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The outcomes of total knee arthroplasty following the incidental finding of tuberculosis and its treatment: A prospective study

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ABSTRACT

Introduction: Extrapulmonary tuberculosis (EPTB) accounts for 16 % of tuberculosis cases globally, with knee joint tuberculosis more prevalent in underdeveloped nations. Total knee arthroplasty (TKA) is commonly used to treat tubercular arthritis of knee, however, there is a marked paucity of research on the outcomes after an incidental diagnosis. The aim of the study is to investigate the outcomes of total knee arthroplasty after an incidental diagnosis of tuberculosis and its management.

Methods: A prospective-observational study was conducted in NCR-Delhi from May 2019 to June 2023, wherein 533 patients had synovial tissue abnormalities and 11 patients reported with positive histopathological examination (HPE) for knee tuberculosis. All the patients whose informed consent was obtained were put on a twelve-month standard treatment (2HRZE or S/10HR) according to World Health Organization (WHO) guidelines for extrapulmonary TB after TKA and were monitored for the outcome of treatment, any postoperative complication, or implant failure.

Result: The mean age of the patients was 63 ± 13 years and 72.7 % of patients were female. The mean hemoglobin, Body Mass Index (BMI), and Erythrocyte Sedimentation Rate (ESR) values were 10.29 ± 1.36 mg/dl, 29.78 ± 6.1 kg/m^2, and 37.37 mm/h respectively and the median of the C-reactive protein (CRP) value was 11 mg/dl at the time of operative procedure. All patients presented with knee-joint pain and swelling and were operated for knee-joint replacement surgery. After one year of standard treatment (2HRZE or S/10HR), no relapses, pain, or progressive radiolucency around the component, or postoperative neurologic or vascular complications were observed. The median range of motion (ROM) was improved from 10 - to 100 to 0–115, the average knee score improved from 44.9 ± 8.9 to 84.9 ± 7.73 points and the average function score improved from 28.82 ± 15.56 to 94.0 ± 7.68 points which were statistically significant at 95 % CI ($p < 0.0001$).

Conclusion: We concluded from this study that any abnormalities in ESR, CRP level prior to, and bone tissue or synovial tissue during operative procedure should be considered for articular tuberculosis and managed according to guidelines. This will make replacement procedures more sustainable and effective by lowering the risk of post-operative infection or implant-related complications and improving patients' quality of life.

1. Introduction

As the primary cause of death worldwide, tuberculosis (TB) is a serious public health concern in both industrialised and developing nations. Reportedly, there were almost 10 million newly diagnosed cases of tuberculosis globally in 2018.[1] Approximately 1.4 million individuals who tested negative for Human Immunodeficiency Virus (HIV) died from tuberculosis in 2021, and an estimated 187,000 individuals who tested positive for HIV also perished. India accounted for 28 % of the total TB cases globally.[2]

As a multi-systemic illness, tuberculosis primarily affects the lungs.[3] Between 10 % and 25 % of cases of extra-pulmonary tuberculosis exhibit musculoskeletal involvement, with the spine being the most often affected region, followed by the hip, knee, and ankle/foot.[4–6] In addition, individuals with weakened immune systems are more susceptible to developing latent tuberculosis in the knee joint.[7] Due to the non-typical and very variable symptoms of joint TB, it might be difficult to make an accurate diagnosis during the initial stages of the disease.

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Patients are often misdiagnosed as having merely the primary condition when, in fact, they have other disorders such as rheumatoid arthritis or early-stage knee TB.[8] If total knee replacement (TKR) is used to treat knee TB as a non-infectious joint illness, it will necessitate more sophisticated treatment, increasing morbidity and financial burden as well as the risk of periprosthetic joint infections.

In a recent investigation, 89 cases of post-operative recurrent joint TB (mainly from joint fusion procedures) were examined. Due to initial misdiagnoses, 32 patients (36.0 %) received antituberculosis chemotherapy that was not conventional, while 45 patients (50.6 %) did not receive antituberculosis chemotherapy at all.[9]

The ideal time to treat patients with osteoarticular tuberculosis is debatable, though a significant disease-free period (ideally 10 years) is recommended by many authors before prosthetic implantation. There have recently been several reports of successful primary TKA for patients suffering from knee TB after the disease has been confirmed to heal.[10] No studies or literature exist that show the outcomes of TKA after an incidental finding of knee TB during the surgical procedure and its management, but this study includes the largest number of patients treated with TKA for knee tuberculosis who did not have a history of prior knee tuberculosis.

We aimed this observational study, to better understand the value of synovial tissue biopsy in the event of finding an abnormal synovial tissue intraoperatively and the results of total knee replacement surgery after an incidental tuberculosis diagnosis and their management.

2. Methods

2.1. Study design

This study followed a prospective observational design.

2.2. Study population

From May 2019 to June 2023, patients at Sarvodaya Multispecialty Hospital in Sector-8, Faridabad, NCR-Delhi who had incidental discoveries of knee tuberculosis during total knee arthroplasty were included in the study.

2.3. Ethical committee

The review board of Sarvodaya multi-specialty hospital ECR/999/Inst/HR/2017 granted the ethical approval to safeguard participant rights and welfare.

3. Procedure

3.1. Inclusion criteria

A total of 533 synovial tissue biopsies were sent for abnormal findings during TKA, and 11 patients who had positive results for extrapulmonary tuberculosis of the knee joint were included in the study.

3.2. Exclusion criteria

Patients with previous exposure to TB infection both pulmonary and extra-pulmonary were excluded from the study.

3.3. Surgical technique

All TKA was performed under spinal anesthesia and femoral block without tourniquet with subvastus approach (SA). After exposure of the knee joint, if inflamed synovial tissue was present (Fig. 1) then thorough debridement was done, and resected synovial tissues were sent for the Acid-Fast Bacilli (AFB) examination, GENE-XPERT examination, and HPE along with synovial fluids examination for gram staining, AFB staining, aerobic and anaerobic culture, and sensitivity. During the procedure, intermittent pulsatile lavage with normal saline and antibiotics was done. Following TKA, the final closure was done in layers using a staple less technique. Patients were mobilized 3–4 h post-surgery with walker support and started on Range of Motion (ROM) and strengthening exercises. On post-operative day 2 first dressing change was done. After histopathological examination reports patients were discharged with anti-tubercular therapy (ATT), according to WHO guidelines for extrapulmonary TB. All patients were followed up every 2 months within the first 6 months followed by, at 12,18, and 24 months post-operatively. ESR was done every 2 months till it came within the normal range in the follow-up period. X-ray knee was done every 6 months to

Fig. 1. Intra-operative findings of synovial tissue of right knee during TKA.

know the implant status during follow-up (Fig. 2) Pre- and post-treatment the Knee Scoring System (KSS) for the clinical and functional American Knee Society Score (AKSS) score was compared. Pre- and post-treatment ROM was also compared to see any significant changes.

3.4. Data collection and statistical analysis

The collected data in the case report forms (CRF) were transferred to Microsoft Excel 2016. For statistical purposes Med Calc. V 12.5 and SPSS V 20 were used. The quantitative variables like age, BMI, Knee Scoring System, and Reduction of movement were presented in median and range, and qualitative variables like gender, presenting complaints, HPE result, history of any TB contacts, diagnosis, type of surgery, and type of TB treatment were expressed as percentage and proportions. Pre- and post-treatment Knee Scoring System was compared using the paired T-test and the test of significance was calculated at 95 % confidence interval.

3.5. Objective

To better understand the value of synovial tissue biopsy in the event of finding abnormal synovial tissue intraoperatively and the results of total knee replacement surgery after an incidental tuberculosis diagnosis and their management.

3.6. Outcome

At the end of the 12 months and during TB treatment, the patients were followed up for any postoperative complication, adverse events following the treatment, and any other complications like implant failure or treatment failure. Pre- and post-treatment the knee scoring system for the clinical and functional score was compared as well as pre-and post-treatment Range of motion was also compared to see any significant changes.

4. Results

Throughout the study period, a total of 3000 patients had surgical procedures, out of whom 533 exhibited intraoperative inflammation in the synovial region together with aberrant fluids. Knee tuberculosis was reported in 11 out of the synovial specimens sent for investigation during the total knee arthroplasty (TKA) operation, accounting for 2.06 % of the patients.

The diagnosis of TB knee was histopathologically confirmed in all patients, as evidenced by the presence of characteristic granulomatous inflammation, characterised by the presence of epithelioid histiocytes surrounded by lymphocytes (Fig. 3). Three patients had positive catridge based nucleic acid amplification test (CBNAAT) results. 72.7 % of the patients were female (n = 8) and the mean age of the patients was 63 ± 13 years. The mean hemoglobin was 10.29 ± 1.36 mg/dl. The mean BMI of the patients was 29.78 ± 6.1 kg/m^2 at the time of operative procedure, which was more than the normal range and considered as the pre-obese patients. The mean ESR value was 37.37 mm/h (15–67), which was higher than the normal (<15 mm/h) at the time of the operative procedure. The median of the CRP value was 11 (1.7–74) which was much higher than the normal range of 0.8–1 mg/dl at the time of operative procedure. 36.36 % of the patients (n = 4) showed the rheumatoid arthritis factor positive for the knee joint and were treated for the same. Moreover, preoperative DEXA scan showed osteoporosis in three patients (27 %), of which two were associated with rheumatoid arthritis. All the patients presented with knee joint pain and swelling at the time of admission (7 in both knee; 3 in the right knee, and 1 in the left knee) without any symptoms of fever, weight loss, anorexia, or night sweats. Of all these patients, 63.6 % patients (n = 7) were operated for the bilateral knee joint replacement surgery.

After testing positive for knee tuberculosis, all positive patients received treatment in accordance with WHO recommendations for extrapulmonary TB, including a two-month intensive phase with isoniazid, rifampicin, pyrazinamide, and ethambutol, followed by a 10-month continuation phase with isoniazid and rifampicin daily (2HRZE/10HR). With the exception of two patients whose ESR and CRP levels were elevated at 6 months after surgery their treatment with ATT was extended to 18 months. The remaining postoperative patients' ESRs returned to the normal range at 6 months. Disease-modifying anti-rheumatic drugs DMARDs) and ATT were used in the treatment of patients with RA.

Following an average follow-up of 22 months (12–33 months), we found no treatment failure, relapse, or tuberculous infection resistance in any of the patients. The median range of motion was improved from 10 to 100 to 0–115 at the most recent follow-up, and the average clinical AKSS score improved from 44.9 ± 8.9 to 84.9 ± 7.73 points and the average function AKSS score improved from 28.82 ± 15.56 to 94.0 ± 7.68 points which was statistically significant at 95 % CI ($p < 0.0001$). During the follow-ups, there were no postoperative complications like pyogenic infection or deep vein thrombosis. The radiographs taken at the most recent follow-up did not show any radiolucency or loosening of the prostheses.

Fig. 2. **(a)** pre-operative (left), **(b)** post-operative (right) and **(c)** 2 – year follow up X-ray of Right Knee.

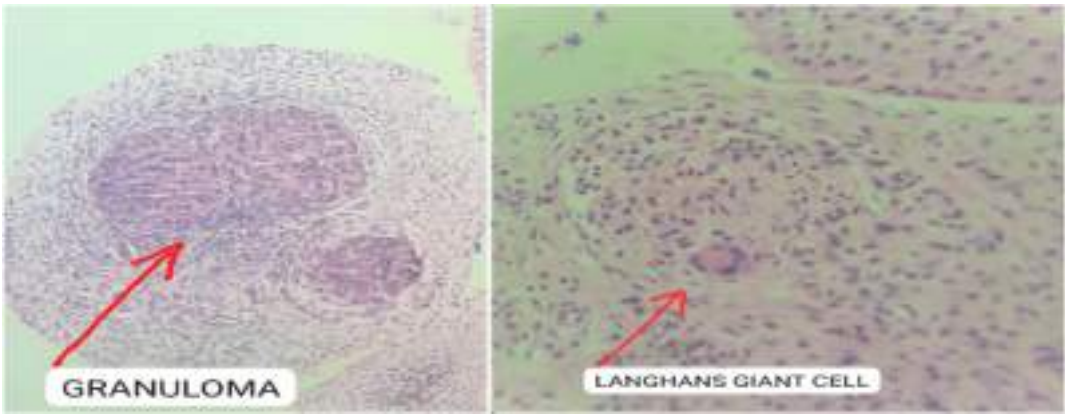

Fig. 3. Histopathological observations of Tuberculosis in patients undergoing TKA.

5. Discussion

One rare kind of tuberculosis is osteoarticular. Consequently, tuberculosis is hardly taken into account while addressing joint issues. Moreover, the clinical manifestations of joint tuberculosis often deviate from the norm; most patients do not exhibit systemic symptoms such as fever, night sweats, or weight loss. In addition, tuberculosis affecting the knee joint primarily presents with symptoms such as knee joint discomfort, swelling, and limited mobility, rather than fever or weight loss as a the usual symptoms of osteoarthritis knee. Ultimately, distinguishing between several possible diagnosis is more challenging in patients with rheumatoid arthritis. Existing literature has proven a correlation between patients with rheumatoid arthritis who are on disease-modifying antirheumatic drugs (DMARDs) and tuberculosis (TB).[11,12]

In this study, incidental findings of extra-pulmonary tuberculosis on synovial biopsy were sent for HPE after TKR was treated with antitubercular treatment and followed postoperatively. With the help of this study, we were able to understand the importance of sending intraoperative synovial tissue and fluid for testing in the event of abnormal findings as well as the survival of implants in patients who had incidental tuberculosis during TKA. All cases in this study had knee pain and swelling, and four patients also showed signs and symptoms of rheumatoid arthritis without any clinical signs of tuberculosis.

Mycobacterium tuberculosis is unlikely to be found in these tissues or joint fluid using molecular diagnostics or clinical pathogenic detection using smear testing. The positive rate of bacterial culture is much lower due to factors like material selection and long-term anti-TB drug use. As a result, clinical diagnosis employs empirical ATT drug therapy.[13] In certain cases, the general pathological exams did not reveal the typical signs such as caseous necrosis and epithelioid degeneration. Instead, only “chronic inflammation” was observed. The absence of supplementary diagnostic techniques such as acid-fast staining, culture, tissue biopsy, and PCR heightened the likelihood of misdiagnosis or failure to detect the condition.

The radiographic alterations in native joints conform to Phemister’s triad of joint tuberculosis, which includes joint space narrowing, subchondral osteopenia, and lateral osseous erosions. These changes bear resemblance to the indications of osteoarthritis.[14,15]

Inflammatory markers including ESR and CRP were usually elevated to some degree in tuberculous arthritis but are non-specific. Erythrocyte sedimentation rate (ESR) tends to be elevated during the acute phase of tuberculosis infection, reflecting an inflammatory response. In contrast, during the chronic or quiescent stages of the disease, ESR levels often return to normal. This fluctuation in ESR levels serves as a potential indicator of the efficacy of antitubercular treatment, with declining ESR values correlating with treatment effectiveness in managing the disease.[16,17] The erythrocyte sedimentation rate (ESR) frequently takes up to 90 days to revert to pre-operative levels and can remain increased for over a year after arthroplasty surgery, posing challenges in its interpretation.[18,19] Nine of these patients had ESR and CRP levels that were above normal at the time of the treatment, and all of them experienced abnormalities in the synovial tissue. Serum ESR and CRP levels were checked every 2 months; in 9 of them, they returned to normal within 6 months postoperatively, therefore ATT was stopped at 12 months. In two patients who had elevated ESR at 12 months, ATT was continued for a further 6 months.

Therefore, TKR can be performed safely in joints where active tuberculosis has been identified postoperatively if the patient is given the right anti-TB medication, which has better results than the alternatives. In a study conducted by Su et al., in 1996, 16 patients with tuberculous arthritis who had undergone knee replacement surgery were examined. Out of these patients, eight were diagnosed with tuberculous arthritis. Three of them received medication for a duration of 2 months, while the remaining five were treated for a period of 10–12 months. For a minimum of 12 months after surgery, the patients’ treatment regimens included the administration of three antituberculosis drugs: isoniazid, ethambutol, and rifampicin. Only one patient with rheumatoid arthritis had tuberculosis recurrence within 14 months after surgery, and the joint fusion was cured.[20] Twelve patients with active tuberculosis who underwent total knee arthroplasty (TKA) were reported in another study by Ozturkmen et al. (2013). Three of the patients had one-phase knee replacements and preoperative antituberculosis treatments, while the other nine patients had one-stage knee replacements and intervals between the two-stage phases of less than six months. Two months following the procedure, the patient received a combination of four antituberculosis medications, and then another 10 months of treatment with two antituberculotic medication. Out of these patients, three exhibited elevated ESRs and CRP levels six months following the surgeries. Consequently, their antituberculosis therapies were prolonged to a duration of 18 months. In that study, the mean interval between the diagnosis of tuberculosis and TKA was 4.0 $\pm$ 1.5 months. In 6.1 $\pm$ 1.8 years, the average follow-up period, not a single patient had a relapse of tuberculosis. The authors held the belief that even if a person had active tuberculosis, it should not be considered a reason to avoid undergoing total knee arthroplasty (TKA). They also argued that there was no requirement for a significant time gap between the diagnosis of tuberculosis and the TKA procedure.[21]

Kadakia et al., 2007 published a case study about an 85-year-old patient who fell and fractured the tibial plateau, requiring therapeutic joint replacement. The patient’s post-operative bone pathology analysis revealed no evidence of caseous necrosis, epithelioid cells, or Langhans giant cells. However, the patient’s surgical incision did not heal properly, and a sinus formed as a result. After a month, the patient developed a persistent, productive cough. Considering a preoperative parietal lobe scarring on a chest radiograph, the sputum and sinus pus were subjected

to laboratory tests, which revealed that both were positive for acid-fast bacteria. Acid-fast bacteria were also found in bone tissue samples obtained during TKA.[22]

Harwin et al., 2013 described another case study, which showed a 60-year-old female patient was preoperatively diagnosed with osteoarthritis. Moderate synovial hyperplasia, edema, cellulose ooze, and vascular wing formation were observed during surgery. This patient was eventually diagnosed with rheumatoid arthritis and had therapeutic joint replacement surgery. The results of this patient's postoperative pathological analyses revealed cellulose-like degeneration and nonspecific inflammation. However, 5 months after the operation, a mass appeared on the patient's medial side of the knee. The mass broke and the prosthesis loosened after a year of observation. The mass contained a cheese-like substance, and tubercle bacilli were cultured. As a result, this case involved a missed diagnosis of knee tuberculosis.[23]

During the follow-up period, no patients experienced implant failure or TB relapse. Further evidence of the efficacy of the treatment was revealed in the considerable mean difference of KSS between clinical score and functional score.

In the latest follow-up X-ray, there were no radiographic findings suggestive of implant loosening or radiolucency in any of our series.

A systemic review on Total Knee Arthroplasty in Patients with Unsuspected Tuberculosis of the Joint conducted by Du Wang et al., 2007 recommended a thorough investigation into the reasons behind elevated ESR and CRP levels detected preoperatively. This recommendation aims to better discern and address potential underlying tuberculosis infections in patients with weakened immune systems. Pathological examination is a reliable method of diagnosing tuberculosis; however, multiple specimens must be examined. Positive *M. tuberculosis* cultures have high diagnostic sensitivity and specificity. Antituberculosis drug treatment is preferred, and debridement and prosthesis retention are required. Two-stage repair should be used for patients with loosening prostheses.[15]

6. Conclusion

Due of its rarity and atypical symptoms, osteoarticular TB is easily misdiagnosed. so attention should be paid to patients with weakened immune systems who have intraoperative aberrant synovial tissue discovered during the procedure should be tested for osteoarticular TB. Additionally, the causes of elevated ESRs and CRP levels should be investigated. Diagnosing tuberculosis using histopathological examination works well but requires submission of several specimens for analysis. The clinical outcomes of TKA in patients diagnosed with TB postsurgery after completing ATT compare favorably with those of noninfected knees. This will make the replacement procedure more sustainable and effective by lowering the risk of post-operative infection or implant-related complications and improving patients' quality of life.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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