Bacterial showdown: Chronic Osteomyelitis Types vs their Microbial Foes

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Abstract
Osteomyelitis is a bone infection which occurs due to the extension from an infected joint or by direct invasion because of trauma or instrumentation. Inoculation of micro-organisms into the bone matrix may occur during fixation of the fracture, implanting prosthesis or due to trauma. The study was conducted from during April 2021 to March 2022 study period, the patients diagnosed as chronic pyogenic osteomyelitis by clinical and radiological examination were included in the study.

Etiology of osteomyelitis such as trauma (45%) and prosthetic implant in-situ (41%) are the major causes. Tibia (42%) followed by femur (34%) are the most common bones involved. Among the 100 cultures, total of 112 pathogens were isolated. Among 112 isolates, 77 (68.8%) were Staphylococcus aureus, 21 (18.8%) were Pseudomonas aeruginosa, 06 (5.4%) were Escherichia coli, 06 (5.4%) were Enterococcus faecalis and 02(1.6%) were Proteus mirabilis. The most common pathogen encountered during the study in cases of chronic pyogenic osteomyelitis was Staphylococcus aureus (68.8%). The antibiotic susceptibility testing showed that 36(46.8%) isolates were MRSA and rest 41 (53.2%) were MSSA. The 36 MRSA strains were tested for Vancomycin sensitivity by E-strip test and all were sensitive for Vancomycin.

Keyword: Chronic pyogenic osteomyelitis, Antibiotic sensitivity testing, MRSA, Staphylococcal bone infection.

Introduction

Osteomyelitis is a bone infection which occurs due to the extension from an infected joint or by direct invasion because of trauma or instrumentation[1]. Inoculation of micro-organisms into the bone matrix may occur during fixation of the fracture, implanting prosthesis or due to trauma. Prosthetic implants provide an environment which favours the micro-organisms for colonization and establishment of infection in the bone**.** The infectious agents attach to foreign material in the body and secrete glycocalyx that inhibits the host defence mechanism and action of antibiotics so that infection can be established which would be difficult to eradicate[6]. Various types of osteomyelitis are: hematogenous osteomyelitis, traumatic osteomyelitis and prothesis implant-failure osteomyelitis. The first description of chronic osteomyelitis was given 250 million years ago[3]. In earlier days, the mode of treatment was irrigation, immobilisation and bandaging. Later osteomyelitis was considered as a bone infection. The discovery and invention of modern medicine and more importantly formulating effective ways made us understand the disease and treat it effectively and to prevent it[10]. The osteomyelitis can be classified as acute and chronic osteomyelitis based on the onset, duration and progression of disease. Broadly the acute osteomyelitis has duration of disease progression not more than 2-4 weeks[4]. Chronic osteomyelitis has duration of disease progression for 6 weeks or more.

Chronic osteomyelitis is a dangerous sequel of delay in diagnosis and management of the acute stage of the disease[3]. The original acute infection of bone may have subsided, or it may persist as low-grade infection subject to repeated recrudescence of the acute process over many months or years[1]. Hematogenous infection with an organism with low virulence property may be chronic from onset. Infection introduced by external wound causes chronic osteomyelitis. Primarily the osteomyelitis is caused by bacterial pathogens. Other pathogenic organisms like fungi and virus can also cause osteomyelitis. It is mostly seen in pediatric age group and immunodeficient people[2]. Signs and symptoms of osteomyelitis include bone pain, pus draining to skin, fatigue, fever, malaise, sweating, weight loss and muscle spasm[1]. Clinical diagnosis of osteomyelitis relies on clinical features and X-Ray findings and MRI. The confirmed diagnosis is by blood culture and or culture of bone biopsy sample or exudate sample[3].

In osteomyelitis, there is isolation of infected material and slow resorption of infected material[1] seen among various types of osteomyelitis such as traumatic and implant failure. Infection of bone is a double-edged sword. Infection increases the blood flow, aggregation of cells, increased calcium transport to the site, which in turn helps in bone remodeling by callus formation.

On the other hand, it has downside which is infection of the bone leading to delayed healing and systemic infection. Hence this study was done to compare various types of osteomyelitis and their bacteriological profile and their anti-microbial susceptibility patterns.

Material and Methods

The study was carried out in Department of Microbiology, Government General Hospital and Medical College, Ongole, Andhra Pradesh from period April 2021 to March 2022. This

analytical study was approved by the Institutional Ethical Committee of Government Medical College, Ongole, Andhra Pradesh. The informed consent was taken from all the patients participating in this study. The patients diagnosed as chronic pyogenic osteomyelitis by clinical and radiological examination are included in the study. The exudate samples from the patients were sent to microbiology lab and processed as per standard microbiological procedures.

Results

Out of 100 cases of clinically diagnosed chronic pyogenic osteomyelitis processed,14 are hematogenous osteomyelitis, 45 are traumatic osteomyelitis and 41 are prosthetic implant osteomyelitis.

Bone involvement in chronic pyogenic osteomyelitis cases: Out of 100 cases of chronic pyogenic osteomyelitis, 34 showed femur bone involvement, 42 showed tibial bone involvement, 2 showed both tibial and femur bone involvement, 3 showed both tibial and fibular bone involvement, 18 showed humerus bone involvement and 1 showed facial bones such as ethmoid and maxillary bone involvement.

Bacterial Isolates Result: Out of 100 exudate samples, 82 were culture positive and 18 were culture negative.

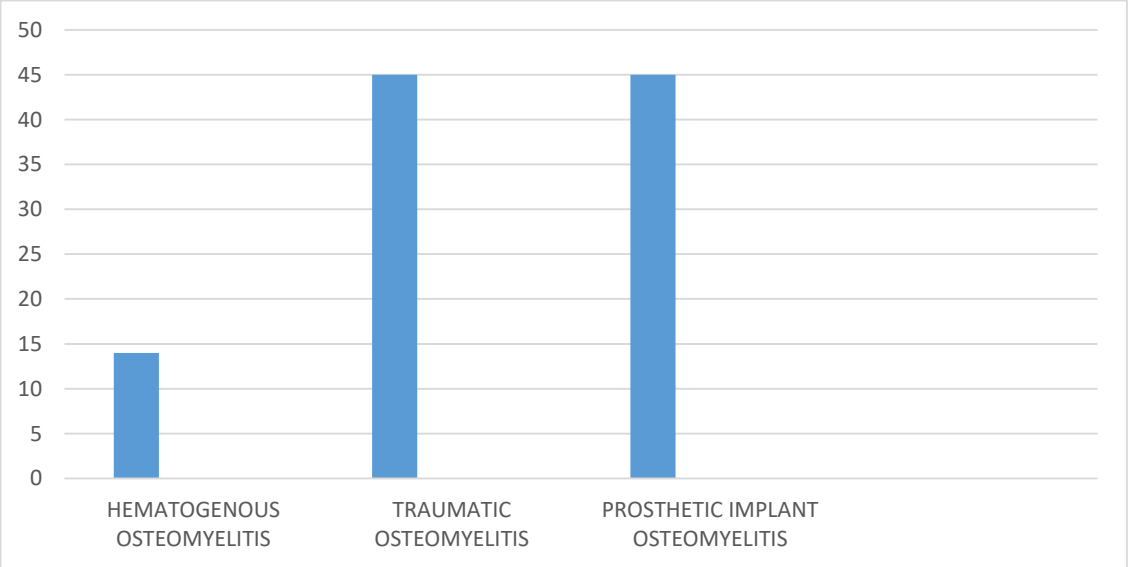
Association between Culture results and Type of chronic osteomyelitis: Out of 82 positive cultures, 41 cases of prosthetic implant associated osteomyelitis showed 39 positive cultures and 2 negative cultures. The 14 cases of hematogenous osteomyelitis cases showed 13 positive cultures and 1 negative culture and the 45 cases of traumatic osteomyelitis showed 30 positive cultures and 15 negative cultures. The statistical analysis (Chi-square test) was performed, showing the relationship between the type of osteomyelitis. Culture results of the samples were significant (p <.01) in this study.

Out of 82 positive cultures, 112 bacterial pathogens were isolated. Most common organisms isolated were *Staphylococcus aureus* (68.8%), *Pseudomonas aeruginosa* (18.8%), *Escherichia coli* (5.4%), *Enterococcus faecalis* (5.4%) and *Proteus mirabilis* (1.6%).

Antimicrobial susceptibility testing results: Out of 112 isolates, 77 isolates were *staphylococcus aureus*. Among 77 isolates, 68 were sensitive for ciprofloxacin (88.3%), 58 were sensitive for trimethoprim/sulfamethoxazole (75.3%), 50 were sensitive for erythromycin (64.9%), 48 were sensitive for gentamicin (62.3%) and 41 were sensitive for cefoxitin (53.2%). All 36 isolates of MRSA (Cefoxitin resistant isolates) were sensitive for Vancomycin Ezy strip (6 µg). Out of 21 *Pseudomonas aeruginosa* isolates, all of them were sensitive to imipenem (100%), followed by ceftazidime and piperacillin/tazobactam (66.7%), ciprofloxacin (61.9%), gentamicin (47.6%) and amikacin (42.9%).

Table 1
Type of Osteomyelitis cases

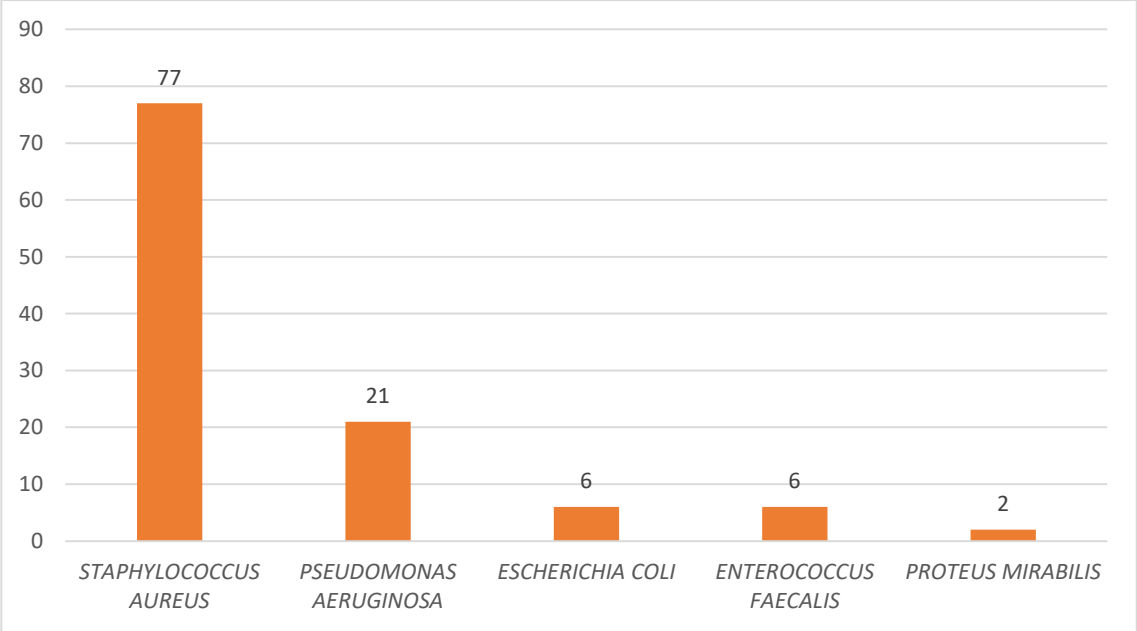
S.N.	Type of Osteomyelitis	Number of cases (percentage)
1.	Hematogenous osteomyelitis	14 (14%)
2.	Traumatic osteomyelitis	45 (45%)
3.	Prosthetic implant osteomyelitis	41 (41%)
Total		100



Graph 1: Type of osteomyelitis

Table 2
Organisms isolated from the clinical Sample

S.N.	Organism	Number	Percentage (%)
1	*Staphylococcus aureus*	77	68.8
2	*Pseudomonas aeruginosa*	21	18.8
3	*Escherichia coli*	06	5.4
4	*Enterococcus faecalis*	06	5.4
5	*Proteus mirabilis*	02	1.6
Total		112	100



Graph 2: Organisms isolated Clinical Sample

Out of 6 *Escherichia coli* isolates, all the isolates were sensitive to Imipenem and ciprofloxacin (100%), followed by trimethoprim/sulfamethoxazole and cefepime (83.3%), cefotaxime (66.6%), ampicillin 50%. Out of 6 *Enterococcus faecalis* isolates, all of the isolates were sensitive to vancomycin and linezolid (100%), followed by ampicillin and erythromycin (83.3%), gentamicin (66.6%) and doxycycline (50%). Out of 2 *Proteus mirabilis* isolates, all the isolates were sensitive to imipenem and ciprofloxacin, trimethoprim/sulfamethoxazole, cefepime, cefotaxime (100%), followed by ampicillin (50%).

Discussion

In present study, out of 100 cases of chronic pyogenic osteomyelitis, 57% were male and 43% female showing almost equal gender distribution. In the present study, chronic pyogenic osteomyelitis was showing majority of 31-50 age group patients (50%), which is correlating with the study done by Vishwajith et al[15] showing that the predominant age group was 31-40 years (30%) followed by 41-50 years old age group. Among the 100 cases, the occurrence of hematogenous - osteomyelitis was 14%, traumatic osteomyelitis was 45%, prosthetic implant induced osteomyelitis was 41%. This study shows that post traumatic osteomyelitis is the most common aetiology for chronic pyogenic osteomyelitis which correlating with the study done by Shah et al[12] where there were 50.67% cases of traumatic history.

In the present study, most common bone involved with chronic pyogenic osteomyelitis is tibia (42%) followed by femur (34%) which is correlating with the Zuluaga et al[17] study where the tibial involvement was 34% and femur (30%). Out of 100 samples, 82 cultures were positive (82%) and 18 culture (18%) had no bacterial growth (negative culture), which is correlating with the study done Wadekar[16] showing 87% positive culture and 13% negative culture in their study.

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In the present study, out of the 82 culture positive samples, the most common pathogen associated with chronic pyogenic osteomyelitis was *Staphylococcus aureus* (75.6%) followed by *Pseudomonas aeruginosa* (15.85%), *Escherichia coli* and *Enterococcus faecalis* 3.65% and *Proteus mirabilis* 1.25%. This is correlating with the studies such as Shah et al[12] (60.6%), Zuluaga et al[17] (43%), Vishwajith et al[15] (48.69%) and Vijayakumar et al[14] (24.2%) where the most common pathogen associated with chronic osteomyelitis was *Staphylococcus aureus*.

In the present study, the antibiogram of 77 isolates of *Staphylococcus aureus* showed that 68 (88.3%) were

sensitive and 9 (11.7%) were resistant to ciprofloxacin, 58 (75.3%) were sensitive and 19(24.7%) were resistant to trimethoprim/sulfamethoxazole, 50 (64.9%) were sensitive and 27 (35.1%) were resistant to erythromycin, 48 (62.3%) were sensitive and 29 (37.7%) were resistant to gentamicin and 41 (53.2%) were sensitive and 36 (46.8%) resistant to cefoxitin. The 36 resistant isolates (46.8%) were methicillin resistant *Staphylococcus aureus* (MRSA) strains. The rest of the 41 sensitive isolates (53.2%) were methicillin sensitive *Staphylococcus aureus* (MSSA). The importance of identifying the transmission of drug-resistant strains of *Staphylococcus aureus* among patients is essential. Hence the MRSA isolates are tested for Vancomycin sensitivity by E-Test, using EZY strip of Vancomycin 30µg, on which all the 36 isolates were sensitive according to the CLSI guidelines, hence there was no vancomycin resistant or intermediate sensitive *Staphylococcus aureus* strain isolated in this study.

Among 21 isolates of *Pseudomonas aeruginosa*, all 21 (100%) isolates were sensitive to imipenem, 14 (66.7%) were sensitive and 7 (33.3%) were resistant to ceftazidime, 14 (66.7%) were sensitive and 7 (33.3%) were resistant to piperacillin/tazobactam, 13 (61.9%) were sensitive and 8 (38.1%) were resistant to ciprofloxacin, 10 (47.6%) were sensitive and 11 (52.4%) were resistant to Gentamicin and 9 (42.9%) were sensitive and 12 (57.1%) were resistant to amikacin correlating with the study done by Shah et al[12] study where all the strains of *Pseudomonas aeruginosa* were sensitive to imipenem and 46.2% of the strains were resistant to amikacin. The other organisms isolated such as *Escherichia coli*, Enterococcus spp and Proteus Spp sensitivity pattern.

Conclusion

The chronic pyogenic osteomyelitis is major cause of morbidity and in some cases mortality in the cases of osteomyelitis. The delayed, inadequate, or improper treatments are the major factors causing chronic pyogenic osteomyelitis. The emergence of the multidrug resistant strains is the major challenge faced while combating the infection. The recent rise in number of Gram-negative bacteria is another important challenge faced by the clinicians. Although there is recent rise in Gram-negative bacteria, still Gram-positive bacteria *Staphylococcus aureus* is the most common pathogen associated with Chronic Pyogenic Osteomyelitis.

The most common etiological factor contributing to the infection is sequel to trauma followed by infected prosthetic implant and spread of infection from septic foci in other parts of body by hematogenous route. The pre-operative, intra-operative and post-operative precautions are to be followed strictly to prevent complications in future. To prevent emergence of multi-drug resistance of the strains, the judicial use of antibiotics is mandatory. This study provides insight to clinicians about the most common etiological factors and type of pathogens associated with chronic pyogenic osteomyelitis and their antimicrobial susceptibility pattern and importance of prompt and adequate treatment in combating this chronic debilitating condition.

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