A study of implant related infections in closed fractures

Dr. Narayanan SK, Devishal R and Dr. Sherafudeenn

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Abstract
Introduction: Infection following insertion of metallic devices is one of the major complications of orthopaedic surgery. When an operation is undertaken, a closed fracture is converted into an open one with the potential danger of it becoming infected. This complication may be catastrophic. It can lead to the loss of a limb and at best, it prolongs the period of morbidity, may make more operations necessary and impairs the quality of the final result. Curbing implant related infections has always been a challenging task for the orthopaedician.

Objective: To know the frequency of infection in orthopaedic implant surgery in a public hospital and to evaluate risk factors, causative organisms, complications and treatment.

Methods: A prospective study was conducted at Sree Gokulam Medical College, Thiruvananthapuram, from May 2015 to April 2020. All closed fracture cases admitted for internal fixation devices were included in the study. The exclusion criteria were open fractures, from May 2015 to April 2020. All closed fracture cases admitted for internal fixation devices were included in the study. The exclusion criteria were open fractures, needing external fixation and immunocompromised state. The follow up was done till infection eradication was attained.

Results: Infection developed in 30 patients, of which 8 was early onset, another 8 were delayed onset and the rest 14 were late onset. Staphylococcus aureus was the most common organism isolated. Smoking and diabetes were significant risk factors. ESR, CRP and procalcitonin were promising tests in detecting infection. Majority of the cases were managed by implant removal, which yielded good results in eradicating infection.

Conclusion: Infection rate was at par with international standards. In view of financial burden on patient and on hospital resources, apt measures to control infections should be a mainstay, and that could in turn substantially decrease morbidity and mortality. Diabetes, prolonged surgery time and smoking show strong correlation with higher infection rates. Most common organism isolated from infected cases was Staphylococcus aureus. Our study showed that implant salvage was effective in eradicating infections of acute onset, and in case of late onset, implant removal seemed to be a better choice.

Keywords: orthopaedic infection, implant surgery

Introduction
Infection following insertion of metallic devices is one of the major complications of orthopaedic surgery. When an operation is undertaken, a closed fracture is converted into an open one with the potential danger of its becoming infected. This complication may be catastrophic. It can lead to the loss of a limb and at best, it prolongs the period of morbidity, may make more operations necessary and impairs the quality of the final result. Bacteria arrive at random near the surface of a biomaterial by direct contamination, contiguous spread from adjacent area or haematogenous spread. The risk of infection in each patient depends on:

1. Patient dependent factors which include nutrition, immunologic status and infection at a remote site
2. Surgeon dependent factors which include prophylactic antibiotics, skin and wound care, operating environment, surgical technique and treatment of impending infections such as in open fractures.

The characteristics of implant associated sepsis are

1. Adhesive bacterial colonization
2. A biomaterial or damaged tissue substratum
3. Resistance to host defense mechanisms and antibiotic therapy
4. Specificity of phenomena (material, organism, location)
5. Presence of characteristic bacteria such as staphylococcus aureus, staphylococcus epidermidis and pseudomonas aeruginosa
6. Transformation of non pathogens or opportunistic pathogens into virulent organisms by the presence of a biomaterial substratum
7. Frequently polymicrobial infection
8. Smaller inoculi required to infect
9. Persistence of the infection until the substratum is removed
10. The absence of tissue cell damage or necrosis
11. The absence of adequate tissue integration at the biomaterial tissue interface

Microorganisms in nature and disease are dependent on substratum attachment for optimal growth and development. Similarly, implanted biomaterials tend to potentiate bacteria on their surfaces so that normally friendly organisms become virulent pathogens. Virulence is also enhanced because both bacteria and biomaterials interfere with host defense mechanisms. Infections centered on biomaterials are difficult to eliminate and usually, require removal of the device.

In the early postoperative days, its detection is particularly difficult, and currently it can be established on the basis of several concurring parameters such as clinical presentation, laboratory markers, imaging study, and microbiologic testing. C-reactive protein (CRP) and, more recently, procalcitonin (PCT) are two laboratory tests of considerable usefulness in clinical practice. CRP is the most available and widely used. CRP is a positive acute-phase protein whose plasma concentration increases rapidly up to 1000-fold from around 1 mg/L, during inflammatory disorders. CRP expression and its induction in the hepatocytes are mainly regulated transcriptionally by interleukin 6 through the activation of several transcription factors. CRP is used to monitor the postoperative course in surgical trauma following orthopedic implants and to detect prosthetic infection.

PCT is a marker of infection; it is produced by the same cells in which calcitonin is synthesized. The short half life (25-30 h in plasma) of PCT, coupled with its virtual absence in health and specificity for bacterial infections, gives it a clear advantage over the other markers when differentiating bacterial infection from noninfective causes of inflammation or viral infection.

When infection occurred after internal fixation, it was formerly advised that, the metal should be removed to control the sepsis. The idea that metal per se is responsible for infection is open to serious doubt. Experience seems to confirm that when internal fixation is secure it should not be removed in the presence of infection and that with debridement, irrigation and antibiotic therapy, union will eventually occur. It may be that the optimum management of an infected nonunion is to combine aggressive treatment of the infection with secure, rigid, internal fixation.

Methods
In this study of infected implants, we have obtained 30 cases of implant related infections in closed fractures, who underwent treatment at Sree Gokulam Medical College and Research Foundation, Thiruvananthapuram between May 2018 to April 2020. Clearance was obtained from hospital ethical committee. The data for this study was collected in a pretested Proforma which includes parameters like age, sex, medical problems, velocity of injury, interval between injury and surgery, duration of surgery and type of implant. All the cases seen during the study period was considered for study purpose.

Once the patient was admitted to the hospital, all the essential information was recorded in the proforma prepared for this study. They were regularly observed during their hospital stay and were discharged with the advice to come to the outpatient department regularly. The patients were followed till infection control was achieved.

Inclusion criteria
- All patients who developed implant related infection in closed fractures

Exclusion criteria
1. Open fractures
2. Fractures requiring external fixator
3. Immunocompromised state

Classification system used in our study was employed by Trampuz et al.

According to the onset of symptoms after implantation
- Early infection (< 2 -4weeks)
- Delayed infection (>4 weeks)
- Late infection (> 10 weeks)

Laboratory investigations like Hemoglobin%, total leucocyte count, differential count, blood grouping, cross-matching, fasting blood sugar, blood urea, serum creatinine, serum ESR, CRP, serum procalcitonin. Urine examined for albumin, sugar and microscopic examination. Pus for culture and sensitivity. X ray of the involved bone were done in all patients.

Management
Conservative management
This consists of local saline irrigation, local cleansing and systemic and oral antibiotics. Antibiotics were administered depending on the pus culture and sensitivity report. The result of recovery was recorded. The result was satisfactory if the discharge from sinus stopped and discharging sinus had healed.

Wound debridement
Patients with poor quality bone at fracture site with stable implant on X ray were managed by antibiotics and wound debridement until infection subsided. If infection persisted, implant was removed once fracture union occurred.

Implant removal
Patients with x ray showing good union of fracture site with loosening of implant underwent implant removal. In patients with unsatisfactory fracture union after removal of implant, external immobilisation by POP slab or external fixator was done.

Follow up
Follow up was done at regular intervals till infection subsided.

Result
Out of 1450 cases operated during the study period at our institution, 30 cases got infected. The infection rate in this study was found to be 2.06%. Of this, 24 (80%) were males and 6 (22%) were female. Maximum aged patient was 80 years. Highest number of the patients were in the age group of
21 to 40 years, with mean age of 42.7 years. In our patients, 73.3% were diabetic and 70% were smokers. 70% cases were following high velocity injury. Majority of the patients i.e., 55.7% were operated during the first week after trauma soon after patient was stabilized and medically fit. The average operating time was 100 mins (30 min-180 min) after anesthesia. 46.7 % of patients developed late onset infection (more than 10 weeks).

Fig 1: In this study plates and screws had a higher percentage of infectivity (56.7) compared to intramedullary implants (26.7).

Fig 2: Staphylococcus aureus was found to be the most common causative organism (46.7 %), than Coagulase negative staphylococcus (26.7 %).

Fig 3: 90% of cases yielded only one species of organism

E coli, Coagulase negative staphylococcus, Staphylococcus aureus, Klebsiella and Pseudomonas were sensitive to Cephalosporin’s. E coli, Klebsiella and Pseudomonas were sensitive to Carbapenems. But, Coagulase negative staphylococcus, Staphylococcus aureus were sensitive to Linezolid. Staphylococcus aureus were sensitive to Cillinamycin. Coagulase negative staphylococcus and Staphylococcus aureus were sensitive to Co-trimoxazole. E coli, Staphylococcus aureus, Klebsiella and Pseudomonas were sensitive to Macrolides. Coagulase negative staphylococcus and Staphylococcus aureus were sensitive to Fluoroquinolones. In our study the range of ESR was between 20 to 120 with a mean of 80.33. 12 cases (40%) had total WBC count more than 10,800 cells/µL/cu mm. 22 patients (73.3%) were positive and 8 (26.7%) were negative for C reactive protein. Serum procalcitonin level was elevated in all cases, with ranges between 0.4 to 9.0. With mean value of 0.9.
In this study only one case was conservatively managed, 36.7% of patients underwent debridement. Eventually, 20 out of 30 patients underwent implant removal (66.7%) to control infection. Following implant infection only one case underwent revision to internal fixation and 4 cases underwent revision to external fixation.

Discussion
In modern era, implant surgery has become one of the commonest orthopaedic operation. Infection following implant surgery is a disaster, both for the patient and the surgeon. No test is 100% sensitive and specific for detection of infection, hence the diagnosis relies on surgeon’s judgement of clinical presentation and interpretation of results. Diabetes mellitus, smoking and prolonged duration of surgery were found to have a strong correlation with incidence of infection in implant surgeries. Marquesue et al. in 2006 correlated diabetes mellitus and infection of implants. Khan et al. [33] in 2008 postulated smoking, diabetes mellitus and increased surgery time with development of infections of implants. There were two groups based on velocity of injury, 70% of cases were high velocity injury and 30% were low velocity injury.

In the present study, 26.6% of cases had early infection, 26.6% had delayed infection and 46.7% had late infection. According to Trampuz and Zimmerli [66], infection in patients can be divided into 3 categories early, delayed and late infection. Early infection refers to infection within 2 weeks of operation. Delayed infection occurs between 2-10 weeks. The suggested causes were contamination from either airborne sources or aseptic surgical technique. The late infection is mainly due to hematogenous seeding.

The infection rate in this study was found to be 2.08%. This is comparable to other studies. The incidence of orthopaedic device related infection is less than 1-2% internationally [58]. In a study by Khan et al. [33], the infection rate was 5.76%. The incidence of infection was higher with fixation with plates and screws and compared to intramedullary implants. In 46.7% cases, the isolated organism was Staphylococcus aureus followed by coagulase negative staphylococcus. Sanderson [50] showed that 35% of infections were caused by staphylococcus aureus. In a study by Trebse [57] in 2005, the most common organism was found to be Staphylococcus aureus 50% of infection in a study of Khan et al. [33] were due to Staphylococcus aureus. According to Antony and William, the causative bacteria grow in glycocalyx enclosed biofilm that was adherent to surfaces of biomaterial. Analysis of joint fluids or swabs of excised tissue of prosthetic surfaces often yielded only one species from what was a polymicrobial population based on electron microscopy [3].

In the present study, 90% of cases yielded only one species of organism. The use of WBC count as a parameter for infection detection was not reliable except in cases of fulminant infection Goel [21] and Trampuz [56] found in two separate studies that the WBC count is not usually abnormal in patients with infected implants.

ESR+CRP had a strong correlation with infection implant surgeries. According to Goel [21], a normal ESR can safely rule out infection but elevated ESR may require further investigation. Increase CRP is also indicative of implant infection.

Our results are, in fact, comparable to various studies that have demonstrated that serum PCT is a helpful diagnostic marker supporting clinical and microbiological findings. Castelli et al. [19] investigated the diagnostic value of PCT and CRP in septic complications after major trauma. They concluded that elevation of PCT signifies possible septic complications during SIRS after major trauma. In addition, high PCT concentration at admission after trauma in ICU patients indicates an increased risk for septic complications. Plain x-ray remains of limited use in the diagnosis of acute infection. Most patients with infection initially had few x-ray changes unless it was prolonged infection. This finding was also found in this study. According to Trampuz, examination of serial x-rays is neither specific nor sensitive. Staphylococcus aureus was found to be sensitive to first and second generation cephalosporins, linezolid and clindamycin. According to Darouiche, methicillin resistant staphylococcus are sensitive to linezolid and clindamycin [63]. Harwood et al. concluded that linezolid has excellent efficacy against gram positive organisms that are resistant to other therapies.

The next common organisms, coagulase negative, staphylococcus was sensitive to first generations cephalosporins linezolid and cotrimoxazole. E.coli, klebsiella and pseudomonas were sensitive to third and fourth
generation cephalosporins, carbapenine and macrolides. According to Widmer cefazidine and mesopenum has good efficacy against pseudomonas. Another study by Agrawal et al. showed E.coli and Klebsiella were sensitive to 3 and 4th generation cephalosporins and macrolides.

According to Russel E. Windsor, antibiotics suppression alone may be the only option in an individual who is a poor surgical candidate. Only organism having exquisite sensitivity to antibiotics can be treated in this way. This method but only suppress if It is possible only in a minority of patients.

In the present study, only 1 patient responded to antibiotic treatment. This patient had early infection and isolated bacteria on pus culture were sensitive to antibiotics. When infection occurred after internal fixation is secure, it should not be removed in the presence of infection and with debridement, irrigation and antibiotic therapy, union will eventually occur. According to Trebse et al., patient with short term infection but stable implant and known pathogen may be successfully treated with retention of implant. In our study patients with acute infection and stable implant with causative organism known were treated with debridement and antibiotics according to sensitivity. This helped in achieving infection control.

In late infection requires aggressive treatment. The higher incidence of infection in patients who have metal implants and the difficulty in eradicating this type of infection may in part. This type of infections may in part be caused by the growth of bacteria in the biofilm on biomaterials as Gristina and Costerton. According to Stockelberg and others, chronic infection may be eradicated by removal of the device as they are not likely to respond to antimicrobial therapy alone.

Study by Masterson et al. showed that a loose prosthesis cannot be successfully treated without implant removal. In the present study, 14 cases of late infection had loosening of implant and with good union of fracture site and was treated by implant removal and antibiotic therapy.

According to Bernard et al., the most commonly used therapy for prosthetic joint infection is a two staged prosthetic exchange separated by 6 weeks of intravenous antibiotic therapy. In our study also, out of 4 patients who underwent reosteosynthesis, only 1 case underwent one stage revision and other 3 cases underwent reimplantation with two stage exchange separated by 3 weeks of intravenous antibiotics.

Conclusions

Most of the patients were in the age group 20-40 years. 80% of patients in the study were males. Infections were commonest in treated fractures caused by high velocity injuries due to road traffic accidents. Majority of the patients i.e., 55.7% were operated during the first week after trauma. The average operating time was 100 mins (30 min-180min) after anesthesia. Diabetes, smoking and prolonged surgery time were found to have a strong correlation with incidence of infection.

During our study period, the infection rate of implant surgeries in our institution was 2.08%. In this study, 26.6% of patients had early infection, 26.6% of patients had delayed infection and 46.7% of patients had late infection. Infection incidence was higher infixation with plates and screw (56.7%) as compared to intramedullary implants (26.3%). In 46.7% of cases the organism isolated was Staphylococcus aureus followed by Coagulase negative staphylococcus (26.7%). In this study 90% cases pus culture yielded only one species. The use of WBC count as a parameter for infection detection was not reliable except in cases of fulminant infection. ESR, CRP and Procalcitonin had a strong correlation with infection in implant surgeries. Plain Xrays remains of limited use in diagnosis of acute infections. Most patients with infections initially had few xray changes unless it was prolonged.

Staphylococcus aureus, the commonest organism was found to be sensitive to 1st and 2nd cephalosporins, linezolid and clindamycin. The next common organism, coagulase negative staphylococcus, was sensitive to first generation cephalosporin, linezolid and cotrimoxazole. E. coli, Klebsiella and pseudomonas were sensitive to 3rd and 4th generation cephalosporins, carbapenem and macrolides.

All cases of acute infection (onset <2 weeks) were given a trial of conservative treatment with patient being taken up for debridement in case of failure of conservative treatment. Implant removal was not done.

In one case of elbow dislocation (OR+IF) the K-wires were removed after a week. And in a case of fracture clavicle, reosteosynthesis of clavicle was done after debridement because fixation was unstable. Infection control was achieved in an average of 13 weeks. Fracture union occurred in 16.5 weeks. Out of 8 cases of delayed infection, 4 were treated by debridement alone. 3 cases were treated by implant removal and further stabilization of fracture with external fixation devices. One case of lateral malleolar fracture was treated by implant removal alone and immobilized in below knee slab till the infection subsided. In this group, a case of fracture shaft of humerus which underwent implant removal and external fixator application is yet to achieve infection control. The average fracture healing time was found to be 14.8 weeks in this group.

All cases of late infection was treated by implant removal with infection eradication time period being 2.5 weeks and mean time period for fracture union was 15.3 weeks. As all cases showed evidence of good fracture healing at the time of implant removal, further immobilization with any means was not carried out.

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