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Challenges and controversies in the treatment of spinal tuberculosis

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ABSTRACT

Current guidelines regarding management of spinal TB are mostly extrapolated from trials on pulmonary disease. Since the British Medical Research Council (BMRC) trials in the 1970s, there are not many good quality studies that substantiate best practice guidelines for the management of this entity. Tuberculous infection of the spine behaves much differently from bacterial osteomyelitis and limited data leads to ambiguity in many cases. Although a few studies have been conducted in patients with spinal TB, most were in the era preceding short course chemotherapy and prior to current radiological and surgical advances. While spinal TB is primarily managed medically, surgical intervention may be needed in certain cases. We discuss areas of uncertainty and challenges that exist with regards to medical treatment, diagnosis, therapeutic endpoints, and a few surgical considerations. Substantial delay in diagnosis continues to be common with this disease even in the developed nations, leading to substantial morbidity. In light of limited evidence, there is an emerging recognition of the need to individualize various aspects of its treatment such as duration, frequency and acknowledging the limitations of various diagnostic and radiological modalities. We aim to consolidate potential areas of research in the diagnosis and management of spinal TB and to revisit the latest published evidence on its redressal.

1. Introduction

Spine is the most common skeletal site of involvement of tuberculosis (TB) [1]. Since the landmark British Medical Research Council (BMRC) trials in the 1970s, there has been very little advancement in the management of spinal TB, and guidance on appropriate use of diagnostic modalities as a test of cure remains ambiguous. With the re-emergence of TB globally due to the HIV epidemic, much of the public health efforts have been focused on pulmonary TB which continues to be the most common manifestation of TB and a significant public health concern. However, there is little guidance on the management of skeletal TB and most of the data comes from studies done in pulmonary manifestation of the disease. Spinal TB continues to be a cause of disability and poor patient satisfaction due to delayed diagnosis or inappropriate management. With the shift in migration patterns on a global scale, the challenges are multifold especially in immigrant populations and a substantial delay to diagnosis continues to occur even in at-risk populations in developed countries [2–5,99]. With the emergence of drug-resistance, the management becomes even more challenging given the treatment courses are generally longer for skeletal than pulmonary TB.

The incidence and prevalence varies between countries and the paucity of accurate data makes an accurate assessment even more challenging. According to the WHO global TB report from 2019 extrapulmonary TB was reported in 15% of new incident TB cases in 2018. Osteoarticular TB has been reported to account for 11.3% of extrapulmonary sites with spinal TB accounting for the vast majority, reported to be up to 50% [6–8]. In one recent study the regional prevalence of musculoskeletal TB was reported to be up to 25% [9]. Treatment at pre-destructive stage by the standard drugs leads to healing in about 95% of patients without significant deformities or neurological complications. However, once symptoms progress to neurological deficits, a significant number of patients may never recover neurological function [10].

2. Challenges and controversies

2.1. Basic concepts

The pathogenesis and management of this entity has key differences relative to bacterial osteomyelitis and the limited data has led to ambiguity in many cases. Bacterial osteomyelitis is typically caused by

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hematogenous arterial spread to metaphysis of the bone where the vascular arcade exists and leads to destruction of the cartilage. However, tubercular osteomyelitis is caused predominantly by spread via the paravertebral venous route and destruction usually starts in the anterior-inferior part of vertebral body with spread under the anterior spinal ligament to adjacent inferior vertebra. Anterior involvement is mostly due to the spread of abscess under the ligaments and periosteum [11]. Contrary to pyogenic osteomyelitis, the disk is typically spared due to lack of bacterial enzymes, until later in the disease course. Keeping in mind these basic differences in principles and approach to mycobacterial bone and joint infections, we aim to revisit more recent literature on spinal tuberculosis with an emphasis on challenges and areas of controversy.

Tuberculous infection of the spine behaves differently from pulmonary TB. A major challenge in the treatment of TB includes multiple mycobacterial populations in the disease locus with different growth kinetics and metabolic characteristics. The organism is a strict aerobe and thrives best in regions with higher tissue oxygen such as lungs, where higher propensity for multibacillary involvement exists. However, in a contained, osseous tissue the organism can still multiply but not to the same extent. These areas are generally paucibacillary with more dormant mycobacteria which are harder to kill and retain viability despite chemotherapy. The treatment often involves using a number of drugs in combination for a long duration, especially in extrapulmonary TB where the challenge lies in trying to destroy this dormant subpopulation once they start replicating [10]. While exogenous reinfection can cause recurrence in high endemic areas [12,13] inadequate killing of these endogenous dormant bacteria can also lead to relapse [13–15].

The duration of treatment in osseous TB can be unusually prolonged, up to a year or two which makes clinical trials investigating relapse-free cure rates extremely difficult. Also, there is also no known methodology to measure the total body burden of *M. tuberculosis* or to predict clinical outcomes. Treatment response is often variable and even in patients with concurrent pulmonary disease, positive predictive value of time to sputum conversion with relapse is low [16].

It has been suspected that the host response to TB often drives the mycobacterium into a phenotypically distinct state. Recent studies show that sputum from treatment naïve TB patients has a mixture of routinely culturable and differentially culturable mycobacteria. This differentially detectable M. tuberculosis (DD TB) does not grow on routine solid media but can be isolated from liquid media. This population was noted to be drug tolerant and dependent on resuscitation-promoting factors (growth stimulatory enzymes secreted by M. tuberculosis). There is emerging evidence that differentially detectable TB may account for variability in host response and by addressing growth kinetics of this subpopulation, treatment could be individualized with possible use of shorter courses in select patients [17–19].

Penetration of antimycobacterial agents into “sanctuary sites” like bones is another concern. Sclerotic bone may block the penetration of drugs into the diseased area. While, older literature had shown reasonable penetration and clinical outcomes, [20–23], more recent studies found variable concentrations of drugs in the area around the sclerotic wall. Even undetected levels inside the sclerotic wall was noticed in one study while the other noted decreased concentration in and outside the sclerotic focus [24,25].

2.2. Medical management

2.2.1. Diagnosis

The introduction of molecular assays like Xpert MTB/ RIF made a significant leap with rapid detection of TB by NAAT as well as Rifampin resistance in less than 2 h. In 2014, the WHO end TB strategy identified diagnostic areas of highest need and TPPs (target product profiles). Besides rapid sputum test, DST(drug susceptibility testing), and triage test, a non sputum biomarker was identified to be of priority [26].

In extrapulmonary, including spinal TB, sputum diagnostics have little utility unless there is concurrent pulmonary involvement. The diagnosis relies on detection of mycobacteria from samples collected by bone biopsy. However, with the surge of personalized medicine, biomarker discovery and application in TB diagnostics would particularly change the existing paradigm in these extrapulmonary patients by avoiding delay in diagnosis and treatment initiation and prevention of subsequent complications that in turn occur from such a delay. Unfortunately, there is extremely limited data in the use of these emerging diagnostic platforms for the diagnosis of most extrapulmonary forms of TB.

An important consideration is the fact that most cases present in primary care settings where specimen transport can be challenging and pretreatment loss to follow up commonplace. In addition, the availability and feasibility of biopsies in many resource-limited settings remains a significant barrier. The challenge remains in development and approval of such non sputum based tests from urine, blood or breath and with good validity that can be decentralized and cost effective at the same time [27]. In addition, the existing guidance on appropriate evaluations of these tests in itself remains elusive although just recently IDSA published set of guidance for evaluation of an ideal non sputum biomarker test with specificity high enough to initiate timely treatment in extrapulmonary TB [28] to target population with limited infrastructure in countries with medium to high TB prevalence.

In a recent systematic review, 44 biomarkers – of which about half were multiple marker biosignatures – were identified in high-quality studies that met the TPP criteria, of which only 2 were incorporated into commercial assays [29]. Only one of these LAM (urine lipoarabinomannan) had received some attention but concerns were raised over poor sensitivity. Other LAM assays showed improved sensitivity [27,30–32] and in HIV-positive patients, both TB DNA and LAM detection in urine is currently an area of interest due to low reliance on sputum diagnostics from immune suppression [33,34].

Also, there remains an overlap between TB and non-TB patients with respect to results from these markers which can suggest that the spectrum of activity may be variable within active TB, may overlap with latent TB infection and even potentially other illnesses. The hope also exists for biomarkers to be a surrogate endpoint and for customization of treatment regimen and tailoring of duration for individual patients. That would in turn potentially solve the problem of long duration of treatment that makes conducting clinical trials with good follow up extremely challenging in extrapulmonary TB. Also, clinical trials assessing newer chemotherapeutic agents would also require at least six months after treatment discontinuation to assess for cure making gathering good evidence for wider application challenging. In addition to biomarkers, the diagnostics to quantify the total body burden of mycobacteria is also non existent. There is a growing need for such tests which could ultimately help with prognosis as well as personalization of various aspects of treatment in extrapulmonary TB.

2.2.2. Frequency of therapy

The guidelines on medical management of osseous TB are mostly extrapolated from clinical trials in pulmonary tuberculosis. Most antitubercular drugs act on the mycobacterial population over an extended period of time (lag effect), with effects lasting for several days. The thrice weekly (sometimes even twice weekly), intermittent therapy is based on this property and its use has been demonstrated to be successful in many cases of pulmonary TB, with the added advantage of improved patient adherence [35,36]. It is important to note, however, that the role of intermittent therapy has not been studied or validated in skeletal or spinal TB [37]. There are in fact some reports of clinical deterioration with this strategy [38].

Major agencies now recommend daily therapy as the first choice for spinal TB with varying modifiers, details are summarized in Table 1. The World Health Organization (WHO) and National Institute for Health and Care Excellence (NICE, United Kingdom) also noted that

Table 1
Frequency of drug therapy.

Society/agency	Treatment frequency	Comments
World Health Organization (2017)	Strong recommendation (high grade of evidence) to use daily therapy in both intensive and continuation phase.	New patients with TB should not receive twice weekly dosing for the full course of treatment unless this is done in the context of formal research.
Infectious Disease Society of America/American Thoracic Society/Centers for Disease Control and Prevention (CDC) combined guidelines for drug susceptible TB (2016)	Expert opinion is to use daily therapy in both intensive and continuation phase.	Guidelines note the lack of studies for validation but that the opinion of experts is to use daily therapy. Daily therapy is defined as either 7 days a week or 5 days a week dosing, both of which are considered equivalent by expert consensus [37].
National Institute for Health and Care Excellence (NICE, United Kingdom, 2016)	Daily therapy is first choice.	Three times weekly dosage should only be considered if risk assessment identifies a need for directly observed therapy AND daily directly observed therapy is not possible [67].

fewer than three times a week therapy should not be offered as if the patient misses one dose, they are essentially missing half or more of the therapeutic dosage. Vitamin B6 is recommended as an addition to patients at risk of neuropathy, and directly observed treatment short-course (DOTS) continues to be endorsed [37,39].

2.2.3. Duration of therapy

For the most part, British MRC trials were the only large scale trials evaluating drug choice and duration of therapy. While the MRC trials did show some success in short course chemotherapy (6 or 9 months) for spinal tuberculosis with certain exceptions, ongoing uncertainty regarding length of treatment in spinal TB exists among many physicians due to concerns regarding early or late recurrence and its associated potential morbidity. These trials [40–42] were done decades ago when surgical interventions were widespread and most of these patients with short course regimens had operative intervention. There was also a lot of heterogeneity in the presentation and complexity of cases, and the treatment regimens used were different with greater failures noted with some regimens. Also, cervical spine disease was mostly excluded. Very few trials exist in patients with extrapulmonary TB outside of the British MRC trials [43,44] and even there, the sample size for patients with skeletal TB has been limited and failures were in fact noticed in many patients with skeletal disease. Currently, there is a difference in expert opinion on length of treatment for extrapulmonary sites including bone [37] with substantial variation in guidelines from major societies. It varies from as little as 6 months to 12 months and even beyond, summarized in Table 2.

In the absence of reliable markers, following clinical response is very crucial. Response is often suggested by a decrease in pain, resolution of fever, improved appetite, and gain in body weight with a serial decrease in inflammatory markers. Failure of sinus tracts and ulcers to heal within a few months of multidrug therapy or their appearance while the patient is on antimycobacterial drugs can suggest drug-resistance, immunodeficiency or rarely paradoxical worsening like immune reconstitution.

2.2.4. Curative end point

Another challenge is defining a curative end-point for unlike pulmonary TB, it is much more difficult to obtain a concrete evidence for culture conversion and eradication of the disease from extrapulmonary sites like spine and bone. Tissue biopsy for test of cure is not pursued given very low yield due to the paucibacillary nature of these sites. Also, since the treatment in extrapulmonary TB is longer, large scale trials with longer follow up are also difficult to conduct. It is important to note that the guidelines that had advocated short course chemotherapy were based on the British MRC trials that utilized X-rays [40,42]. Studies are needed to look into more recent and advanced imaging modalities to determine treatment endpoints.

There is not much guidance on soft issue or vertebral changes on MRI that signify response during or after antituberculous therapy. Some experts claim that despite a good clinical response, during the first 5–6 months of chemotherapy, MRI findings may be discordant with the clinical evolution and at times show an increase in the size of epidural abscess, osseous destruction and bone edema [3,10,45]. The interpretation of this discordant response in clinical practice remains challenging. The radiological evidence of healing might lag behind biological response by about three months. There might also be an immunologic response to dead/dying mycobacteria. In such cases, MRI might not differentiate between the inflammatory response of active disease and that of repair [10]. However, if there is clinical worsening along with persistence or worsening of marrow edema, destruction, and abscess, the drug regimen should be reconsidered, and surgery/tissue sampling for repeat tissue diagnosis as well as treatment pursued to exclude drug-resistance or an alternative or coexisting diagnosis.

Despite being on similar regimens, radiological evolution of healing tends to vary among individual patients. Generally, healing is suggested by MRI evidence of complete resolution of pre and paravertebral collections, resolution of vertebral body marrow edema, and replacement of marrow edema by fat or calcification. Published literature suggested MRI evidence of healing at the end of 8 months of combination drug therapy occurred only in about one third of the cases [46] which is

Table 2
Duration of drug therapy.

Society/agency	Treatment duration	Comments
Infectious Disease Society of America/American Thoracic Society/Centers for Disease Control and Prevention (CDC) combined guidelines for drug susceptible TB (2016)	6–9 months	Experts favor 9 months citing difficulty in assessing treatment response. In the setting of orthopedic hardware, an extension of treatment up to 12 months has also been recommended, though these guidelines acknowledge that there is a wider range on expert opinion on length of treatment for extrapulmonary sites including bone [37].
World Health Organization (2017)	9 months	Duration longer than that for pulmonary TB citing the difficulty in monitoring treatment response.
National Institute for Health and Care Excellence (NICE, United Kingdom, 2016)	Without central nervous system involvement: 6 months With CNS involvement or patients with coexisting HIV: 9 months [67].	

another reason as to why duration of treatment must be individualized by taking clinical, lab and radiological factors into consideration.

In 2016, Central Tuberculosis Division of India came out with a new set of recommendations specifically pertaining to spinal TB [47] where endpoints are decided on a case by case basis. The standard of care is to obtain follow up serial X-rays every 3 months or so and based on clinical response, repeat MRI at 6, 9, 12 and 18 months with imaging features to be interpreted in light of clinical response. Follow ups are suggested about every 6 months for a total of two years.

Because of the limitations of MRI especially in distinguishing active from healing disease, positron emission tomography- computed tomography (PET-CT) has also been proposed to be useful as a follow-up modality. Application of PET/CT or HRCT scans as potential imaging biomarkers and curative end points has been studied in pulmonary multidrug-resistant (MDR) TB [48]. Fluorodeoxyglucose (FDG) uptake in spinal TB normalizes about 3–4 months after treatment and it is suggested that relative uptake quantification with standardized uptake value (SUV) could distinguish between residual and resolved lesions [49–52]. Current research is underway further studying the usefulness of PET/CT as a tool to determine resolution in spinal TB. The feasibility of the use of widespread MRI and/or PET/CT is another challenge in many under-resourced settings where TB is endemic.

2.3. Surgical management

The literature shows widespread use of combined medical and surgical techniques in the management of spinal TB. In a systematic review of case-series published between 1980 and 2011, surgery was reported in 28 out of 37 articles with spinal TB [53]. In the US between 2002 and 2011, approximately 20% of patients with spinal TB underwent surgery, mostly in thoracolumbar area, and about half of those underwent instrumentation of three or more levels [54].

The impact of radical surgery and outpatient chemotherapy were also studied by British MRC trials [55,56]. The historical practice of bed rest offered no advantage. In uncomplicated patients undergoing medical treatment had similar long term results at 15 years with no late relapses or paraplegia. Radical surgery, however, led to earlier bony fusion and lesser kyphosis in those with complicated deforming disease. Two systematic reviews compared chemotherapy alone versus chemotherapy with surgery. Only two trials (from 1970–1980s) fulfilled the inclusion criteria, and concluded that there was no statistical difference in outcomes between the two groups [57,58]. They also noted that surgery had no effect on the resultant kyphosis angle, but the incidence of kyphosis for all study subjects was considerably high at the onset ($>30^{\circ}$), which is usually an indication for operative intervention regardless. These reviews were limited by a very small sample size and the fact that tremendous surgical and medical advancements followed all these trials.

More and more evidence has emerged in recent years showing good outcomes in those managed by chemotherapy alone or with minimally invasive surgeries for stabilization or percutaneous fixations. [59–61]. Improved immediate postoperative outcomes were noted in one study with radical debridement, however, no difference in long term deformity or neurologic status was noted when compared with stabilization alone [62]. Also, with the widespread use of highly efficacious combination drugs, the trend has naturally shifted to more of a conservative approach.

Another important point to consider is that studies looking into outcomes mostly included thoracolumbar cases which is the most common site of involvement and patients with cervical involvement were largely excluded given the risk of major neuro deficits due to the proximity of cervical spinal cord and the risk of tracheal compression from abscess collection in the retropharyngeal space. However, a recent study reported good outcomes with medical therapy alone in a vast majority of patients even with cervical spine involvement. In this study 57.9% of the patients had a neuro deficit but only 9.5% required surgery for progressive neuro deficits. Most were managed conservatively, but those with advanced spinal cord involvement or compression had poor outcomes and the authors suggested an aggressive surgical approach in that population [63].

Paraspinal and epidural abscesses also tend to resolve with chemotherapy [2]. However, controversy still exists and some propose later intervention may lead to greater risk of failures than earlier intervention. Failure estimates were noted to be heterogeneous between studies leading to uncertainty about actual outcomes [64]. Surgical drainage is therefore reserved for worsening abscess or mechanical pressure related symptoms owing to their size or location [65,66].

International guidelines acknowledge the dearth of high quality evidence to recommend for or against surgery. However, they conclude the trials found no additional benefit with surgical debridement over chemotherapy alone in most cases and conclude the decision to be made on a case by case basis [37,67]. Currently, spinal TB is treated medically in the absence of major neurological deficits or concerns for major deformity.

Many things need to be factored in the decision for surgery including the patient's age and comorbidities, location of the lesion, especially in relation to the dura, number of vertebral bodies involved, kyphosis angle and neuro deficits to name a few [68]. Sometimes, when diagnosis cannot be confirmed by other means or when exclusion of drug-resistance is necessary surgery may be the only alternative. Many studies indicate that progression may correlate with the size and number of vertebral lesions [69–71]. Major indications also include failed medical management (despite 3–6 months of effective medical treatment), concern for spinal instability from kyphosis, worsening abscess or one causing difficulty in swallowing or breathing, as in the case of cervical/ thoracic lesions, or persistent or recurrent neurological symptoms or cord compression [37,68,72,73]. Early surgical consultation, therefore, should be sought in complicated cases. Unfortunately, the decision to intervene can be particularly challenging in resource-limited settings where much of the disease burden exists and so does the need for cost effective interventions.

2.4. Complications

2.4.1. Neurological involvement

Contrary to bacterial osteomyelitis, development of a neurologic deficit is generally a gradual process in TB. In the absence of published evidence, experts may differ in their approach for cases with early neurological involvement where some have advocated for medical treatment alone in very early phases without major weakness under close supervision [66,74,75]. However, this observation mostly come from case series. In one series of 50 patients with radiologic epidural cord compression but early neurological signs, i.e., with clumsy gait, hyperreflexia, clonus and early motor deficits, forty-seven of the fifty patients recovered with medical treatment alone [74]. Some argue that neurologic deficits due to spinal tuberculosis tend to behave differently than traumatic causes of spinal injury, with a much greater degree of recovery of neurologic function [76]. In the absence of good sample size and lack of randomization, such an approach should be cautiously followed, and may be of value in situations where surgery might be risky. Close monitoring of the patient's neurological status is important and any worsening would be a strong indication for surgery.

Late paraplegia may sometimes occur when the initial lesion heals with residual severe deformity, which can even manifest years later. It is considered to be due to spinal cord stretching leading to gliosis and is often described on imaging as myelomalacia [77].

2.4.2. Deformity and kyphosis

Kyphosis is an end result of vertebral collapse in spinal tuberculosis. Although a certain degree of kyphosis is inevitable and acceptable, the aim is to de accelerate its progression as much as possible. The deformity progresses in the active phase of disease as well as after the

infection is eradicated [70,78]. This progression is also influenced by the severity of kyphosis before treatment, the level of the lesion, and age of the patient.

In adults, the progression of kyphosis after healing is rare [70]. Children however, are at risk of severe kyphosis for they continue to have significant changes in the growing spine even after the disease is healed [70,78,79]. The risk for late onset paraplegia resulting from long standing kyphosis is more relevant in childhood TB [66,70,80] where prediction scores have been used and early surgical management may be required in the active stage of the disease to prevent such complications [77,78].

Kyphosis has even been reported to continue to increase for six months, even after anterior decompression and bone grafting [81,82]. The resultant deformity from surgery depends on the location of the lesion for the same degree of kyphosis, with lumbar lesion of less cosmetic and mechanical significance than cervical or thoracic lesions. Features such as the location of lesion (cervico thoracic and thoracolumbar junction lesions), destruction of three or more vertebral bodies, loss of vertical height equivalent to or more than 1.5 times the vertebral body height, signs of instability or progression of kyphotic deformity in successive X-rays are high risk for severe kyphotic deformity and strong consideration for surgery is given in these cases [70,83].

2.5. Drug resistance and newer agents

Multidrug resistant TB (MDR- TB) is defined as resistance to isoniazid and rifampicin, the two most potent drugs used in TB. Extensively drug resistant TB (XDR-TB) is defined as MDR-TB plus resistance to a fluoroquinolone and at least one second-line injectable (i.e. amikacin, kanamycin, capreomycin). WHO global TB report 2019 estimated 3.4% of new cases and 18% of previously treated cases had MDR or rifampin resistance (RR) in 2018. There were about half a million new cases of RR TB, of which 78% had MDR-TB. Three countries accounted for almost half of the world's cases of MDR/RR-TB: India (27%), China (14%) and the Russian Federation (9%). Drug resistance continues to pose a major concern and the incidence does not seem to decline. Even in the US, although the number of TB cases have declined steadily since 1990s, the proportion of MDR TB has remained relatively constant between 1 and 2% [84].

The development of resistance poses further challenges in spinal TB patients, given the difficulties in obtaining a definitive diagnosis due to the paucibacillary nature of the disease. Also, biopsy may not always be possible in resource limited settings. Generally, drug-resistance is suspected when there is no significant clinical improvement after adequate therapy for at least 2–3 months or persistent growth of MTB at other sites beyond 2 months of therapy. Therefore, every effort must be made to obtain a microbiologic diagnosis prior to initiation of therapy [85,86].

Regimens typically include at least 4–5 active drugs for prolonged periods of time, and require aggressive monitoring for adverse effects and for clinical/radiographic response. The minimum recommended duration of therapy is typically 18–24 months. Short course chemotherapy regimens for MDR-TB have not yet been adequately studied in extrapulmonary TB.

There is no formal data about efficacy newer drugs in osteoarticular TB. Most of the recent evidence comes from XDR TB in patients with pulmonary manifestation [87–89]. Effective use of linezolid, clofazimine and quinoline in combinations with other second and third line agents has been reported in limited case series and case reports [90,91]. Linezolid was recently shown to have effective concentrations in diseased bone in patients with spinal TB even after 24 h of drug administration [92], which previously had only been studied until 2 h after administration.

Bedaquiline is active against both replicating and dormant mycobacteria [93] which makes it very effective and better clinical outcomes were observed in some studies compared with other newer agents and shorter courses seemed promising with the inclusion of bedaquiline [94–96] yet the first case report of acquired resistance was first reported in 2015 [97,98]. In a recent study of 14 MDR/ XDR TB patients in the US, out of which 36% had extrapulmonary disease, bedaquiline was well tolerated in most patients with good outcomes. However, no post treatment data was collected [87].

3. Conclusion

Guidelines regarding management of spinal TB are often extrapolated from trials on pulmonary disease. Fewer studies that were conducted in spinal TB preceded short course chemotherapy as well as current radiological and surgical advances. The delay in diagnosis and treatment continues to be a pattern with this entity. To prevent complications, spinal TB disease requires prompt initiation of antitubercular chemotherapy yet delays are commonplace relative to pulmonary disease. It also behaves differently than bacterial osteomyelitis and in general surgical intervention is generally avoided unless there are concerns for complications and advanced disease. Although short course chemotherapy has changed the paradigm of management of TB, uncertainty continues to exist with regards to duration, curative endpoint, and promising use of newer agents to shorten the course. Conducting high quality trials is a challenge given long treatment duration. The global call for development and validation of non sputum biomarkers for diagnosis and tailoring treatment duration can be one potential advance to make such trials possible in future and move towards personalized and evidence-based management for improved treatment outcomes of this morbid disease.

Ethical statement

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, and revision of the manuscript. Furthermore, each author certifies that this material has not been and will not be submitted to or published in any other publication before its appearance in your journal.

Declaration of Competing Interest

We have no conflict of interest to declare and have adhered to ethical guidelines.

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