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Etiology and Drug Resistance Pattern of Osteomyelitis Associated with Combat-Related Injuries in Iraqi Patients.

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Abstract:

Osteomyelitis is a progressive infection of bone that results in inflammatory destruction of the bone. The aim of this study was to determine etiological agents of osteomyelitis and management of it in Iraqi Patients admitted in an Iranian Hospital. This study carried out by Doctors without Borders (MSF group) in Imam Hussein Hospital of Mehran with cooperation of Milad Hospital. Surgical debridement, bone graft, fixation and antibiotic therapy were the major management programs and. The most prevalent organisms isolated from patients included *Staphylococcus aureus*, *E.coli* and *Klebsiella pneumoniae*. The majority of these microorganisms were resistant to third generation of cephalosporins. Colistin was the sole antibiotic which most of gram-negative rods were susceptible to it. Nearly 34 % isolates of *S.aureus* were resistant to methicillin. All isolates of *S.aureus* were susceptible to vancomycin.

Introduction:

Since the beginning of America military operation in Iraq they have been reported thousands injuries among military soldiers and Iraqi civilians. Orthopedic

injuries have made up 65% of the total number of injuries during every major conflict. The soft -tissue defects produced in conjunction with open fracture in war-related trauma, contamination of wounds at time of injury, and the asso-

ciated prolonged hospital courses with potential exposure to nosocomial pathogens among compact casualties.^(1, 2) Early and aggressive managements of extremity wounds, starting with intervention near the battlefield, however in Iraq war, many civilians are injured because of booming and blasting. According to recent reports ,40% of all admissions and 70% of a hospitalized patients in Iraq and Afghanistan are civilian patients.⁽³⁾ There is not enough facilities for management of these victims, for this reasons wound and bone infections remain an important source of mortality and morbidity in these patients. The etiology of war wound infections has changed from the clostridia infections seen before World War I to the polymicrobial infection seen during the Vietnam conflict, with an increase in the frequency of drug resistant infections. Recovery of multidrug resistant gram-negative organisms, notably *Acinetobacter* spp, *Pseudomonas aeruginosa* ,and *Klebsiella pneumoniae* is increasing being reported from the wound in Iraq (Operation Iraqi Freedom) [OIF] and Afghanistan Operation Ending Freedom [OFE] casualties.^(1,4,5,6)

The high-energy weaponry of compact can result in massive tissue damage, In addition ,increasingly drug resistant bacteria are being recovered from OIF and OFE casualties.⁽¹⁾ The aim of this study was to determine etiological agents of osteomyelitis and management of it in Iraqi Patients admitted in an Iranian Hospital.

Materials and Methods:

This study carried out by Doctors without Borders (MSF group) in Imam Hussein Hospital of Mehran. This city located in Ilam province, near the border of Iran and Iraq .During our study from April 2008 to September 2008, 44 Iraqi patients with compact related osteomyelitis hospitalized in Imam Hussein hospital of Mehran.The majority of Patients suffered from osteomyelitis in Knee, Tibia, femur, Humorous or other parts of their body. The age of patients ranged between 17-61 years olds. Treatment protocol included bone graft, amputation, debridement, drainage screw fixation, arthrolysis, plate removal, external fixation and others. Data for these patients were retrospectively extracted from inpatient and outpatient medical records and included date of injury, fracture site, antibiotic prophylaxis on admission time to hospital, initial surgical management, specimen type (bone or tissue), initial culture and susceptibility testing results, surgical and pharmacological treatment of early wound infections, response to therapy, follow-up culture results, imaging results and definitive management. Samples for initial culture were obtained in the operating room from deep tissue during each patient's first surgical debridement on arrival at Imam Hussein hospital. All specimens were sent to Milad Hospital of Tehran for culture and susceptibility testing. All swabs samples and tissue specimens were sent in transport medium to microbiology laboratory of Milad Hospital in Tehran. Briefly after preparation of direct smear for Gram stain all specimen streaked across trypticase soy agar with 5% sheep blood and MacConkey agar and incubated at 35°C

for 18-24h, Isolated organisms were identified by using standard bacteriological methods.^(7,8) Susceptibility testing performed by disk diffusion methods as recommended by Clinical Laboratory Standards Institute ⁽⁹⁾ The Results of specimens culture and susceptibility testing were e-mailed as soon as possible to Mehran Imam Hussein hospital for establishment of treatment protocol.

Results:

During our study 44 Iraqi patients who had orthopedic problems including chronic osteomyelitis admitted to Imam Hussein hospital of Mehran. In total 89 specimens were processed in microbiology laboratory of Milad Hospital of Tehran. The majority of patients suffered from disorder and infection in knee, tibia, femur humerus ankle and others. The clinical specimens included tibia, wound, bone discharge and others. Treatment protocol included bone graft, amputation, debridement, drainage, screw fixation plate removal, arthrolysis. Of 89 specimens 32 (35.9%) were yielded negative culture, while 57 specimens had positive culture. The most prevalent isolated pathogen was *Staphylococcus aureus* with 15 isolates. The other prevalent organisms were *Klebsiella pneumoniae* and *E.coli* each with 10 isolates. Results of susceptibility testing showed that nearly 34% of *S.aureus* isolates were resistant to methicillin. All isolates of *S.aureus* were susceptible to vancomycin and chloramphenicol. Nearly 60 % isolates were susceptible to erythromycin and clindamycin. 72.6% isolates of *S .aureus* were susceptible to gentamycin, Co-trimoxazole and ceftriaxone. Ampicillin, cephalex-

in, ceftazidim, cefotaxime were the most effective antibiotics against *E.coli* and all isolates of this organism were susceptible to above mentioned antibiotics. The other effective antibiotics against *E,coli* were amikacin, imipenem and chloramphenicol. Drug resistance among isolates of *K.pneumoniae* in comparison with *E.coli* was prevalent. Nearly 90% of isolate of *K.pneumoniae* were Extended Spectrum Beta- lactamase (ESBLs) Positive All isolates of this organism were susceptible to amikacin. The other effective antibiotic against *K.pneumoniae* included imipenem and ciprofloxacin. Ampicillin and ciprofloxacin were two antibiotics which were active against of *Proteus mirabilis* isolates. The colistin was the sole antibiotic which *P.aeruginosa* and *A.baumannii* isolates were susceptible to it. In our study there was an other microorganisms such as Morganella morganii, Enterococcus faecalis, Klebsiella oxytoca which were isolated from clinical specimens, However the number of this organism was not enough for detection of drug resistance pattern.

Discussion:

Musculoskeletal war wounds often involve massive injury to bone and soft tissue that differ markedly in character and extent compared with most injuries seen in civilian practice. These complex injuries have challenged orthopaedic surgeons to the limits of their treatment abilities on the battlefield, during medical evacuation, and in subsequent definitive or reconstructive treatment. Newer methodologies are being used in the treatment of these wounds to prevent so-called second hit complications, decrease

complications associated with prolonged medical evacuation, reduce the incidence of infection, and restore optimal function. Basic science advances hold the promise of providing foundations for future treatment options that may improve both bone and soft-tissue healing. Research on the treatment of these often devastating wounds also will have broad applicability to trauma resulting from acts of terrorism or from natural disasters.^(1,11,12) Osteomyelitis is a progressive infection of bone that results in inflammatory destruction of the bone, bone necrosis, and new bone formation and may progress to a chronic and persistent state. The major categories of osteomyelitis are based on the source of infection (hematogenous or secondary to a contiguous focus of infection) and whether vascular insufficiency (either local or systemic) exists. While large-organism inoculation and/or host compromise can predispose patients to the development of osteomyelitis, the virulence of the infecting pathogen also has a significant role. One species in particular, *Staphylococcus aureus*, is able to cause an acute bone infection even with a low inoculum in a healthy host. In addition, through the timed expression of its arsenal of virulence factors and aided by its ability to develop antibiotic resistance rapidly, *S. aureus* progresses to a chronic, biofilm-mediated infection. Once a chronic infection develops, bacterial clearance cannot be attained by the host immune system or antimicrobial therapy. At this point, surgical removal of the focus of infection is usually necessary for complete infection resolution.^(13, 14)

Overall there is a higher prevalence of wound infection in patients suffering combat-related injuries. Recently a number of reports have described drug resistance pathogens, such as *A.baumannii*, infecting combat casualties.⁽⁵⁾ In our study we isolated only one strain of *A baumannii*. Fortunately this isolate were susceptible to many antibiotics. Previous studies have revealed that gram-positive organisms such as *S.aureus* predominate in the cultures of traumatic wounds. Our find also confirmed that *S,aureus* with 26.3% isolates was the predominant organism. The presence nearly 70% of gram -negative bacteria in our study is similar previous study. However, it remains unclear whether these wounds become contaminated at time of injury, during initial management or during hospitalization in our facility.^(15,16,17)

One of the major limitations in our study was our inability to obtain the details of each patients management course before transfer to our hospital. These data especially included results of culture obtained at the time of injury and during each subsequent debridement performed before.

In conclusion our study showed that osteomyelitis is the major complication, in war victims in Iraqi civilians patients. *S.aureus*,*E.coli* and *K.pneumoniae* were the major causative agents; Treatment protocol included surgical operation and antibiotic therapy.

Table 1- frequency of different microorganisms isolated from Iraqi patients hospitalized in Mehran Hospital

Microorganism	frequency	Percent
Staphylococcus aureus	15	26.3
E.coli	10	17.5
Klebseilla pneumonia	10	17.5
Proteus mirabilis	6	8.7
Pseudomonas aeruginosa	5	8.7
Morganella morganii	3	5.2
Acinetobacter baumannii	2	3.5
Staphylococcus warneri	1	1.75
Staphylococcus capitis	1	1.75
Enterobacter aeruginosa	1	1.75
Bacillus spp	1	1.75
Klebsiella oxytoca	1	1.75
Acinetobacter baumannii	1	1.75
Total	57	100

Table2-percent of Antibiotic resistance among prevalent gram-negative bacilli

Antibiotic	CIP	CT	AN	IPM	GM	AM	SXT	CN	CAZ	CRO	C	TE	CTX
E.coli	60	60	10	30	90	90	90	100	100	100	20	90	100
K.pneumonia	90	40	0	10	90	60	90	90	90	90	90	70	90
P.aeruginosa	0	60	90	0	40	-	-		20	80	-	100	80
P.mirabilis	0	0	0	0	83	100	83	83	49.8	66.8	66.8	66.8	66.8
M.morgani	0	0	0	0	33.4	100	33.4	33.4	33.4	33.4	33.4	33.4	33.4

Ciprofloxacin (CIP), ceftazoxime (CT), Amikacin (AN), Imipenem (IPM), Gentamycin (GM), Ampicillin (AM), Co-trimoxazole (SXT), cefotaxime (CXT), Cephalexin (CN), Cef-tazidime (CAZ), Ceftriaxone (CRO), Chloramphenicol (C), Tetracycline (TE), Cefotaxime (CTX)

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