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RATIONAL USE OF ANTIBIOTICS IN OSTEOMYELITIS

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ABSTRACT

Osteomyelitis (OM) is a progressive infection of the bone marrow and cortex caused by bacteria or fungi resulting in inflammatory destruction of the bone. The incidence of disease is related to joint replacements, complex surgical interventions and wound infections. Aim was to evaluate the rational use of antibiotics to reduce the further incidence of infection & mortality related to OM.This was a retrospective study carried out in different hospitals of Lahore. A total of 35 patients with the complaint of Osteomyelitis were selected randomly from the Jinnah Hospital, Lahore; Mayo Hospital, Lahore between the period of 7th June 2010 to 28th June 2010.Study method adopted was performa. Through our study we came to know that males are more commonly affected than females. 57.14% patients have compromised health status because host deficiencies are involved in the direct inoculation of micro-organism & spread of infection. Most commonly affected bone by OM is Tibia(51.4%) and Femur(34.28%). S.aureus was most common causative agent of OM in 78.26% of patients.Most commonly prescribed antibiotics for OM are Cephalosporins 57.14%, Fusidic acid and Linezolid 34.28%, Other Penicillins & Fluoroquinolones 20%. We concluded that rational antimicrobial treatment often involves a combination of antibiotics, either given orally or parentally based on results regarding microorganism sensitivity, patient compliance & health status of patients. A minimum of 4-6 weeks of oral or parenteral antimicrobial therapy along with surgery has become a standard therapy for Osteomyelitis.

Key Words: *Osteomyelitis(OM), Staphylococcus aureus, Antibiotics, Patient Compliance.*

INTRODUCTION

The words Osteomyelitis is derived from two words “osteon” (bone) and “myelo” (marrow) which are combined with “itis” (inflammation) to define the clinical state in which bone is infected with micro organisms. Osteomyelitis is an infection of the medullary or cortical bone**[1].** It is caused by a pyogenic organism and is a progressive infection of the bone leading to destruction of the bone & often deformity.This disease has multiple aspects according to the clinical presentation and evolution, the causative microorganism, the site of infection, and, finally, the patient's age and immunological status**[2,3].**

Bone infections are currently classified by the Waldvogel or the Cierny-Mader classification.Waldvogel classification is an etiologic system and the Cierny-Mader classification is descriptive, both classifications can be simultaneously used **[3,4].** The Waldvogel classification system divides osteomyelitis into the categories of hematogenous, contiguous and chronic **[5].** The more recent Cierny-Mader staging system is based on the status of the disease process, not etiology, chronicity or other factors. The terms “acute” and “chronic” are not used in the Cierny-Mader system. The stages in this system are dynamic and may be altered by changes in the medical condition of the patient (host), successful antibiotic therapy and other treatments **[6].**

The most frequently observed etiological agents of Osteomyelitis are: Staphylococcus aureus, Gram negative species such as Pseudomonas aeruginosa, E. coli and group B Streptococcus spp. In the majority of cases the metaphysis of the long bone are the most commonly implicated sites, although infection may spread to the contiguous epiphysis and joint in neonates patients with sickle cell disease and those with nail puncture wounds**[7,8,9].** The lower extremities are most commonly affected **[8].** Hematogenous spread is considered to be the most important route. The incidence is increasing in older patients. The source of infection in the elderly has been

related to the use of intravenous access devices and the asymptomatic urinary infections.

In young patients the increase has been correlated with the growing number of intravenous drug abusers and with immigrants from areas where tuberculosis is still endemic. Fever is present in 10-45% of patients. Spinal infections may cause severe neurological compromise in few cases **[10].** Children and adults with hematogenous osteomyelitis may present with acute signs of infection including pain of limb involved, fever, irritability, lethargy, and local signs of inflammation **[11,12].**

Patients with contiguous focus osteomyelitis often present with localized bone and joint pain, erythema, swelling, and drainage around the area of trauma, surgery, or wound infection. Signs of bacteremia such as fever, chills, and night sweats may be present in the acute phase of osteomyelitis but are not seen in the chronic phase. Both hematogenous and contiguous focus osteomyelitis can progress to a chronic condition. Local bone loss, sequestrum formation, and bone sclerosis are common. Persistent drainage and/or sinus tracts are often found adjacent to the area of infection. When osteomyelitis is suspected, imaging techniques such as X-rays, MRI & CT-scans used in association with blood and tissue cultures are the most reliable diagnostic tests**[13,14,15].**

When an etiology of osteomyelitis is identified, antibiotics are modified based on culture and susceptibility data. Decisions about antibiotics should be made after assessments of pertinent clinical information, laboratory and microbiology information, ease of administration, patient compliance, potential adverse effects, cost, local resistance patterns and available evidence supporting various treatment options **[16].**

The principles of treatment are symptomatic measures, bedrest and operative intervention, if necessary, with drainage of pus and debridement of any necrotic material, together with antibiotic treatment in sufficient concentration and for sufficient duration**[8].** Antibiotic classes used in the treatment of osteomyelitis include penicillins, beta-lactamase inhibitors, cephalosporins, other beta-lactams (aztreonam and imipenem), vancomycin, clindamycin, rifampin, aminoglycosides, fluoroquinolones, trimethoprim-sulfamethoxazole, metronidazole. Traditional treatments have used operative procedures followed by 4 to 6 weeks of parenteral antibiotics **[17].** Parenteral high-dose beta-lactam agents yield clinical success for many patients with chronic osteomyelitis, particularly with prolonged administration and surgical debridement. Over the last decade, the initial success of oral quinolone therapy for gram-negative osteomyelitis was exploited further for staphylococcal diseases. The early results with quinolones and rifampin for prosthesis-related infection are encouraging **[18,19].**

The efficacy and safety of three oral fluoroquinolones (lomefloxacin, levofloxacin, and ciprofloxacin) for the treatment of chronic osteomyelitis were analyzed and determined that oral fluoroquinolones can be safe, effective therapy if they are given for a prolonged course as treatment for infections caused by susceptible gram-positive as well as gram-negative organisms and in combination with adequate surgical debridement **[20,21].** Management of osteomyelitis is a multidisciplinary and individualized process. A rational approach to management includes careful consideration of the pathogenesis, microbiology, diagnostic options, and surgical and medical treatment of this diseases.

MATERIALS AND METHODS:-

This retrospective study was carried out between 7th June 2010 to 28th June 2010.Thirty five patients with bacteriologically &/or radiologically confirmed osteomyelitis were selected randomly from inpatient and outpatient rheumatology departments of Jinnah Hospital, Sheikh Zaid Hospital and Mayo Hospital of Lahore. The patients fulfilling the following inclusion criteria were selected for the study: Male and female patients having characteristic clinical signs and symptoms of bone infection with age >1 year and patients receiving antimicrobial therapy were selected. The

following patients were excluded from the study : Patients with infected joints, diagnosed with other rheumatic disorders like rheumatoid arthritis and those treated with surgical interventions only. Patients were regarded as having a functional loss if one of the following conditions existed: persistent pain, inability to weight bear, significantly deviated gait, and loss of range of motion across the adjacent joint. The data was collected from medical records of each patient who met the inclusion criteria: date of birth, gender, date of admission, history of presenting complaint, other symptoms present, risk factors, clinical signs, current medication, laboratory, radiological, bacteriological and histopathological findings, type and duration of antimicrobial therapy, any interventions and complications, discharge diagnosis and outcomes.

Results:-

Thirty five patients with different stages of OM were studied. The prescription was analyzed for rational use of medication, diagnosis of patients and cautions advised to them along with treatment plan. Figure 1 shows that 68.57% of patients observed were males while females were only 31.42%. Figure 2 reveals that in majority of patients (51.4%) the location of osteomyelitis was in tibia while other bones involved were: femur 34.28%, fibula 14.2%, phalanges 5.71%, humerus and ankles 2.85% each. Figure 3 shows that most of osteomyelitis patients (57.14%) have compromised health status.

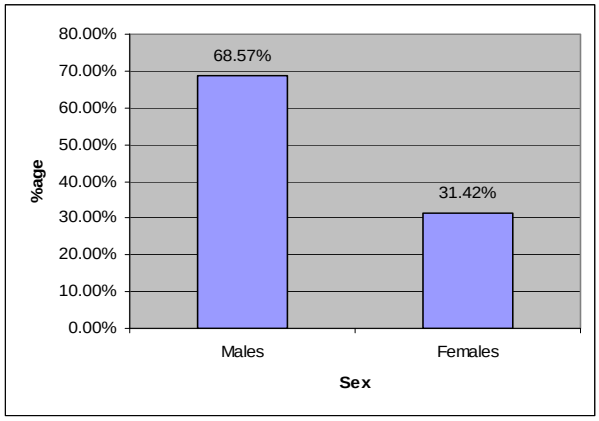

Figure-1: Frequency of male and female patients.

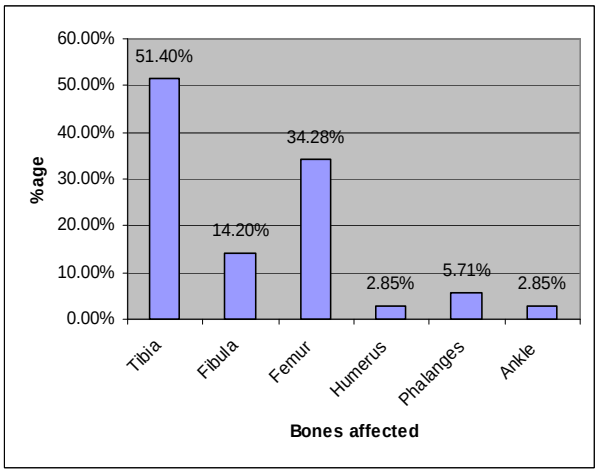

Figure-2: Bone affected by Osteomyelitis.

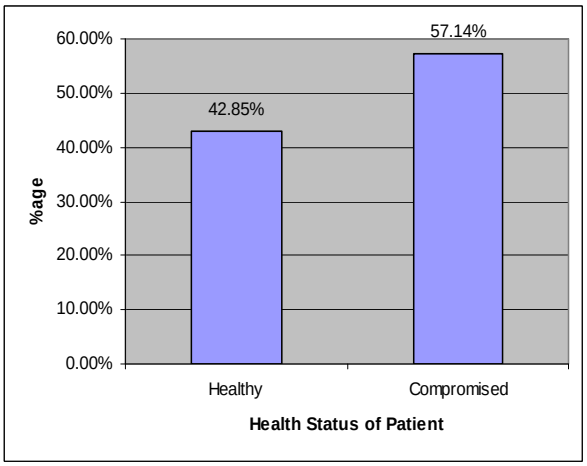

Figure-3: Health status of the Osteomyelitis patients.

Figure 4 shows that almost 100% patients presented with pain, swelling, tenderness and abscess ,80% of patients had sinuses with purulent discharge and 14.28% with fever. Figure 5 shows that culture sensitivity test (CST) were performed in 100% patients and yielded 65.71% positive cultures and 34.28% negative cultures. Figure 6 reveals the most common causative organisms of osteomyelitis. These were 69.56% *S.aureus*, 17.39% *E.coli* and P.aeruginosa each, 13.04% Proteus species and 4.34% Cauliform species. Figure 7 shows that cephalosporins was the most common initial choice (57.14%) while other antibiotics prescribed were: Fusidic acid & Linezolid 34.28%, Penicillins & Fluoroquinolones 20% each and aminoglycosides 8.57%.

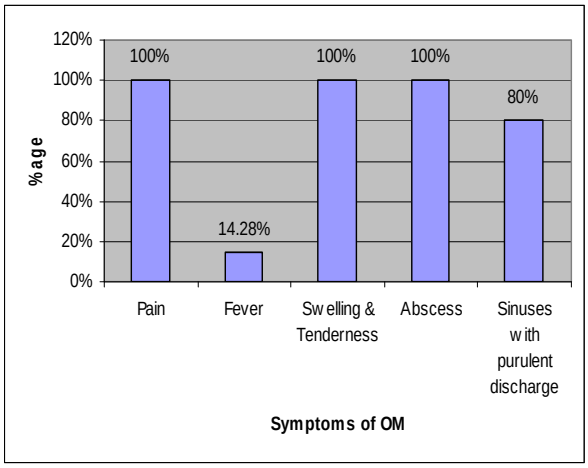

Figure-4: Frequency of appearance of symptoms in Osteomyelitis patients.

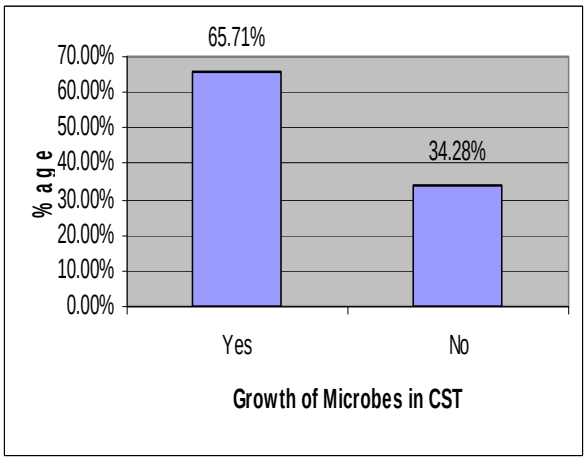

Figure-5: Growth of microbes in Culture Sensitivity Test (CST).

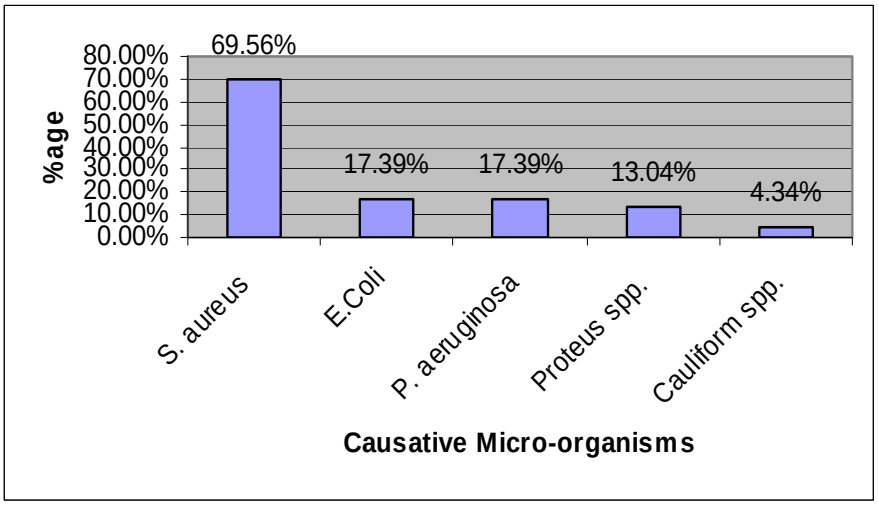

Figure-6: Causative micro-organisms for Osteomyelitis.

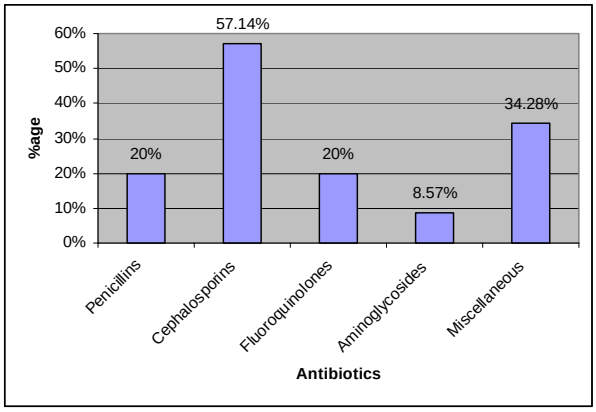

Figure-7: Antibiotics used for treatment of Osteomyelitis.

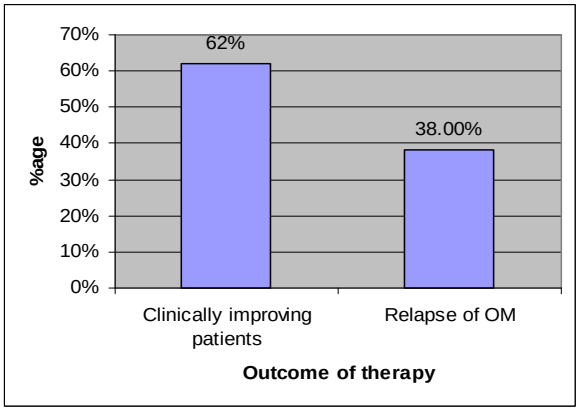

Figure-8: Outcomes of antibiotic therapy.

Figure 8 reveals that 62% of patients were showing some improvement in their condition while 38% showed relapses. Figure 9 reveals the disease resistance to a course of antimicrobial therapy and almost 42.85% of patients developed resistance to their previous antibiotic regimen. Figure 10 shows the incidence of side effects after the use of antibiotics and almost 17% of patients reported nephrotoxicity, 12% hepatotoxicity, 9% antibiotic-associated diarrhea and 3% reported rashes while 59% of patients had no side effects.

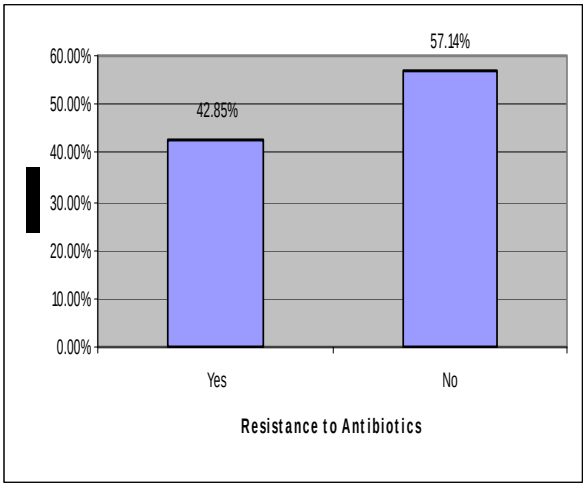

Figure-9: Resistance to antibiotics in Osteomyelitis patients.

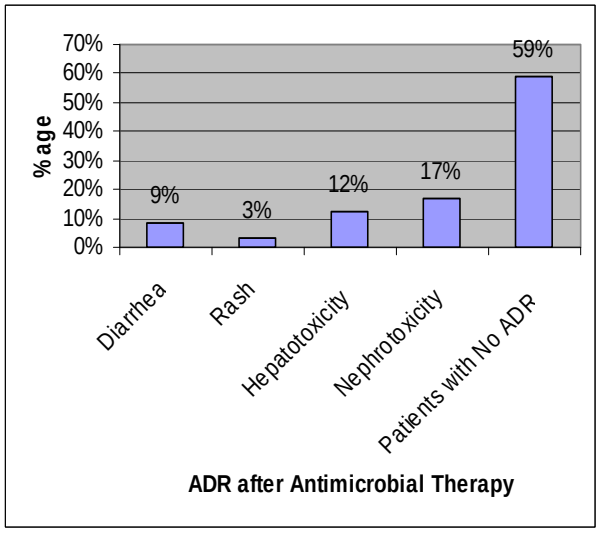

Figure-10: Incidence of ADRs after antimicrobial therapy.

Discussion:

Osteomyelitis is an infection of the medullary or cortical bone. The current incidence is 1 in 5000. This disease has multiple aspects according to the clinical presentation and evolution, the causative microorganism, the site of infection, and, finally, the patient's age and immunological status. The majority of infections of bone or joint are caused by spread of bacteria through the bloodstream or occasionally by entry of organisms through an open wound, by puncture or by extension of infection from adjacent tissue. Males have a higher rate of contiguous focus osteomyelitis than do females. The incidence is increasing in older patients. The source of infection in the elderly has been related to the use of intravenous access devices and the asymptomatic urinary infections. The onset of symptoms is typically insidious with neck or back pain often underestimated by the patient. Fever is present in 10-45% of patients, probably because patients are usually taking analgesic medications. The location of the pain depends on the site of infection. The condition can affect any bone in the body and people who suffer from osteomyelitis are often affected in the femur, or upper leg bone, or the lower leg bone (the tibia) as well as the bones found in the arm. Host (systemic or local) deficiencies often lead to bacteremia that favor the development of hematogenous osteomyelitis. Host deficiencies are also involved in the direct inoculation of organisms and/or contiguous spread of infection from an adjacent area of soft-tissue infection. When osteomyelitis is suspected, imaging techniques are used in association with blood and tissue cultures. Blood cultures are crucial in the evaluation of osteomyelitis. The isolation of the pathogen or pathogens in cultures of specimens from the bone lesion, blood, or joint fluid determines the etiology of osteomyelitis. Multiple organisms are usually isolated from infected bone. *Staphylococcus aureus* remains the most commonly isolated pathogen. However, gram-negative bacilli and anaerobic organisms are also frequently isolated. Appropriate therapy for osteomyelitis includes adequate drainage,

thorough debridement, wound protection, and specific antimicrobial coverage. Several antibiotic regimens have been proposed for osteomyelitis treatment. Decisions about antibiotics should be made after assessments of pertinent clinical information, laboratory and microbiology information, ease of administration, patient compliance, potential adverse effects, cost, local resistance patterns and available evidence supporting various treatment options. The antibiotics, which show a really good therapeutic efficacy, are beta-lactams, (mainly the newer cephalosporin's), used alone or in combination with other drugs. More recently great interest has been shown in the use of fluoroquinolones, because they can be taken by the oral route, are well tolerated for long-regimen treatments, have a good bone distribution and a rapid efficacy on many gram positive and negative bacteria. In particular, attention should be paid to good nutrition, to a smoking cessation program, and to control of specific diseases such as diabetes. Rapid and efficient treatment is a necessary condition for avoiding therapeutically failures or relapsing infections. The safety of prolonged use of the various antimicrobial agents and the cost and feasibility of the therapeutic regimen should be the parameters for a rational choice of the antibiotic. Furthermore, a number of different laboratory tests should be requested for patients with osteomyelitis to monitor drug toxicity (serum creatinine level and liver function tests), nutritional status (serum albumin level and total iron-binding capacity), and comorbidities (e.g., blood glucose levels for patients with diabetes).

Conclusion :-

Osteomyelitis (OM) remains challenging and expensive to treat, despite advances in antibiotics and new operative techniques. Drugs are the only part of the overall treatment for patients with OM and all patients require a holistic approach to OM assessment and management. In this study we concluded that appropriate treatment of osteomyelitis involves adequate antimicrobial therapy and operative debridement of all necrotic bone and soft tissues. Antimicrobial treatment often involves a combination of antibiotics and the decision to use oral or parenteral antibiotics should be based on results regarding microorganism sensitivity, patient compliance, infectious disease consultation, and the surgeon's experience. During treatment, patients should be followed closely for signs and symptoms of worsening infection. After the completion of treatment, follow-up should be based on the response to therapy and the overall health of the patient. Pharmacists are in ideal situation to improve compliance by educating patient and clinician and by establishing a supportive relationship with patient.

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