antibiotic therapy should be guided carefully by culture and sensitivity is an effective treatment modality. This will prevent development of drug resistance and indiscriminate use of antibiotics.

REFERENCES

[1] Lew DP, Waldvogel FA. Osteomyelitis. Lancet. 2004;364(9431):369-79.
[2] Romanò CL, Romanò D, Logoluso N, Drago L. Bone and joint infections in adults: A comprehensive classification proposal. Eur Orthop Traumatol. 2011;1(6):207-17.
[3] Lew DP, Waldvogel FA. Osteomyelitis. N Engl J Med. 1997;336:999-1007. PMID: 9077380.
[4] Souza Jorge L, Gomes Chueire A, Baptista Rossit AR. Osteomyelitis: Current challenge. Braz J Infect Dis. 2010;14(3):310. PMID: 20835519.
[5] Conterno LO, Turchi MD. Antibiotics for treating chronic osteomyelitis in adults. Cochrane Database Syst Rev. 2013;9:CD004439. Doi: 10.1002/14651858.CD004439.
[6] Pineda C, Vargas A, Rodriguez AV. Imaging of osteomyelitis: Current concepts. Infect Dis Clin N Am. 2006;20:789-825.
[7] Hatzenbuehler J, Pulling TJ. Diagnosis and management of osteomyelitis. Am Fam Physician. 2011;84(9):1027-33. PMID: 22046943.
[8] Kindsfater K, Jonassen EA. Osteomyelitis in grade II and III open tibia fractures with late debridement. J Orthop Trauma. 1995;9(2):121-27. PMID: 7776031.
[9] De Boeck H. Osteomyelitis and septic arthritis in children. Acta Ortho Belg. 2005;71(5):505-15.
[10] Maraga NF, Gomez MM, Rathore MH. Outpatient parenteral antimicrobial therapy in osteoaricular infection in children. J Paed Orthop. 2002;22(4):506-10.
[11] Mader JT, Calhoun J, et al. Genral concept of osteomyelitis. In: Principal and practice of Infectious diseases,(Eds.). 6th Edn Elsevier, Churchill Livingstone, Philadelphia. 2005; pp:1182-1196.
[12] Waldvogel FA, Medoff G, Swartz MN. Osteomyelitis- A review of clinical features, therapeutic considerations and unusual aspects3: osteomyelitis associated with vascular insufficiency. N Engl J Med. 1970;282:316-22.
[13] Cierny G, Mader JT, Penninck JJ. A clinical staging system for adult osteomyelitis. Clin Orthop Relat Res. 2003;414:07-24.
[14] Calhoun JH, Manring MM, Shirtliff M. Osteomyelitis of the long bones. Seminplast Surg. 2009;23:59-72.
[15] Chihara S, Segreti J. Osteomyelitis. Dis Mon. 2010;56(1):05-31.
[16] Sia IG, Berbari EF. Infection and musculoskeletal conditions: Osteomyelitis: Best Pract Res Clin Rheumatol. 2006;20(6):1065-81.
[17] Dagan R. Management of acute hematogenous osteomyelitis and septic arthritis in the pediatric patient. Pediatr Infect Dis J. 1993;12(1):88-92.
[18] Zuluaga AF, Galvis W, Saldarriaga JG, Agudelo M, Salazar BE, et al. Etiologic diagnosis of chronic osteomyelitis. Arch Intern Med. 2006;166:95-100.
[19] Berbari EF, Steckelberg JM, Osmon DR. Osteomyelitis. In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 7th ed. Philadelphia, PA: Churchill Livingston 2010. 1457- 68.
[20] Abid AS, Ehan AH, Yonis AR. Epidemiological and bacteriological study of chronic osteomyelitis. Tikrit Medical Journal. 2008;14(1):59-62.
[21] Mandell GL, Bennett JE, Raphael D. Mandell, douglas and bennett's principles and practice of infectious diseases. 7th ed.Philadelphia: Elsevier Churchill Livingstone. 2010;1:1322-30.
[22] Canale ST, James HB. Campbell's Operative Orthopaedics, 11th ed. vol. 1.Mosby: St Louis Missouri; 2008. Pp. 695-709.
[23] Rudresh SM, Nagarathnamma T. Extended spectrum β-lactamase producing Enterobacteriaceae & antibiotic coresistance. Indian J Med Res. 2011;133:116-18.
[24] Hodiwala A, Dhoke R, Urhekar AD. Incidence of metallo-betalactamase producing *Pseudomonas, Acinetobacter* & Enterobacterial isolates in hospitalised patients. Int J Pharmacy Biol Sci. 2013;3:79-83.
[25] Chakraborty D, Basu S, Das S. A study on infections caused by metallo beta lactamase producing Gram negative bacteria in intensive care unit patient AJ Infect Dis. 2010;6:34-39.
[26] Khadri H, Alzohairy M. Prevalence and antibiotic susceptibility pattern of methicillin-resistant and coagulase-negative Staphylococci in a tertiary care hospital in India. Int J Med Med Sci. 2010;2(4):116-20.
[27] Khonglah TG, Borgohain B, Khongwir, Ahmed KA. Extremity chronic osteomyelitis in a population of North East India: Epidemiology, clinical characteristics and management. International Journal of Research in Orthopaedics. 2020;4(6):06-23.
[28] Collee JG, Fraser AG, Marmion BP, Simmons et al. Mackie & mccartney, Practical Medical Microbiology, Churchill Livingstone, 2006; 14th edition: 135-141,152,255,796-798.
[29] Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Seven Informational Supplement; CLSI Document M02-A12 and M07-A10, CLSI. 2020.
[30] Wadekar MD, Anuradha K, Venkatesha D. Chronic osteomyelitis: aetiology and antibiotic susceptibility pattern. International Journal of Recent Trends in Science and Technology. 2014;9(3):337-40.
[31] Singh A, Biswas PP, Sen A. Bacteriological profile of osteomyelitis cases with special reference to antibiotic susceptibility pattern of isolates in a tertiary care hospital of eastern India. J Evolution Med Dent Sci. 2016;5(53):3496-501. Doi: 10.14260/jemds/2016/807.
[32] Shah RV, Sanghavi RV. Bacteriological profile in chronic osteomyelitis. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2017;16(10):47-50.
[33] Khatoon R, Khan SA, Jahan N. Antibiotic resistance pattern among aerobic bacterial isolates from osteomyelitis cases attending a Tertiary care hospital of North India with special reference to ESBL, AmpC, MBL and MRSA production. Int J Res Med Sci. 2017;5:482-90.
[34] Padmini B, Deepa S. Microbiological profile of chronic osteomyelitis in a tertiary care hospital. Int J Curr Microbiol App Sci. 2021;10(05):826-34.
[35] Suguneswari G, Heraman Singh A, Basu R. Bacteriological profile of osteomyelitis in a tertiary care hospital at Visakhapatnam, Andhra Pradesh. Int J Cur Res Rev. 2013;05(20):52-58.

PARTICULARS OF CONTRIBUTORS:
1. Microbiologist, Department of Microbiology, Regency Hospital, Kanpur, Uttar Pradesh, India.
2. Assistant Professor, Department of Microbiology, Rama Medical College, Kanpur, Uttar Pradesh, India.
3. Professor, Department of Microbiology, Rama Medical College, Kanpur, Uttar Pradesh, India.
4. Tutor, Department of Microbiology, Rama Medical College, Kanpur, Uttar Pradesh, India.
5. Research Associate, Department of Microbiology, Rama Medical College, Kanpur, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. R Sujatha,
Professor, Department of Microbiology, Rama Medical College,
Kanpu-209217, Uttar Pradesh, India.
E-mail: drsujatha152@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 07, 2022
- Manual Googling: Jan 12, 2023
- iThenticate Software: Feb 21, 2023 (20%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 06, 2022**
Date of Peer Review: **Jan 06, 2023**
Date of Acceptance: **Feb 27, 2023**
Date of Publishing: **Apr 01, 2023**