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Review Article

Comprehensive review of osteoarticular tuberculosis: from epidemiology to emerging therapies

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ABSTRACT

Osteoarticular tuberculosis (OATB) remains a significant global health challenge with high morbidity and potential for permanent disability. Recent advancements in diagnostics, pharmacotherapy, and adjunctive treatments have shown promise for improving the outcomes of patients with OATB. This review summarizes the latest developments in the field, focusing on epidemiology, pathogenesis, diagnostic innovations, novel anti-tuberculosis drugs, combination therapy approaches, surgical interventions, adjunctive therapies, and the importance of multidisciplinary approaches. Emerging diagnostic technologies such as advanced imaging modalities, molecular assays, and nanotechnology-based tests have enhanced the speed and accuracy of OATB detection. Newer anti-tuberculosis drugs, including bedaquiline, delamanid, and pretomanid, have demonstrated efficacy in multidrug-resistant (MDR) and extensively drug-resistant (XDR) cases, whereas DprE1 inhibitors and oxazolidinone alternatives show promise in early phase trials. Minimally invasive surgical techniques, joint-preserving procedures, and reconstructive methods using 3D-printed implants and antibiotic-loaded materials have improved functional outcomes. Immunomodulators, bone grafts, and regenerative medicine have been explored as adjunctive therapies. Effective management of OATB requires collaboration among various specialists, and integrated care models facilitate personalized treatment plans. Challenges remain, including drug resistance, and the need for further research to establish optimal regimens and durations specific to OATB. By highlighting key advancements and their potential impact on patient outcomes, this review underscores the importance of a multidisciplinary evolving paradigm for treating OATB in the era of precision medicine.

Keywords: Osteoarticular tuberculosis, Extrapulmonary tuberculosis, Multidrug-resistant tuberculosis, Antitubercular agents, Molecular diagnostic techniques, Surgical procedures, Immunotherapy, Regenerative medicine

INTRODUCTION

Osteoarticular tuberculosis (OATB) is a form of extrapulmonary tuberculosis (EPTB) that affects the bones, joints, and spine, most commonly involving the vertebral column (Pott's spine), hip, and knee joints. It accounts for approximately 10-15% of all EPTB cases and 1-3% of total tuberculosis cases globally.[1,2] Despite representing a relatively small proportion of TB cases, OATB carries significant morbidity owing to the potential for structural deformity, neurological compromise, and long-term functional impairment if not diagnosed and treated early.[3]

OATB pathogenesis involves the hematogenous spread of *Mycobacterium tuberculosis* from a primary pulmonary or lymphatic focus to osseous tissues. The disease course is typically insidious, with non-specific symptoms, such as chronic pain, swelling, or stiffness, often leading to delayed diagnosis and treatment.[4] This delay, combined

with the poor penetration of antitubercular drugs (ATT) into avascular or necrotic bone tissues, complicates management and contributes to residual deformities or recurrence.[5]

Traditionally, the mainstay of OATB treatment has been prolonged ATT for over 9-12 months, often supplemented by surgical intervention in cases of neurological compromise, spinal instability, or nonresponsiveness to medical therapy.[6] However, the emergence of MDR and XDR TB has challenged the conventional treatment strategies. First-line ATT regimens are often ineffective in these cases, necessitating the use of second-line and novel drugs with enhanced efficacy and better bone-penetration profiles.[7]

Recent years have witnessed significant advancements in OATB management, particularly in the domains of rapid molecular diagnostics, novel antitubercular pharmacotherapies, host-directed therapies, and surgical innovations. The development of new agents, such as bedaquiline, delamanid, pretomanid, and DprE1 inhibitors, has transformed the treatment landscape, particularly for drug-resistant TB strains. [8,9] Simultaneously, regenerative techniques such as mesenchymal stem cell therapy and 3D-printed bone grafts are being investigated to enhance structural recovery and reduce long-term disability.[10,11]

Moreover, the integration of host-directed therapies and immunomodulators aims to boost the host immune response while minimizing tissue damage, thereby offering a promising adjunct to antimicrobial treatments. [12] Molecular tools such as Xpert MTB/RIF Ultra, next-generation sequencing (NGS), and PET-MRI have enhanced the early diagnosis and monitoring of OATB, allowing timely intervention and individualized treatment planning .[13,14]

Given the evolving nature of tuberculosis management and the high functional cost associated with osteoarticular involvement, there is a pressing need to review and contextualize these recent advancements. This article aims to provide a comprehensive overview of current innovations in diagnosis, medical management, surgical approaches, and adjunctive therapies for OATB, highlighting their clinical applicability and potential to improve patient outcomes.

EPIDEMIOLOGY

OATB represents a significant subset of EPTB cases, accounting for approximately 10-15% of EPTB cases and 1-3% of all tuberculosis cases globally.[1] Among osteoarticular sites, the spine is the most frequently involved, followed by weight-bearing joints, such as the hip and knee.[6] The burden of OATB is disproportionately higher in developing countries with high TB prevalence, particularly in Southeast Asia, sub-Saharan Africa, and parts of Eastern Europe. [2]

According to the world health organization (WHO) global tuberculosis report 2023, an estimated 10.6 million people will develop TB worldwide in 2022, with approximately 1.6 million TB-related deaths. Although pulmonary TB constitutes the majority of cases, the rate of EPTB, including skeletal TB, has shown a relative increase owing to better diagnostic modalities and heightened clinical awareness.[2] Immunocompromised populations, such as individuals with HIV/AIDS, diabetes, or those undergoing immunosuppressive therapy, are at greater risk of developing EPTB, including OATB.[15]

Drug-resistant TB is an emerging concern in osteoarticular infections. Studies have reported an approximate overall drug resistance incidence of 12.5%, with a primary drug resistance of 11.1% in consecutive cases of OATB, further complicating the treatment strategies.[16]

Understanding the epidemiological trends of OATB sets the stage for a deeper exploration of its pathogenesis, which is crucial for developing effective diagnostic and therapeutic strategies.

PATHOGENESIS

The pathogenesis of OATB begins with the hematogenous dissemination of *Mycobacterium tuberculosis* from a primary focus, commonly pulmonary or lymphatic, to distant skeletal sites.[4] In the spine, bacilli typically seed the metaphyseal regions of vertebral bodies owing to their rich vascular supply. Involvement of the adjacent intervertebral discs occurs through direct extension, resulting in spondylodiscitis and vertebral collapse.[5]

Infection leads to granulomatous inflammation, caseation necrosis, and subsequent bone destruction. If unchecked, this process results in deformity, instability, and neurological compromise in spinal TB or joint destruction in peripheral OATB. The paucibacillary nature of skeletal TB often leads to delayed culture positivity and contributes to diagnostic challenges.[17]

Synovial membrane involvement is typically the first sign of infection in joints. Mycobacteria cause chronic synovitis that progressively erodes the cartilage and bone. The immune response, mediated by activated macrophages, T-cells, and cytokines, such as TNF-α and IFN-γ, plays a dual role by both containing the infection and promoting tissue destruction.[12]

Bone lesions in TB are often characterized by cold abscess formation, sequestrum development, and sinus tract formation in advanced cases. These features distinguish it from pyogenic osteomyelitis, which typically presents with acute inflammation and systemic toxicity.[14]

The slow and insidious course of the disease, lack of early symptoms, and low bacillary load often lead to diagnostic delays, contributing to advanced-stage presentations with irreversible joint or spinal damage.

DIAGNOSTIC ADVANCEMENTS

The diagnosis of OATB has historically posed a challenge owing to its insidious onset, non-specific symptoms, and paucibacillary nature. However, significant advancements in imaging modalities, molecular diagnostics, and biomarker identification have enhanced early detection and accurate diagnosis, facilitating timely intervention and improved outcomes.

IMPROVED IMAGING TECHNIQUES

Radiographic imaging remains a cornerstone in the diagnosis of OATB, with conventional radiography being the initial modality. However, advanced imaging techniques play a critical role in early disease detection, anatomical delineation, and surgical planning.

Magnetic resonance imaging (MRI) is considered the gold standard for spinal tuberculosis because of its superior sensitivity in detecting marrow edema, abscess formation, disc involvement, and spinal cord compression before changes become evident on radiography. MRI also helps differentiate tubercular spondylitis from pyogenic and neoplastic etiologies based on characteristic findings, such as contiguous vertebral involvement and preserved disc spaces in the early stages.[18]

Computed tomography (CT) provides detailed information on bone destruction, sequestrum formation, and spinal stability. It is especially valuable for assessing posterior element involvement and the guiding CT-guided biopsies.[19]

Hybrid imaging techniques, such as positron emission tomography-computed tomography (PET-CT) and PET-MRI, are emerging tools that aid in the functional and anatomical assessment of active disease. PET-CT using 18F-FDG has shown promise in identifying metabolically active lesions and monitoring responses to therapy.[14]

MOLECULAR DIAGNOSTIC METHODS

Molecular diagnostics have revolutionized tuberculosis detection, offering rapid, sensitive, and specific results, even in paucibacillary cases. The Xpert MTB/RIF assay, endorsed by the WHO, allows the simultaneous detection of *Mycobacterium tuberculosis* and rifampicin resistance directly from tissue or pus samples within hours.[20]

An enhanced version, Xpert MTB/RIF ultra, has shown increased sensitivity in detecting lower bacterial loads in extrapulmonary samples, including synovial fluid and bone biopsies.[13] This has reduced diagnostic delays and enabled the early initiation of appropriate therapy.

Line probe assays (LPAs), such as geno type MTB DR plus, detect resistance to first-line drugs, such as isoniazid and rifampicin, while MTB DRsl identifies resistance to second-line agents, aiding in the management of drug-resistant cases.[21]

NGS is an emerging diagnostic modality capable of identifying the full resistance profile of bacilli. It can detect low levels of heteroresistance and uncommon mutations, thereby providing a comprehensive genetic blueprint for drug susceptibility. [22]

Table 1: Summary of diagnostic modalities for OATB.

Diagnostic tool	Principle	Sample type	Sensitivity	Remarks
Xpert MTB/ RIF ultra	PCR-based molecular test	Tissue, synovial fluid	High	Also detects rifampicin resistance
MRI	Imaging	N/A	Very High	Best for early spinal disease
ADA	Enzyme activity	Synovial/pleural fluid	Moderate to high	Non-specific, adjunctive use
NGS	DNA sequencing	Tissue	High	Detects drug resistance profiles

BIOMARKERS FOR EARLY DETECTION

Biomarker research on OATB is still in its early stages, but several promising markers have emerged that may support diagnosis and disease monitoring.

Adenosine deaminase (ADA) levels in synovial or pleural fluid have been widely studied as supportive evidence of TB. ADA values >40 IU/L in joint fluid have shown high sensitivity and specificity in suspected tubercular arthritis.[23]

Interferon-gamma release assays (IGRAs), including QuantiFERON-TB Gold, detect latent or active TB infections by measuring T cell-mediated responses to *M. tuberculosis* antigens. Although not specific to OATB, they are helpful in confirming TB exposure in clinically suggestive cases.[24]

Other exploratory biomarkers include serum neopterin, matrix metalloproteinases (MMPs), and cytokine profiles, which may aid in distinguishing active from latent TB or in assessing treatment response. However, their clinical applicability remains unclear.[25]

MEDICAL MANAGEMENT

Medical therapy remains the mainstay treatment for OATB. The standard approach involves prolonged administration of first-line ATT, which are effective in most cases, particularly when initiated early and adhered to appropriately.

Standard First-line ATT

The classical regimen for drug-susceptible OATB comprises two phases. The intensive phase lasts for two months and includes the administration of four drugs: Isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E). This is followed by the continuation phase, which lasts for 10-12 months and typically involves Isoniazid and Rifampicin, with or without ethambutol. The extended duration of therapy is crucial because of the poor vascularity of the bone and joint tissues, which hampers drug penetration and delays bacillary clearance. Continuous clinical and radiologic monitoring is necessary to evaluate the treatment response. The WHO currently recommends a minimum of 9 to 12 months of therapy for skeletal tuberculosis, although the optimal treatment duration remains under active investigation.[1,6]

EMERGING CHALLENGES AND THE NEED FOR NOVEL AGENTS

Emerging challenges continue to undermine the effectiveness of first-line drugs for the treatment of OATB. One major concern is the increasing incidence of MDR-TB, which complicates treatment protocols and reduces therapeutic success. Additionally, the diagnosis of OATB is often delayed owing to its non-specific clinical presentation and the paucibacillary nature of the disease, making early detection difficult.

Another limitation is the suboptimal penetration of standard antitubercular drugs into the osseous and synovial tissues, which can result in inadequate local drug concentrations and treatment failure. Collectively, these factors highlight the urgent need for the development and implementation of novel antitubercular agents, particularly for managing drug-resistant or refractory cases of OATB.

NOVEL ANTI-TUBERCULOSIS DRUGS

In response to the rising burden of MDR and XDR tuberculosis described earlier, several novel antitubercular agents have been developed and are now being incorporated into treatment regimens for refractory or drug-resistant OATB. Key agents include:

Bedaquiline

A diarylquinoline that inhibits mycobacterial ATP synthase, has shown potent activity against MDR-TB. It is now a WHO-recommended agent for MDR regimens and has shown promise in osteoarticular TB when used in combination with linezolid and levofloxacin. [26]

Delamanid

A nitrodihydroimidazooxazole derivative, inhibits mycolic acid synthesis. Although data specific to skeletal TB are limited, delamanid is increasingly used in extended regimens for EPTB.[27]

Linezolid

Initially oxazolidinone antibiotic, exhibits excellent bone penetration and has proven effective in both pulmonary and EP-MDR-TB cases, albeit with hematologic and neurologic toxicity risks with long-term use.[28]

Pretomanid

In combination with bedaquiline and linezolid (BPaL regimen), is part of an all-oral shorter-course therapy approved for highly resistant TB. Although primarily evaluated in pulmonary TB, the combination holds promise for resistant skeletal TB.[29]

Table 2: Novel anti-TB drugs and their mechanisms.

Drug	Mechanism	Indications	Key advantages	Limitations
Bedaquiline	ATP synthase inhibition	MDR-TB	Oral, effective	Cardiotoxicity
Delamanid	Mycolic acid inhibition	XDR/MDR-TB	Works with bedaquiline	Limited OATB data
Pretomanid	Cell wall and respiratory inhibition	BPaL regimen	Potent	Only for resistant cases

These agents are increasingly included in regimens for resistant or relapsed OATB, especially in cases confirmed by drug susceptibility testing (DST) or molecular diagnostics.

COMBINATION THERAPY APPROACHES

The standard therapy for drug-sensitive OATB mirrors that for pulmonary TB. Current WHO guidelines recommend a 6–9-month regimen, beginning with a 2-month intensive phase of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE), followed by a continuation phase with isoniazid and rifampicin (HR) for an additional 4-7 months.[30]

For spinal and weight-bearing joint TB, many clinicians advocate extended therapy for up to 12 months because of the high risk of relapse, delayed healing, and difficulty in monitoring the response.[31] However, studies have shown that shorter regimens (6-9 months) can be equally effective when initiated early, and patient adherence is ensured.[32]

Adjunctive corticosteroids are occasionally used in cases of severe inflammation, neurological involvement, or

spinal cord compression; however, their use remains controversial and should be individualized.[33]

In MDR-TB, therapy must be tailored based on the DST profiles and often requires second-line agents in combination, such as fluoroquinolones, bedaquiline, linezolid, and cycloserine, typically for 18-20 months.[7]

TREATMENT DURATION OPTIMIZATION

The ideal treatment duration for OATB remains an area of ongoing debate. While conventional approaches often favor extended regimens (12-18 months), recent randomized trials and WHO recommendations suggest that 6-9 months of treatment may suffice for uncomplicated cases.[34]

Treatment response is monitored clinically and radiologically, as microbiological conversion is often not feasible owing to the paucibacillary nature of the infection. MRI changes may lag behind clinical improvement; hence, a combination of symptom resolution, normalization of inflammatory markers (ESR and CRP), and radiological stability are used to determine treatment completion.[17]

Future directions include the use of therapeutic drug monitoring (TDM) to optimize dosing and the development of host-directed therapies (HDTs) to modulate the immune response and reduce treatment duration.[12]

SURGICAL INTERVENTIONS

Although the cornerstone of OATB management remains medical therapy, surgery plays a crucial role in selected cases. Indications for surgical intervention include diagnostic uncertainty, neurological compromise, spinal instability, joint destruction, abscess formation, and non-responsiveness to medical treatment.

Recent advances have led to the development of minimally invasive techniques, joint-preserving approaches, and reconstructive surgeries to enhance functional outcomes while minimizing morbidity.

MINIMALLY INVASIVE TECHNIQUES

The evolution of minimally invasive surgery (MIS) for spinal and joint tuberculosis has significantly reduced the operative morbidity and improved patient outcomes. Techniques such as percutaneous abscess drainage, endoscopic debridement, and video-assisted thoracoscopic surgery (VATS) are increasingly being employed for debridement and stabilization of spinal tuberculosis. VATS debridement for thoracic spinal TB offers excellent visualization, minimal blood loss, and reduced postoperative pain, with outcomes that are comparable to those of open surgical procedures.[35] Percutaneous pedicle screw fixation has emerged as a preferred technique for spinal TB, particularly in early or non-kyphotic lesions, as it facilitates early mobilization and stabilization while minimizing soft tissue disruption.[36] Similarly, arthroscopic debridement has gained traction in the management of peripheral joint tuberculosis, especially in the knee and shoulder, by allowing effective synovectomy and lavage with minimal joint trauma. [37]

JOINT-PRESERVING PROCEDURES

In early-stage joint tuberculosis, preservation of joint architecture is crucial for preventing long-term disability. Arthroscopic synovectomy and curettage, when combined with ATT, can effectively halt disease progression, particularly in joints such as the knee, hip, and shoulder.[38] In cases of hip tuberculosis, procedures like core decompression and open debridement are recommended for patients presenting with early avascular necrosis or joint effusion without collapse, with the goal of delaying the need for joint replacement. Additionally, osteotomies such as triple osteotomy or pelvic support osteotomy may be considered, especially in younger patients, to correct deformities and maintain joint function without resorting to prosthetic implantations. These joint-preserving strategies are especially important in the pediatric and adolescent populations, where prosthetic replacement can lead to significant long-term challenges.[39]

RECONSTRUCTION METHODS

Advanced-stage OATB frequently leads to joint destruction, deformity, and instability, necessitating reconstruction procedures to restore function and relieve pain. Total joint arthroplasty (THA), such as total hip or knee replacement, is now commonly performed in patients with quiescent or healed tuberculosis. With the use of modern implants and appropriate preoperative ATT, outcomes are comparable to those achieved in arthroplasty for non-infectious conditions.[40] In spinal tuberculosis, reconstruction often involves anterior or posterior approaches with cage placement, autologous bone grafts, and pedicle screw instrumentation to correct deformity and provide stabilization, particularly in cases of kyphosis or vertebral collapse.[41] For large bony defects, especially in the upper extremities, wrist, or ankle, biological reconstruction using vascularized fibular grafts or allografts is a viable option.[1] Although reconstructive surgery in TB was once considered controversial because of the risk of disease reactivation, recent studies have demonstrated that with sufficient antitubercular treatment and confirmed infection quiescence, such procedures are safe and can significantly enhance the quality of life.

ADJUNCTIVE THERAPIES

Adjunctive therapies are emerging as valuable complements to standard anti-tuberculosis treatment and surgery for managing OATB. These approaches aim to enhance immune response, accelerate bone healing, and prevent long-term complications. Among these, immunomodulators, bone grafts and substitutes, and

regenerative medicine techniques are gaining traction as adjuncts to conventional treatment protocols.

IMMUNOMODULATORS

Given the host-dependent nature of tuberculosis progression, modulation of the immune response has emerged as a promising area of focus in the management of extrapulmonary TB. Immunomodulators are designed to strengthen host defence mechanisms, minimize inflammation-induced tissue damage, and improve the efficacy of antitubercular drugs. *Mycobacterium* w (Mw), also known as Sepsivac, has been explored as an immunotherapeutic agent aimed at enhancing Th1 immune responses, with ongoing investigations into its potential role in extrapulmonary TB, including spinal tuberculosis.[42] Recombinant interferon-gamma (IFN-γ) has demonstrated encouraging results in early studies by promoting macrophage activation and reducing the bacterial burden in MDR TB (MDR-TB), although its clinical application remains limited.[43] Additionally, vitamin D supplementation, especially in populations with documented deficiency, has been linked to increased cathelicidin production and better clinical outcomes; however, more robust clinical trials are needed to confirm these findings.[44] While direct evidence for OATB is still sparse and primarily derived from pulmonary TB studies, such immunomodulatory agents may offer added benefit in cases with delayed healing or recurrent disease.

BONE GRAFTS AND SUBSTITUTES

Bone loss and structural defects are common complications of OATB, particularly in cases involving the spine and the large joints. Although autologous bone grafts remain the gold standard for reconstruction, they are associated with donor site morbidity and may be inadequate for addressing large defects. To overcome these limitations, alternatives such as allografts, demineralized bone matrix (DBM), and synthetic substitutes-including calcium phosphate and hydroxyapatite-have been utilized with comparable outcomes in spinal TB reconstruction.[45] Bioactive ceramics, particularly β-tricalcium phosphate, provide osteoconductive scaffolding and are gaining popularity in both spinal and joint TB reconstruction.[46] When combined with growth factors such as bone morphogenetic proteins (BMPs), these materials have the potential to enhance osteogenesis and promote spinal fusion. However, their application in infection settings remains cautious because of concerns regarding the possible reactivation of dormant mycobacterial infections.[47]

Table 3: Adjunctive therapies under investigation.

Therapy	Type	Proposed benefit	Clinical status
MSC therapy	Regenerative	Bone regeneration	Experimental
IFN-γ	Immunomodulatory	Enhanced macrophage activity	Limited use
BMPs	Growth factors	Osteoinduction	Investigational in TB

REGENERATIVE MEDICINE APPROACHES

Advances in regenerative medicine, including the use of stem cells and tissue-engineered scaffolds, hold significant promise for the repair of osteoarticular defects resulting from tuberculosis. Mesenchymal stem cells (MSCs) derived from bone marrow or adipose tissue have demonstrated potential in preclinical studies for enhancing bone regeneration and modulating immune responses in chronic infections.[48] Scaffold-based delivery systems incorporating stem cells or biological agents such as vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) may further promote local healing in large bone defects caused by TB-induced destruction. Although clinical research in this area is still in its early stages.[49] Gene therapy is an emerging approach, with experimental studies focusing on enhancing local osteogenesis and antimicrobial activity. For example, Bao et al identified N-Myc downstream-regulated gene 1 (NDRG1) as a candidate for modulating host immune responses in murine macrophages infected with *Mycobacterium tuberculosis*, suggesting that targeted gene regulation could bolster intracellular bactericidal activity and complement conventional therapy.[50] While these innovative strategies remain largely investigational and represent promising future directions, particularly for managing drug-resistant and structurally debilitating cases of osteoarticular tuberculosis.

CHALLENGES AND FUTURE DIRECTIONS

Despite significant progress in the understanding and management of OATB, multiple challenges that hinder optimal patient outcomes remain. These include increased drug resistance, delayed diagnosis, and limited access to advanced therapies in low-resource settings. Personalized treatment strategies, development of effective vaccines, and targeted host-directed therapies represent critical areas for future research and clinical development.

DRUG RESISTANCE CHALLENGES

The emergence of MDR-TB and XDR-TB has had a profound impact on the management of OATB. MDR-TB in osteoarticular cases is linked to significantly prolonged treatment durations, increased need for surgical intervention, and higher morbidity.[51] Treatment regimens for MDR/XDR-TB typically rely on second-line drugs, which are often less effective, more toxic, and substantially more expensive, posing major challenges for

patients and healthcare systems alike.[52] Furthermore, DST specific to extrapulmonary TB isolates, including those from skeletal tissues, remain underdeveloped, leading to delays in selecting the most effective therapeutic regimen. There is a critical need for rapid and reliable DST platforms tailored specifically to skeletal TB, particularly in high-burden regions.[53]

PERSONALIZED TREATMENT STRATEGIES

As our understanding of host-pathogen interactions in tuberculosis continues to advance, individualized treatment strategies are gaining increasing relevance. Pharmacogenomics and TDM offer the potential to personalize antitubercular drug dosing, ensuring therapeutic efficacy while reducing the risk of drug-related toxicity.[54] Additionally, the use of imaging biomarkers, host immune profiling, and assessments of local disease burden can inform clinical decisions regarding the timing of surgical intervention, duration of therapy, and the necessity for adjunctive treatments.[55] Emerging technologies such as machine learning models and AI-based decision support systems are also being investigated for their ability to predict treatment outcomes and stratify patients based on clinical and laboratory data. These personalized approaches hold particular promise for optimizing resource utilization in regions with high TB prevalence and limited diagnostic infrastructure.[56]

POTENTIAL VACCINE DEVELOPMENT OPPORTUNITIES

Although the Bacillus Calmette-Guérin (BCG) vaccine provides protection against disseminated tuberculosis in children, its effectiveness in preventing adult pulmonary and extrapulmonary TB-including OATB-remains limited.[57] Several novel vaccine candidates are currently under development, with M72/AS01E demonstrating promising efficacy against latent TB infections.[58] Vaccine strategies aimed at enhancing T cell-mediated immunity, augmenting the protective effects of BCG, and delaying disease reactivation are being actively explored for potential application in skeletal TB. Additionally, post-exposure prophylactic vaccines may offer significant value in high-burden endemic regions and among healthcare workers at a risk of occupational exposure. The development of an effective therapeutic vaccine continues to be a high-priority objective to combat the global burden of TB, including its challenging osteoarticular forms.[59]

CONCLUSION

Despite being an ancient disease, OATB continues to pose significant clinical challenges owing to its diverse clinical presentation, diagnostic delays, and escalating problem of drug resistance. However, in recent years, substantial advancements have revolutionized the diagnosis and management of OATB. The application of modern imaging techniques, molecular diagnostic tools, and biomarker-based research has facilitated earlier and more accurate detections. Simultaneously, the development of novel antitubercular drugs and the introduction of shorter and more effective treatment regimens have enhanced therapeutic outcomes.

Surgical management has also evolved, with minimally invasive procedures and biologically enhanced reconstructive techniques contributing to improved recovery and reduced morbidities. Adjunctive therapies such as immunomodulators, bone substitutes, and regenerative strategies offer additional avenues for comprehensive management. The implementation of multidisciplinary and integrated care models ensures personalized and holistic treatment, which is particularly important for managing complex or drug-resistant cases.

Nevertheless, several challenges persist, notably, the burden of MDR and XDR-TB, the absence of a highly effective vaccine for adults, and the lack of standardized treatment guidelines for extrapulmonary TB, including OATB.

Future research efforts must prioritize the enhancement of rapid diagnostic tools, especially in low-resource settings, broader application of TDM and host-directed therapies, acceleration of clinical trials focused on vaccines and biologics, and development of precision medicine-based, individualized treatment strategies. As global strategies for TB control continue to evolve, OATB must receive increased attention in both research and health policy to mitigate disability, improve quality of life, and progress toward the ultimate goal of TB elimination.

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