doi: 10.5216/rpt.v48i2.57806

REVIEW

BONE AND ARTICULAR IMPAIRMENT IN TUBERCULOSIS. AN IMPORTANT EXTRAPULMONARY INVOLVEMENT: A REVIEW

Ricardo Vieira Teles Filho[1], Guilherme de Matos Abe[1], Lucas Henrique Souza de Azevêdo[1], Nilo Carrijo Melo[2], Marcelo Fouad Rabahi[3] and Murilo Tavares Daher[1,2]

ABSTRACT

This is a literature review on the pathogenesis and epidemiology of bone tuberculosis (BTB). Full-text papers from 2001 to 2017 were included. After inclusion criteria were met, 23 papers were selected for analysis. Results show that in most cases of BTB, the spine is the main site involved, regardless of the geographical regions analyzed; hip and knee involvement are also frequent. These three sites are the most prevalent, totaling approximately 70 - 80% of infections. The major forms of involvement are tuberculous spondylitis, tuberculous osteomyelitis, primarily in areas of long-bone growth, as well as cases of chronic disease leading to tuberculous arthritis, mainly in endemic areas. The results also indicated that bone involvement is still prevalent, being the fifth cause of extrapulmonary disease involvement in Brazil. This review highlights the role of tuberculosis in public health, especially in economically active groups where BTB is most prevalent.

KEY WORDS: Tuberculosis; bone tuberculosis; epidemiology; Pott's disease; spine.

INTRODUCTION

Tuberculosis (TB) is still an important public health issue. In 2016, 10.4 million people contracted the disease and, of these, about 1.3 million died. As stated by the World Health Organization (WHO), TB is the deadliest single-agent infectious disease, surpassing HIV (WHO, 2017). In Brazil, 69,569 new cases of TB were recorded in 2017, with 4,426 deaths in 2016 (Brasil, 2017).

The pulmonary site is notably the most frequently affected by TB. Extrapulmonary involvement is present in only about 10% of the cases, being classified according to location: laryngeal, peripheral ganglionic,

1. Department of Orthopedics and Traumatology, Faculty of Medicine (FM), Federal University of Goiás (UFG), Goiânia, Goiás, Brazil.
2. Dr. Henrique Santillo Rehabilitation Center (CRER), Goiânia, GO, Brazil.
3. Department of Internal Medicine, FM, UFG, Goiânia, Goiás, Brazil.

Corresponding author: Ricardo Vieira Teles Filho. Avenida dos Alpes, Quadra 49, Lote 11, Setor União, CEP 74313-760, Goiânia, Goiás, Brazil. E-mail: ricardovteles@gmail.com

Received for publication: 21/3/2019. Reviewed: 5/6/2019. Accepted: 19/7/2019.

meningoencephalic, bone, genitourinary, miliary, cutaneous or ocular (Lopes et al., 2006). Bone TB (BTB) and articular TB most commonly affect the spine, the hip joint and the knee, although also occurring in several other sites (Garg et al., 2011; Kilborn et al., 2015). Spinal TB (STB), or Pott's disease, accounts for 1 to 2% of all cases of extrapulmonary TB (ExTB) (Batirel et al., 2015; Ledbetter et al., 2016) and most commonly affects the lumbar and lower thoracic spine (Leonard et al., 2017).

In general, BTB manifests as arthritis and / or osteomyelitis, with inflammation and / or joint infection. Furthermore, it presents indolent progression when compared to non-specific osteomyelitis and septic arthritis, although with greater morbidity (Norbis et al., 2014; Pigrau-Serralach et al., 2013). Among the risk factors associated with the development of TB, geographic location, age, immunosuppressive treatment, diabetes mellitus, and HIV infection are of epidemiological importance (Garg et al., 2011).

The purpose of this paper is, therefore, to determine the profile of bone and joint impairment in TB through a review of the sites involved and the epidemiological profile that may help to establish clinical hypotheses in cases of ExTB, based on the high prevalence of TB in Brazil and the great importance of bone involvement in this disease.

METHODS

The articles selected for this review were published in national and international journals from 2001 to 2017. Systematic review studies and meta-analyses were also included. Since this review aims to delineate the characteristics of bone and joint involvement by *Mycobacterium tuberculosis* (MTB), only studies that focused directly on BTB and its relations were included.

The following descriptors were used: "Tuberculosis", "Epidemiology", and "Bone tuberculosis" in articles made available by Scielo, BVS and Bireme System (MEDLINE, LILACS and BDENF). Their respective bibliography was also researched for articles to complement the review. Repeated articles, dissertations, theses, articles of validation and any that did not present the complete available text were excluded.

Considering this is a descriptive study and not directly involving human beings and their possible identification, the submission of the research project to the Ethics Committee was not necessary.

RESULTS AND DISCUSSION

73 relevant papers were found, 23 of which were selected after reading their abstracts and applying the inclusion criteria. Subsequently, complete versions of the papers were obtained for analysis (Table).

Table. Selected papers for analysis and review.

Authors	Year	Country	Clinical Apresentation	Boneor Joint Affected
Davidson P.T., Horowitz I.	1970	USA	Arthritis, Osteomyelitis and Spondylitis,	Hip, Knee and Spine
Naim-ur-Rahman	1980	Saudi Arabia	Osteomyelitis and Spondylitis	Spine
Colmenero J.D. *et al*	2004	Spain	Osteomyelitis	Spine
Franco-Paredes C. *et al*	2006	USA	Arthritis	Femur, Knee, Psoas muscle and Spine
Hong L. *et al*	2010	China	Arthritis, OsteomyelitisandSpondylitis,	Clavicles, Ribs, Spine, Scapulas and Sternum
Shikhare S. *et al*	2011	Singapore	Osteomyelitis and Spondylitis	Calcaneus, Hand, Knee, Spine, Scapula and Ulna
Pattamapaspong N., Muttarak M., Sivasomboon C.	2011	Thailand	Arthritis and Tenosynovitis	Flexor tendon sheaths, Knee, Hip Shoulder and Wrist
Al-Qattan M.M. *et al*	2011	Canada	Monoarthritis and Tenosynovitis	Hand
Garg R.K., Somvanshi D.S.	2011	India	Osteomyelitis and Spondylitis	Spine
Tahasildar N. *et al*	2012	India	Arthritis	Hip
Pigrau-Serrallach C., Rodriguez-Pardo D.	2013	Spain	Bursitis, Sacroiliitis and Spondylitis	Spine, Sacroiliac joint and Trochanteric Bursa
Kim S-J., Kim J.H.	2013	USA	Osteomyelitis	Knee
Norbis L. *et al*	2014	Italy	Spondylitis	Spine
Murray M.R., Schroeder G.D., Hsu W.K.	2015	USA	Osteomyelitis and Spondylitis	Spine
Kilborn T., van Rensburg P.J., Candy S.	2015	South Africa	Osteomyelitis and Spondylitis	Spine
Batirel A. *et al*	2015	Turkey	Spondylitis	Spine
Ledbetter L.N. *et al*	2016	USA	Neuroarthropathy	Spine
Kumar K.	2016	USA	Osteomyelitis and Spondylitis	Spine
Sahli H. *et al*	2017	Tunisia	Arthritis	Hand
Leonard M.K., Blumberg H.M.	2017	USA	Arthritis, Osteomyelitis and Spondylitis	Knee, Hip, Rib and Spine
Huaman M.A., Brawley R., Ashkin D.	2017	USA	Osteomyelitis and Spondylitis	Spine
Hogan J.I., Nelson S.B.	2017	USA	Arthritis, Osteomyelitis, Spondylitis and Tenosynovitis	Knee, Hip and Spine
Narayan V. *et al*	2018	USA	Spondylolisthesis	Spine

EPIDEMIOLOGY

BTB cases account for about 2 to 3% of all TB cases notified in the United States and in some reported series in the United Kingdom, for more than 6% of the cases. In these countries, there are reports of an increasing racial disparity in the latest years, with most cases reported amongst minorities and individuals born overseas (CDC, 2015; Hodson & Ormerod, 1990). These immigrants were responsible for increasing the incidence of the disease in those countries. Due to the indolent course of the disease and its low clinical suspicion in areas with low TB incidence, diagnostic delay is frequent in developed countries (Talbot., 2007; Colmenero et al., 2004).

In countries where TB is endemic, older children and young adults are more commonly affected by BTB, whereas in developed countries the disease is more frequently observed in the elderly (Ludwig & Lazarus, 2007). Historically, BTB affected the infant age group and young adults shortly after the development of primary infection. In areas with limited resources, it is still frequent, whereas in developed countries BTB results more commonly from relapses (Davidson et al., 1970).

Regarding risk factors, ExTB is more common amongst HIV infected patients, however BTB did not present the same proportion ratio when compared to seronegative patients (Kim & Kim, 2013; Leibert et al., 1996). The advent of anti-tumor necrosis factor α (TNF- α) therapy is a risk factor associated with disseminated TB amongst patients with TB latent infection, and studies have noted that it includes the development of serious musculoskeletal lesions (Franco-Paredes et al., 2006).

Data from DATASUS (Department of Informatics in the Unified Health System in Brazil), which utilizes SINAN (Notification of Injury Information System) as a source of recorded confirmed TB cases in Brazil, showed that, in 2017, of the 89,487 TB cases, 13,357 were classified as ExTB, and, of these, 639 as BTB, corresponding to 4.8% of the ExTB cases – which places it in the 5th position regarding ExTB forms. The Northern Region presented the highest percentage increase in the total amount of TB and BTB cases from 2001 to 2017: in 2001, 7,582 TB cases were diagnosed, of which 37 were classified as BTB. In 2017, the total amount of cases in this region increased by 33%, to 10,109 cases, and BTB cases increased by 59.6%, to 59 cases – which corresponded to 9.2% of the total BTB cases in Brazil for that year.

In 2017 45 BTB cases were diagnosed in patients 19 or less years of age in the entire country, which corresponded to 7.0% of the total. 429 recorded BTB cases were diagnosed in patients 20 to 59 years old, corresponding to 67.1% of the total. 164 cases were recorded in patients 60 or more years of age, corresponding to 25.7% of the total.

It must be noted that the notification system still fails to report the sites and degree of involvement of the cases, which limits comparison with international literature and worldwide BTB epidemiology. This limitation, as well as the many variants in underreporting, impair the analysis of the BTB scenario in the country in previous periods.

PATHOGENESIS

MTB is an aerobic bacterium, but it also behaves as a facultative anaerobic bacterium, thus being able to remain in its host for a long time. Tuberculosis arthritis and osteomyelitis derive from reactivation foci of stored bacilli originated from the hematogenous spread of the primary infection. The musculoskeletal system receives hematogenic strains originating from primary sites, mainly the lungs and the genitourinary tract, and shows less replication than in this primary site (Leonard et al., 2017; Norbis et al., 2014).

The broad vascularization of vertebrae and long bones is the major determinant in the preferential affection of these by the bacillus, especially the metaphyseal region (Pigrau-Serrallach et al., 2013). Infrequently, MTB are carried from the lungs to distant sites such as the spine; in this case, the route may be the paravertebral venous plexus or the paraaortic lymph nodes' draining lymphatics. The osteoarticular infections caused by nontuberculous mycobacteria (NTM) usually arise secondarily to inoculation, after a trauma or surgical procedures (Hogan et al., 2017).

From the dissemination, a granuloma is formed in the site of the injury, with prostaglandin E 2 (PGE-2) being released to increase the inflammatory recruitment, and a necrosis focus is formed as result of the response to the infectious cells, in which are involved both bacterial enzymes, that digest and destroy the surrounding tissue, and the host's exacerbated protective response (Norbis et al., 2014). The resulting inflammatory focus leads to caseous necrosis and to the typical TB granulomas, which then lead to an increase of compression in these foci and to the collapse of the joint or the vertebral bone. In addition, there may be nerve root compression or secondary neurologic disorders (Hong et al., 2010).

In general, immunocompromised conditions, whether acquired or drug-induced, are important risk factors for the contraction of TB infection. In this context, the relation of STB with HIV should be highlighted, since TB is the main opportunistic infection in such patients. This is justified because patients with the acquired immune deficiency syndrome (AIDS) present heavily compromised cellular immunity, due to the progressive depletion of TCD4+ lymphocytes, resulting in increased risk for TB infection, relapse and extrapulmonary spread, in comparison to healthy individuals (Batirel et al., 2015; Naim-ur-Rahman, 1980).

Tuberculous Spondylitis

Tuberculous spondylitis, known as Pott's disease, initially results from involvement of the subchondral region of the terminal endplate by MTB. In the beginning, it does not affect the disc, due to poor vascularization, despite the rich blood supply to the vertebrae, which in turn suffers lytic destruction without the formation of new bone tissue (sclerosis). The anterior region of the vertebra is the most damaged part whereas its posterior components are only slightly affected. Tuberculous discitis in children may occur as a primary disease, as a result of the remaining blood supply to the intervertebral disk. However, after childhood, in view of the disc's avascular structure, its involvement may only happen due to continuity of foci originating from the vertebral body (Calderone et al., 1996).

The destruction of the anterior region of the vertebral body results in kyphosis (Figure 1). The severity of kyphosis is related to the amount of damage to the anterior regions of the vertebrae. There may be compression of neurologic structures due to angular deformity or due to direct compression by the caseous tissue. Furthermore, paraspinal abscesses may be present. (Figure 2) (Kumar et al.,2016; Narayan et al., 2018).

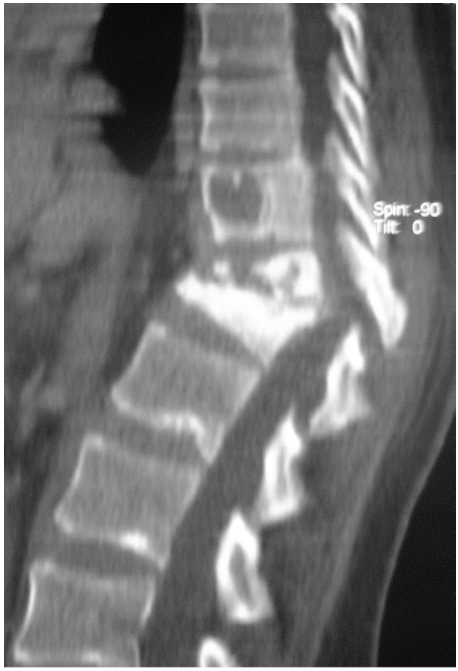

Figure 1. Computer tomography (CT) of the thoracic spine showing destruction of vertebral bodies and kyphosis of the segment at T10-T12.

Tuberculous Osteomyelitis

Tuberculous osteomyelitis may affect bones and joints. In this disorder, there is a significant difference in clinical manifestations according to the affected age group. In children there is the characteristic involvement of several bones with multiple lesions, especially in the feet and hands (Figure 3). However, after childhood, patients present single lesions that may involve any bone.

Tuberculous osteomyelitis occurs mainly in the metaphyseal region of long bones such as the femur and tibia. In children, intra-articular involvement is common due to contiguous dissemination (Shikhare et al., 2011). When growth plates are involved, there may be shortening and deformation of the affected limb (Huaman et al., 2017; Murray et al., 2015).

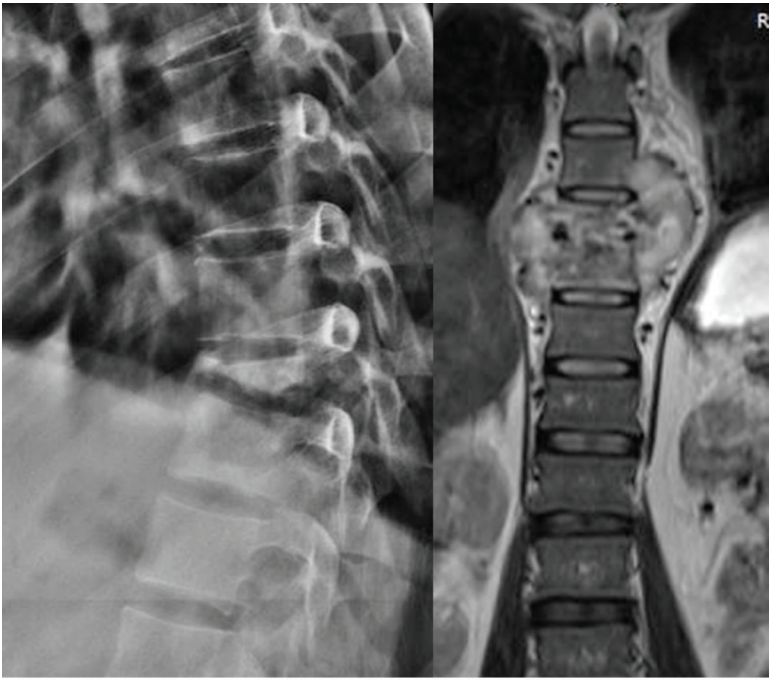

Figure 2. Patient with acquired immunodeficiency syndrome under treatment for pulmonary TB that evolved with decreased muscle strength in the lower limbs. The images show the destruction of the vertebral body and a paraspinal abscess. The left lateral radiography shows collapse of the intervertebral disc and vertebral bodies at T10-T12 that are sclerotic. The right T2 image by Magnetic Resonance Imaging (MRI) presents a paravertebral abscess and destruction of the thoracic vertebra and the intervertebral discs, associated with an exuberant paravertebral soft tissue component and dorsal kyphosis.

Tuberculous Arthritis

Although tuberculous arthritis can affect any joint, it tends to appear in joints that are subjected to greater weight loads such as the knee and hip. The impairment of the intra-articular region may occur due to hematogenic or contiguous spread, the latter occurring through the erosion of the epiphyseal (in adults) or metaphyseal (in children) bone (Al-Qattan et al., 2011). Involvement due to contiguous spread may also occur from other organs (Tahasildar et al., 2012). Once the joint space and the synovial fluid have been affected, the result is erosive arthritis with the formation of pannus that manifests clinically with joint deformities, commonly seen in other types of advanced arthritis such as rheumatoid arthritis. Tuberculous arthritis is monoarticular in about 90% of the cases (Pattamapaspong et al., 2011; Sahli et al.,2017).

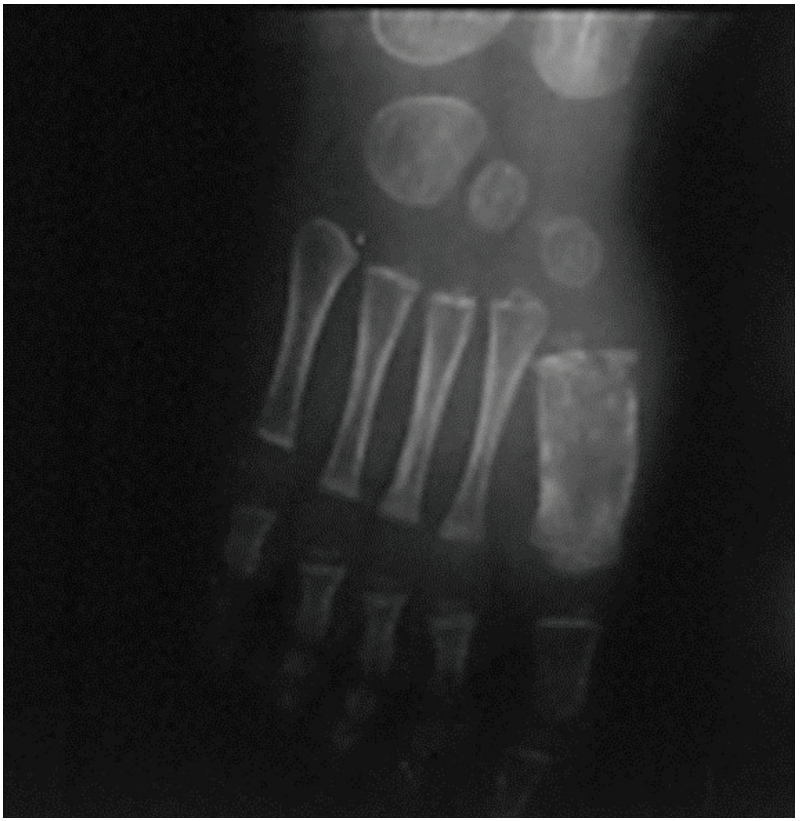

Figure 3. X-ray of a 2-year-old child with tuberculous dactylitis showing the diaphyseal enlargement and osteolytic lesion with blurred limits of the first metatarsal bone, demonstrating a decrease in bone density that is characteristic in this type of condition.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of BTB is reasoned on clinical and imaging findings. Radiological study is of great relevance for the diagnosis; lytic patterns (osteolytic, subperiosteal with sclerotic margins and fragmentation) indicating bone destruction are highly suggestive for BTB if there is clinical and epidemiological reason for suspicion (Pigrau-Serralach et al., 2013). Hematological data is of little contribution for laboratory research, and the number of leukocytes is not very sensitive to change. The tuberculosis skin test (also known as the tuberculin or PPD test) is positive in most cases, even though it cannot be considered when dealing with endemic areas and immunocompromised populations. The gold standard for diagnosis is the isolation of MTB from samples by aspiration cytology-biopsy and culture, or by histological bone specimen, which will also be useful in determining resistance to medication (Norbis et al., 2014; Pigrau-Serralach et al., 2013). Multiplex real-time PCR may be useful for diagnosis and can distinguish typical from atypical mycobacteria in synovial biopsy, but as this method does not identify if the microorganism is alive or dead, it is not indicated to establish the activity of the disease.

BTB, especially tuberculous spondylitis, must initially be differentiated from metastatic neoplasms that affect the vertebrae, such as myeloma, and some solid tumors (Ledbetter et al., 2016). It should also be differentiated from pyogenic diseases in cases of abscesses and inflammatory arthritis. The focus for the differential diagnosis always depends on well-established clinical and epidemiological suspicions with suggestive image findings (Kumar et al.,2016; Narayan et al., 2018).

TREATMENT

Preference should be given to clinical treatment in cases without significant motor and neurological damage; in cases with neurological deficits, surgical treatment may be indicated, varying according to the particularity of each case. In tuberculous osteomyelitis combined anti-tuberculosis drugs produce similar long-term results when compared to the surgical approach by debridement and fusion or anterior debridement alone (Pigrau-Serralach et al., 2013). The combined use of rifampicin, isoniazid, ethambutol, and pyrazinamide for 2 months followed by the association of rifampicin and isoniazid for a total period of 6-18 months is the most frequent protocol used for BTB treatment which should start as soon as possible.

WHO recommends 9 month treatment for BTB (WHO, 2010). The Brazilian Ministry of Health recommends a two phase treatment for meningoencephalic and osteoarticular TB totaling 12 months: an intensive (or attack) phase in the first 2 months with a complete regimen, to rapidly

reduce the bacilli population and eliminate bacilli naturally resistant to any drugs. Subsequently a maintenance phase over the remaining 10 months with a double regimen of rifampicin and isoniazid for both adults and adolescents, with varied doses of medication according to age group and weight, with a view to eliminating latent or persistent bacilli and reducing the possibility of disease recurrence (Brazil, 2018).

In cases of vertebral involvement, the surgical approach is indicated when there is neurologic damage, large abscesses and instability or deformity (kyphotic angles of 30 degrees or more), and non-response to clinical treatment with antibiotics due to resistance (Colmenero et al., 2004).

CONCLUDING REMARKS

BTB is still one of the main sites of extrapulmonary involvement. Even though any joint or bone may be damaged by TB, there is greater involvement of the spine and large joints, such as the hip and knee, which are responsible for the majority of cases. In countries where TB is endemic, older children and young adults are most commonly affected by BTB, while in developed countries the disease is often reported in the elderly. The population most affected by this disease in Brazil, in the analyzed period, consisted of young people in the workforce. The main forms of clinical presentation are tuberculous spondylitis, tuberculous osteomyelitis and tuberculous arthritis. The diagnosis is mostly based on clinical and radiological studies with laboratory support for differential cases. The mainstay of treatment is a multidrug anti-tuberculosis chemotherapy combination (rifampicin, isoniazid, ethambutol, and pyrazinamide); surgery is recommended in special cases, mainly when there is neuroarticular damage.

REFERENCES

1. Al-Qattan MM, Al-Namla A, Al-Thunayan A, Al-Omawi M. Tuberculosis of the Hand. *J Hand Surg Am 36*: 1413-1421, 2011.
2. Batirel A, Erdem H, Sengoz G, Pehlivanoglu F, Ramosaco E, Gülsün S, et al. The course of spinal tuberculosis (Pott disease): Results of the multinational, multicentre Backbone-2 study. *Clin Microbiol Infect 21*: 1008-1018, 2015.
3. Brasil. Ministério da Saúde. *Brasil Livre da Tuberculose: Plano Nacional pelo Fim da Tuberculose como Problema de Saúde Pública / Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância das Doenças Transmissíve*is. 2017. Available in: http://bvsms.saude.gov.br/bvs/publicacoes/brasil_livre_tuberculose_plano_nacional.pdf Accessed at 01/12/2018.
4. Brasil. Ministério da Saúde. *Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. Manual de Recomendações para o Controle da Tuberculose no Brasil / Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância das Doenças Transmissíveis*. 2ed. 2018. Available in: http://portalarquivos2.saude.gov.br/images/pdf/2019/marco/28/manual-recomendacoes.pdf Accessed at 25/06/2019.

5. Calderone RR, Larsen JM. Overview and classification of spinal infections. *Orthop Clin North Am 27*: 1-8, 1996.
6. CDC. *Reported Tuberculosis in the United States.* CDC: Atlanta, GA. 2015.
7. Colmenero JD, Jiménez-Mejías ME, Reguera JM, Palomino-Nicás J, Ruiz-Mesa JD, Márquez-Rivas J, Lozano A, Pachón J. Tuberculous vertebral osteomyelitis in the new millennium: still a diagnostic and therapeutic challenge. *Eur J Clin Microbiol Infect Dis 23*: 477-483, 2004.
8. Davidson PT, Horowitz I. Skeletal tuberculosis. A review with patient presentations and discussion. *Am J Med 48*: 77-84, 1970.
9. Franco-Paredes C, Díaz-Borjon A, Senger MA, Barragan L, Leonard M. The ever-expanding association between rheumatologic diseases and tuberculosis. *Am J Med 119*: 470-447, 2006.
10. Garg RK, Somvanshi DS. Spinal tuberculosis: A review. *J Spinal Cord Med 34*: 440-454, 2011.
11. Hodgson SP, Ormerod LP. Ten-year experience of bone and joint tuberculosis in Blackburn 1978-1987. *J R Coll Surg Edinb 35*: 259-262, 1990.
12. Hogan JI, Nelson SB. Mycobacterial Musculoskeletal Infections. *Infect Dis Clin 31*: 1-14, 2017.
13. Hong L, Wu JG, Ding JG, Wang XY, Zheng MH, Fu RQ, Li WB, Peng WX, He WF, Sun QF. Multifocal skeletal tuberculosis: Experience in diagnosis and treatment. *Médecine Mal Infect 40*: 6-11, 2010.
14. Huaman MA, Brawley R, Ashkin D. Multidrug-resistant tuberculosis in transplant recipients: Case report and review of the literature. *Transpl Infect Dis 19*: 12672, 2017.
15. Kilborn T, van Rensburg PJ, Candy S. Pediatric and Adult Spinal Tuberculosis. *Neuroimaging Clin N Am 25:* 209-231, 2015.
16. Kim S-J, Kim JH. Late onset *Mycobacterium tuberculosis* infection after total knee arthroplasty: A systematic review and pooled analysis. *Scand J Infect Dis 45*: 907-914, 2013.
17. Kumar K. Spinal tuberculosis, natural history of disease, classifications and principles of management with historical perspective. *Eur J Orthop Surg Traumatol 26*: 551-558, 2016.
18. Ledbetter LN, Salzman KL, Sanders RK, Shah LM. Spinal Neuroarthropathy: Pathophysiology, Clinical and Imaging Features, and Differential Diagnosis. *Radio Graphics 36*: 783-799, 2016.
19. Leibert E, Schluger NW, Bonk S, Rom WN. Spinal tuberculosis in patients with human immunodeficiency virus infection: clinical presentation, therapy and outcome. *Tuber Lung Dis 77*: 329-334, 1996.
20. Leonard MK, Blumberg HM. Musculoskeletal Tuberculosis. *Microbiol Spectr 5:* 1-2, 2017.
21. Lopes AJ, Capone D, Mogami R, Tessarollo B, da Cunha DL, Capone RB, Siqueira HB, Jansen JM. Quais são os desafios para o diagnóstico da tuberculose extrapulmonar? Tuberculose extrapulmonar: aspectos clínicos e de imagem. *Pulmão RJ 15*: 253-261, 2006.
22. Ludwig B, Lazarus AA. Musculoskeletal Tuberculosis. *Disease-a-Month 53*: 39-45, 2007.
23. Murray MR, Schroeder GD, Hsu WK. Granulomatous Vertebral Osteomyelitis: An Update. *J Am Acad Orthop Surg 23*: 529-538, 2015.
24. Naim-ur-Rahman. Atypical forms of spinal tuberculosis. *J Bone Joint Surg Br 62B*: 162-165, 1980.
25. Narayan V, Mohammed N, Savardekar AR, Patra DP, Nanda A. Tuberculous Spondylolisthesis: A Reappraisal of the Clinicoradiologic Spectrum and Surgical Treatment Paradigm. *World Neurosurg 114*: 361-367, 2018.
26. Norbis L, Alagna R, Tortoli E, Codecasa LR, Migliori GB, Cirillo DM. Challenges and perspectives in the diagnosis of extrapulmonary tuberculosis. *Expert Rev Anti Infect Ther 12*: 633-647, 2014.

27. Pattamapaspong N, Muttarak M, Sivasomboon C. Tuberculosis Arthritis and Tenosynovitis. *Semin Musculoskelet Radiol 15*: 459-469, 2011.

28. Pigrau-Serrallach C, Rodríguez-Pardo D. Bone and joint tuberculosis. *Eur Spine J 22*: 556-566, 2013.

29. Sahli H, Roueched L, Sbai M, Bachali A, Tekaya R. The epidemiology of tuberculous dactylitis: A case report and review of literature. *Int J Mycobacteriology 6:* 333, 2017.

30. Shikhare S, Singh D, Shimpi T, Peh WCG. Tuberculous Osteomyelitis and Spondylodiscitis. *Semin Musculoskelet Radiol 15*: 446-458, 2011.

31. Tahasildar N, Sudesh P, Tripathy SK, BK S. Bilateral pathological dislocation of the hip secondary to tuberculous arthritis following disseminated tuberculosis. *J Pediatr Orthop B 21:* 567-573, 2012.

32. Talbot J, Bismil Q, Saralaya D, Newton D, Frizzel R, Shaw D. Musculoskeletal Tuberculosis in Bradford – A 6-Year Review. *Ann R Coll Surg Engl 89*: 405-409, 2007.

33. World Health Organization. *Bending the curve - ending TB: Annual report 2017*. WHO Regional Office for South-East Asia. 2017. available in: http://www.who.int/iris/handle/10665/254762. Accessed at 01/12/2018.

34. World Health Organization. *Guidelines for treatment of tuberculosis.* 4th edition. 2010. ISBN: 9789241547833. WHO/HTM/TB/2009.420 available in: https://www.who.int/tb/publications/2010/9789241547833/en/. Accessed at 04/06/2019.