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RESEARCH ARTICLE

PERIPROSTHETIC JOINT INFECTION FOLLOWING TOTAL KNEE ARTHROPLASTY: CONTEMPORARY CONCEPTS IN DIAGNOSIS AND MANAGEMENT

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Abstract

Periprosthetic joint infection (PJI) is one of the most serious complicati ons following total knee arthroplasty and remains a leading cause of early revision surgery. It is associated with high morbidity, prolonged hospitalisation, increased healthcare costs, and inferior functional outcomes. Despite advances in implant design, surgical techniques, and perioperative infection control measures, PJI continues to challenge arthroplasty surgeons. With the increasing volume of knee arthroplasty procedures worldwide, the burden of PJI is expected to rise further. Traditionally, two-stage revision arthroplasty has been considered the gold standard for treatment; however, single-stage revision is gaining acceptance in carefully selected patients. This review discusses the epidemiology, pathogenesis, clinical presentation, diagnostic criteria, and contemporary management strategies for PJI following total knee arthroplasty.

Introduction:-

Total knee arthroplasty (TKA) is a reliable and effective treatment for end-stage knee arthritis. However, periprosthetic joint infection (PJI) remains a devastating complication that compromises clinical outcomes. Although the incidence is relatively low, the absolute number of cases is increasing due to the rising number of arthroplasty procedures.

Epidemiology and Risk Factors:-

The reported incidence of PJI after primary TKA ranges from 1% to 2%, increasing significantly after revision surgery. Patient-related risk factors include diabetes mellitus, obesity, smoking, immunosuppression, malnutrition, and inflammatory arthritis. Surgical factors such as prolonged operative time and wound complications also contribute.

Pathogenesis:-

PJI occurs due to bacterial contamination during surgery or hematogenous spread. Biofilm formation on implant surfaces plays a critical role in chronic infection, rendering bacteria resistant to host immunity and antibiotics.

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Clinical Presentation:-
Patients may present with pain, swelling, erythema, wound discharge, or sinus tract formation. Late infections often present with implant loosening and persistent pain.

Diagnosis:-
Diagnosis requires a combination of clinical evaluation, laboratory markers, imaging, and microbiological analysis. Elevated ESR and CRP are commonly used screening tests. Joint aspiration with synovial fluid analysis and culture is essential. The MSIS and ICM criteria provide standardized diagnostic frameworks.Interleukin-6 (IL-6) is a cytokine that is released in the present of bacterial infection or tissue damage. A 2010 meta-analys showed superiority of IL-6 over CRP and ESR in diagnosing PJ, with a sensitivity of 97% and specificity of 91 %,15 With the combined use of IL-6 and serum CRP, Elgeidi et al. reported i sensitivity of 100%, specificity of 99% and accuracy of 98%" However, the main problem remains the expense and lack of availability of the test.D-dimer is a product of fibrin-clot dissolution by plasmin, and this is a commonly performed test. The increased fibrinolytic activity associated with infections results in increased D-dimer levels. Mixed results have been reported in the literature in comparison to ESR and CRP, with added problems that D-dimer is raised in the normal postoperative course, and with other conditions such as thromboembolism.Pro-calcitonin (PCT) has recently attracted research interest in PJ, primarily due to its utility in identifying bacterial infections. PCT is normally produced by the thyroid gland, whereas in infectious conditions it is produced by macrophages and liver-derived monocytic cells. Again, there has been variability in the success of its use in diagnosing PJI, limiting its routine uptake by clinicians.

Serological markers:-
C-reactive protein (CRP) and erythrocyte sedimentation rate:-
(ESR) are widely available cheap blood tests that should be performed on all cases undergoing revision surgery, In acute ilection with an inflammatory presentation, CRP and ESR arecommonly raised, with the 2018 International ConsensusMeeting (1CM) on PJ stating an acute PJ should have a CRP>100 mg/litre, '* It has been shown that the CRP level normalizes at approximately & weeks post-surgery, while the BSR level may be elevated for up to 1 year after an uncomplicated total hip or knee arthroplasty, In acute infections, the sensitivity of ESR is 42-94%, and its reported specifieity ranges frem 33 to 87% in the literature, The sensitivity of CRP is 74-94%, and its specificity varies between 20% and 100%.In chronie infection, CRP elevation may be minimal, and It may vary with the virulence of the causative organism, with the ICM setting a criteria of 10 mg/litre for chronic PJI. Fernández.Sampedro et al. analysed a total of 498 patients, including 77 late PJs." In these late PJis, the sensitivity of CRP was only 62.3%,' potentially leading to many false negative results. Greidanus et al. showed that using a combination threshold of CRP>13.5 mg/litre and ESR >22.5 mm/hour, if both tests were negative then the negative predictive value was 96%, but if both tests were positive, the positive predictive value was 84%.!* The problem remains that neither ESR or CRP are specific to infec-tion, and they can be raised in many conditions.

Synovial fluid analysis:-
Synovial cell counts; this method estimates the total number of leukocytes, along with an assessment of the polymorphonuclear neutrophil (PMN) percentage. Various cut-off settings have been used with various sensitivity and specificity values in a variety of diferent scenarios. The original synovial leukocyte count cut-off value of >10,000 cells/ul, proposed by the International Consensus Meeting, has been shown to have low sensitivity by multiple authors, in both acute and chronic PJs. Cytological assessments can be affected by many host-related factors and by whether the patient has received antibiotics.a-defensin (AD) is an antimicrobial peptide secreted by syno-vium neutrophils in reaction to infection, and targets the cell membrane of the infecting agent. It has been reported to exhibit a sensitivity range of 96-100% and a specificity exceeding 90%.Significantly, this biomarker's diagnostic accuracy is notcompromised by the administration of antibiotics, and it possesses the capability to identify a broad spectrum of microbial agents exhibiting a diverse range of virulence. A recent large-scale meta-analysis reported that laboratory-based synovial AD and synovial calprotectin were the two best independent preoperative diagnostic tests for diagnosing PJI.? The assay is available in two configurations: a qualitative lateral flow test (LFT), which presents lower diagnostic accuracy, and a quantitative method, the enzyme-linked immunosorbent assay (ELISA).

Leucocyte esterase (LE) :
assay presents a swift diagnostic method for identifying potential PJI. This enzyme is characteristically released by neutrophils as a response mechanism to infectious stimuli. A positive (*+') reading on the LE test may suggest the existence of an acute infection, while a double-positive ('++') serves as a threshold indicative of a chronic infection.

Despite the notable advantages of this test, including cost-effectiveness, wide availability and rapidity, the interpretation of outcomes remains susceptible to observer bias.20 Calprotectin ;is a protein secreted by neutrophils, and stimulates leucocyte migration as part of the inflammatory response. Han-touly et al. conducted a comprehensive meta-analysis comprising 618 subjects across eight studies looking at the diagnostic accuracycalprotectin.? They found a cumulative sensitivity and specificity of 92% and 93% respectively.Synovial CRP, and the combination of synovial CRP and serumCRP, has demonstrated superior diagnostic precision relative tothe exclusive use of serum CRP alone. In a study conducted by Baker et al., an analysis was undertaken of 621 patients being evaluated for a revision arthroplasty due to potential PJ1.22 Both serum and synovial CRP levels were examined, and the combination of the two resulted in an enhancement in diagnostic ac-curacy. They reported sensitivity as 74.6% and specificity of 98%, which were superior to serum CRP alone.D-lactate ; is a metabolic by-product derived from bacterial ac-tivity, typically present within infected tissues. It has been recommended as a screening test by Karbysheva et al., who tested 224 patients with suspected PJI synovial fluid and found that it had a 92.4% sensitivity and 88.6% specificity.23 However, as D-lactate mirrors bacterial activity, lower levels are seen in low-virulence infections.

Management Strategies:-
Management options include DAIR, single-stage revision, and two-stage revision. Two-stage revision remains the gold standard for chronic infection, whereas single-stage revision is suitable for selected cases with known organisms and good soft tissues.

DAIR:-
Debridement, antibiotics and implant retention (DAIR) is a controversial but increasingly common method of treating PJI. It has been indicated for acute and haematogenous infections in a functioning, well-fixed implant; however, some units have suggested that reasonable results can be achieved with chronic in-fections, especially if combined with local antibiotic delivery. A lack of a precise definition of what is undertaken during a DAIR (including what is exchanged), the use of local antibiotics and duration of post-operative antibiotics have hampered interpretation of reported results (Figure 2).

The best reported results for DAIR describe the following key steps:
1. The surgery should be performed by experienced PJI sur-geons. Many reports previously confused DAIR with a'washout' performed out-of-hours by on-call surgeons. A DAIR should be performed on a planned list by an experienced arthroplasty surgeon who regularly treats PJI.
2. A complete exposure of the joint is required. A DAIR should be undertaken with a standard revision TKR exposure, to allow examination of the whole joint space and bone/implant interfaces. It should not be undertaken arthroscopically.
3. Multiple tissue samples should be taken. At least five tissue samples should be taken for microbiological culture and two for histological examination. Ideally, samples should be taken with a no-touch technique with clean instruments from the medial/lateral gutters, suprapatellar pouch, poste rior capsule, and prosthetic-bone membrane.
4. Debridement is a full synovectomy. The debridement in a DAIR should be equivalent to that of a single or stagedTevision. Any modular component (e.g. polyethylene inseror extension piece in a tumour prosthesis) should be removed to facilitate adequate access to the prosthetic cav. ity. A sharp surgical removal of a synovium from the medial/lateral gutters, suprapatellar pouch,posteriorcapsule, and prosthetic-bone junction should be undertaken.
5. Scrubbing of retained implants. The surfaces of the retained implant and the prosthetic-bone junction should be scrubbed or cleaned with an antiseptic solution (chlorhexidine or diluted iodine solution) to disrupt any biofilm.
6. High-volume lavage. A lavage with saline or antiseptic solution should be undertaken, with 5-7 litres of fluid.
7. Fresh modular components. New modular components should be used to reconstruct the joint. In some low economic regions, the components (especially for tumour prostheses) are sterilized and reinserted; however, the gold-standard should be new implants.
8. Addition of antibiotic-loaded carriers. Increasingly, absorbable calcium antibiotic carriers are used with either broad spectrum antibiotics (covering both Gram-negative and Gram-positive organisms) or tailored antibiotics. The use of tailored antibiotics requires a preoperative aspiration toidentify the organism and its antibiogram.
9. Closure over a drain and occlusive dressing. The use of a suction drain is recommended, to manage the dead space and to help with wound management (especially if antibiotic carriers are used). Many authors now recommend the use of closed incision negative pressure dressings to reduce wound leakage.

10. Extended antibiotic coverage postoperatively. In the first few days following surgery, intravenous antibiotics shouldremain broad, until the infecting organism(s) are identified, and then tailored oral antibiotics should be continued for 3-6 months postoperatively.
The reported success rates for DAIR vary from 18% to 100%, but in a systemic review of reported results by Qasim et al., the mean success rate in controlling infection was 64% 29 The authors have reported the results of DAIR with local antibiotic carriers with 83% success at 2 years (unpublished).Factors that have been shown to influence the success of

DAIRs include:
1. Patient factors (host). Patient-related factors, including immunocompromise and the condition of the soft tissues (most surgeons feel that a sinus is a contraindication to a DAIR) are risk factors for failure, as DAIR relies on the host to combat any residual infection.
2. Duration of symptoms. Success rates of 28-62% have been shown with DAIR for late chronic or established PJI, as compared to 31-100% with acute infections. Furthermore, acute postoperative infection has shown better results as compared to haematogenous spread.
3. Microbiology. DAIR has been shown to be most effective in treating PJIs in non-immunocompromised hosts infected with low-virulence organisms with a favourable antibio-gram. Several studies have shown that infection with Staph aureus .

Treatment;
Single-stage revision:-
Single-stage revision surgery has been popular in Europe for many years with large arthroplasty centres such as Endoklinik (Hamburg); however, it has been less popular in the USA andfor TKRs compared to THRs (Figure 3). Traditionally, single-stage revision has been most indicated for a first-time PJI in a good host with good skin and a PJI with an organism sensitive to oral antibiotics; however, many authors now will contemplate single-stage revision in poorer hosts, recurrent infection and those with a sinus. Knowledge of the causative organism is important in single-stage revision, so that tailored antibiotics can be used intra- and postoperatively, necessitating preoperative aspiration.Razi et al. reported a consecutive series of 84 cases of single-stage revision TR that were performed for infected primary TKRs (44%) and for infected revision TKRs (56%), and all patients had previously received antibiotics." Patients wereexcluded from single-stage exchange if they were systemically septic, if the soft-tissue envelope was considered at risk and primary wound closure was not likely to be achievable, if massive bone resection was required, or if there was disruption of the extensor mechanism. Patients were not excluded forculture-negative PJI or the presence of a sinus. This meant that 75% (π = 84/112) of infected TKRs referred during the study period were eligible for a single-stage revision (DAIR in 6 patients, two-stage revision in 17 patients and knee arthrodesis in 5 patients). Their results showed that 91% of patients remainedinfection-free at 5 years, and this was not influenced by culture-negative infections, preoperative ASA status or revision of revision implants. They did, however, report that polymicrobial infections had a significantly higher rate of failure, and may be best-treated with a two-stage revision.

Two-stage revision:-
the management of infecteg bias, where ly thowever, many a the papers include reporting blas, where oy those patients mo made it to their second apents on ere plete a in the succen proup. The number of patients who complete a first-stage rer. grouput who do not reach a second operation is reported to be lo sion b, and this is one of the main reasons cited by proponents of single stage revision. However, there remains little doubt that in the worst case scenario', where there are polymicrobial in. fections, fungal, multi drug-resistant infection and those with very significant bone or soft tissue loss, that two-stage revisionoffers better results than single-stage revision.The first stage operation is where there is a complete removal of the implants and debridement of the effective joint space, followed by insertion of an antibiotic-laden spacer with tailored antibiotics. There is debate in the literature whether articulating or static spacers are better. Proponents of articulating spacers suggest the increased elution profile of antibiotics and possibly better early range of motion (ROM) following second-stage surgery, whilst proponents of the static spacer suggest an improvedsofttissue recovery and ability to delay second-stage due to spacer stability; however, studies suggest that reinfection and eventual ROM does not vary between types. After the operation the patient is commenced on antibiotics for a significant period.Recently, as with other techniques, many authors are advocating increased elution of antibiotics with carriers in addition to antibiotics contained within the PMMA.
How long the interval should be between stages, the duration of antibiotics and when to proceed to the second-stage operation remain controversial. A majority of clinicians would use a total of a minimum of 6 weeks duration of

antibiotics between stages, with a 2-week antibiotic holiday. However, there are proponents of a shorter duration, or even no parenteral antibiotics, and some prefer to continue antibiotics to until the second stage. A recent randomized clinical trial, the Solario study, reported at the European Bone and Infection Society in 2024, analysed 500 orthopaedic infections treated with local antibiotic delivery and found that a short course of antibiotics (7 days) postoperatively showed no difference in infection control compared to a longer (>4 weeks) course, with fewer adverse events.The second stage is normally performed when the clinical signs of infection have settled, inflammatory markers are nearcessation d there has been no flare-up of infection followingcessation of antibiotics. The spacer is removed, the cavity debrided again, and a reconstruction is performed.

Salvage options;

When multiple attempts at curing infection have failed, patients are unfit for further major surgery or soft tissues are poor, preventing a functional total knee replacement, then several main options exist.Above knee amputation (AKA) is an obvious, but often too-frequently used treatment for recurrent infection. After an infected primary TKR, there is a 0.025% amputation rate; however, this can increase to 5.1% after persistent infection despite revision TKR surgery, with an incidence of 37% in infected tumour prostheses. Most elderly patients will be unable to use a prosthetic leg due to the high energy demands, and phantom limb pain remain a significant complication. The authors believe that AKA should be a last resort or a specific patient choice, with a limb salvage rate of 91% in their series of recurrent infections.Arthrodesis (KA): a primary bone-to-bone knee arthrodesis, or the use of arthrodesis implants, has reduced the need for an AKA in salvage cases. AKA has the advantage of not requiring a functioning extensor mechanism. Wilding et al. reported the outcome of eight silver-coated knee arthrodesis prostheses in patients facing an AKA after failed knee PJI. There were no subsequent amputations, deaths or implant revisions. One case of recurrent infection was successfully treated with washout and debridement. The mean pre-arthrodesis and post-arthrodesisOxford Knee Score difference was +8.9 points (P = 0.086),with significantly improved pain (P = 0.019), night pain (P =0.021) and ease of standing (P = 0.003).Prolonged suppressive antibiotic therapy (PSAT): when patients refuse either arthrodesis or amputation, long-term antibiotic suppression is a potential alternative option. The antibiotics will not cure the infection, but may make it more manageable and reduce hospital admissions. In one series of 136 elderly patients treated with PSAT, failure was defined as: (i) local or systemic progression of the infection (failure), (ii) death and iii) discontinuation or switch of PSAT.45 There were 46 (33.8%) patientswith an event: 25 (18%) with an adverse drug reaction leading to definitive discontinuation or switch of PSAT, 8 (5.9%) with progression of sepsis, and 13 (9.6%) died. Among patients under follow-up, the survival rate without an event at 2 years was 61%.

Outcomes:-

Two-stage revision achieves infection eradication rates exceeding 85%. Emerging evidence suggests comparable outcomes with single-stage revision in selected patients.

Conclusion:-

PJI remains a significant challenge in knee arthroplasty. Early diagnosis, appropriate surgical strategy, and multidisciplinary care are essential for successful outcomes.

Table 1: Comparison of One-Stage and Two-Stage Revision

Parameter	One-Stage Revision	Two-Stage Revision
Indication	Selected cases	Chronic infection
Hospital stay	Shorter	Longer
Morbidity	Lower	Higher
Eradication rate	Comparable in selected cases	>85%

Figure 1: Treatment Algorithm for PJI (Textual Flowchart)

Suspected PJI → Clinical & laboratory evaluation → Joint aspiration → Acute infection → DAIR Chronic infection → Assess host & organism → Suitable → One-stage revision | Not suitable → Two-stage revision

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