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REVIEW ARTICLE

Tuberculosis of the spine. A systematic review of case series

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Abstract
Purpose The objective of this systematic review was to characterise the methodological issues, as well as clinical, diagnosis, microbiological and treatment characteristics of patients with spinal tuberculosis.
Methods We conducted a systematic review including prospective or retrospective case series written in English, Spanish, French, German and Italian published in the period from January 1980 to March 2011.
Results Thirty-seven articles were included with a total of 1,997 patients; the median of the percentage of men was 53% (interquartile range [IQR] 48–64) and the median of the patients mean age was 43.4 (IQR 37–55). The most common symptom reported was back pain, and thoracic spine was the most frequent segment involved. Spinal plain radiography was done in 35 studies (94.6%), magnetic resonance imaging (MRI) in 26 (70.2%), computed tomography scan (CT-scan) in 13 (35%) and microbiological diagnosis in 29 (78.3%). Surgical treatment was reported in 28 articles 75.7%; finally, 24 articles reported follow-up, and in 15 of them at least 80% of patients improved.
Conclusions Spinal TB is still an important public health issue, it must be suspected in the presence of back pain or characteristic images and should be confirmed with microbiological procedures. Chemotherapy treatment is often used; in contrast, there is heterogeneity in the percentage of patients treated by surgery.

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Introduction

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, and is one of the oldest disease in the world. It has been described in almost all ancient civilisations, and tuberculous bacilli has even been found in prehistoric skeletal remains [1].

The disease has been an important public health issue, having serious medical, social and financial impacts, especially in developing countries. TB incidence has been rising since the 1980s and early 1990s, causing 2–3 million deaths annually worldwide [2]. Despite a marked improvement in the socioeconomic status of many countries and the availability of effective antitubercular drugs, the impact of the acquired immunodeficiency syndrome (AIDS) pandemic and immigration have increased the rate of the disease [3]. Immigrants have not been diagnosed in their own countries or have not been fully treated, which make them infective, which is why tuberculosis is a world-wide public health problem [4].

Extra-pulmonary TB accounts for about 15–20% of TB cases [5]. Although the true incidence of spinal TB is not certain, it has been estimated that it occurs in 1.7% of the world population. Vertebral tuberculosis is the most common form of skeletal tuberculosis, constituting approximately 50% of all cases [6].

Spinal tuberculosis was discovered by Pott in 1776 and is the result of haematogenous dissemination from a primary focus. The infection reaches the skeletal system through vascular channels, generally the arteries, as a result of bacillemia, or rarely in the axial skeleton through Batson's plexus of veins [1]. The infection spreads to the adjacent vertebral bodies under the longitudinal ligaments. The most common site is the thoracolumbar junction, but any segment of the spine can be involved; nevertheless, TB of the cervical region accounts for 10% of all cases of spinal TB. Atlantoaxial junctions are the least common sites for

presentation of spinal TB, accounting for just 1% of all cases [7].

The symptoms are back or neck pain and non specific complaints such as weight loss and fever; thus, the diagnosis can reliably be made on a clinical and radiological basis, if the disease is suspected. On the other hand, microbiology access can increase diagnostic accuracy [8].

Before the advent of chemotherapy in 1994, treatment was basically bed rest, but after the treatment with chemotherapy and surgery the outcome began to improve [1]. Surgical treatment is considered in cases of severe spinal instability or progressive neurological symptoms with evidence of cord compression or deformation [9].

Finally, the prognosis depends on many factors. It is better if there is partial cord compression, if the neural complications are of short duration, if there is early onset cord involvement and neural complications developed slowly and if the patient is young, and does not have any other disease [8].

Actually, spinal TB is a great challenge to physicians because of the nonspecific and wide spectrum of clinical presentations that result in delay of diagnosis and the risk of significant potential morbidity and mortality due to several complications. Early diagnosis and treatment is the key to avoiding this long-term disability [9].

The objective of the systematic review was to characterise the methodological issues, the clinical manifestations, microbiological features, diagnosis methods, treatment procedures and outcomes during follow-up of patients with spinal tuberculosis.

Material and methods

Data sources and search strategy

We carried out systematic searches of the literature in the following bibliographical databases: MEDLINE (PubMed), CINAHL, EMBASE and the ISI Web of Sciences. Search criteria included articles published in the period from January 1980 to March 2011, and only included articles published in English, Spanish, French, German and Italian. The search terms used were "tuberculosis, spinal", "Pott disease" and "Pott's Disease". The search strategy for MEDLINE was as follows: "tuberculosis, spinal" [MeSH Terms] OR pott disease [Text Word] OR Pott's Disease [Text Word] AND ("1980/01/01"[PDAT] : "2011/03/24"[PDAT]). The search strategy was adapted for the other databases. In addition, reference sections of the original studies were screened manually.

Selection criteria

Studies included in the review met the following criteria: prospective or retrospective descriptive case series of spinal TB in hospital settings with information about clinical manifestations, diagnosis methods, microbiological features, treatment and outcomes during follow-up. We excluded article studies that did not provide sufficient data for the study variables, case series with less than four patients, atypical presentation, non hospital settings and case series with only data about one specific location.

Selection studies procedure

Relevant papers were selected by screening the titles (first step), abstracts (second step) and entire articles (third step) retrieved during the database searches. During each respective phase, the title, abstract, or entire article was screened to ensure they met the selection criteria. Assessment of eligibility criteria for inclusion or exclusion studies was performed independently by two investigators (A.O. and G.L.). Any disagreement during the selection procedure was resolved by discussion and consensus.

Data extraction and study variables

Data were extracted from the included studies by the two researchers (O.A. and L.G.) and entered into a Microsoft Excel database. The following characteristics were collected from each study: methodological issues (year of study, country, study period, number of hospitals and sample size), epidemiological characteristics (age, sex, time to diagnosis, HIV infection, previous treatment or diagnosis of pulmonary TB, proportion of spinal TB between TB cases, proportion of spinal TB between all extra-pulmonary TB cases), diagnosis characteristics (plain radiograph of the spine, magnetic resonance imaging (MRI) , computed tomography (CT) scan, tuberculin skin test, microbiological and histological diagnosis obtained by surgery biopsy or either CT-guided needle biopsy or CT-guided drainage), clinical manifestations, location of spinal TB, number of vertebrae involved and treatment characteristics (duration of chemotherapy, surgical treatment, and outcome during follow-up).

The study variables for each of the included studies were summarised in descriptive tables.

Results

Selected papers

The database search identified 5,576 titles (MEDLINE (PubMed), 1,522 titles; EMBASE, 2,086 titles; CINAHL, 968 titles; and ISI Web of Sciences, 1,000 titles). Combining the results of the four electronic searches and removing duplicate records left titles of 2,605 unique records to be screened independently. Screening of the titles and abstracts

resulted in a selection of 58 articles that appeared to meet all the selection criteria. Of the potentially relevant publications retrieved during our initial search, 22 were excluded based on the exclusion criteria (Fig. 1). Searching through the references of the included studies provided a new paper. Finally, 37 studies were included in the review.

Methodological characteristics

In relation to the year of publication, eight (21.6%) studies were published during 2010. The countries primarily represented were Spain (five) and France (three). The article with the longest period of study was 15 years (1990–2005). In 75.6% of the articles, data were obtained from one hospital only. A total of 1,997 patients were included in the review. Number of patients per article ranged from six to 255 (Table 1).

Epidemiology

Table 2 shows the epidemiological features of the included studies. The median of the patients mean age of all studies was 43.4 (interquartile range [IQR] 37–55), and the age range was nine to 76 years old. The median of the percentage of men was 53% (IQR 48–64). In 14 (37.8%) studies were no data on time to diagnosis, and in the rest the mean was 6.5 months (standard deviation [SD] 2.5) and the range was 3–12.

Human Immunodeficiency Virus (HIV) test was not performed in 19 (51.3%) studies and two studies excluded HIV patients. Only 12 studies had information about previous treatment or diagnosis of pulmonary TB. A total of 78.4% (29) of the articles did not report the proportion of spinal TB in patients with a diagnosis of TB; however, of the reported cases the highest prevalence was 5.3%. On the other hand, six (16.2%) studies reported the percentage of spinal TB in patients with extra pulmonary TB and the range varied from 1.3 to 17.3%.

Diagnosis procedures and microbiological features

Clinical diagnosis of spinal TB was not present in five (13.5%) articles as inclusion criteria. Spinal plain radiography was performed in 94.6% (35) of the studies. More than 20% of the patients showed normal results in only four of the studies

In addition to radiography, MRI as a diagnostic test was performed in 26 (70.2%) articles, and a positive or altered result greater than 95% was obtained in 77.7% of the articles. CT scan was used in 13 studies where 61.5% (eight) showed a positive result greater than or equal to

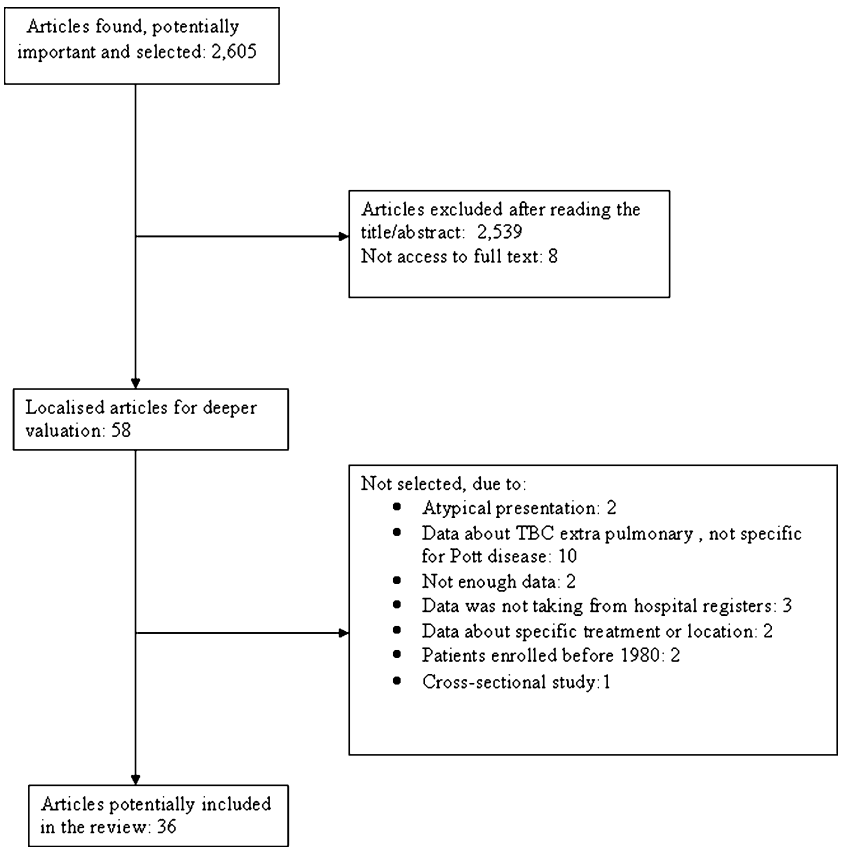

Fig. 1 Study selection flow diagram

Table 1 Methodological features of included articles

Author	Year publication	Country	Study period	Number of hospital settings	Number of patients
Prazuck et al. [33]	1989	Burkina Faso	1986–1987	1	45
Campos et al. [34]	1989	Peru	1984–1986	2	27
Richter et al. [35]	1991	Tanzania	1987–1988	1	47
Fam et al. [36]	1993	Canada	1981–1990	1	7
Puigdengolas et al. [37]	1993	Spain	1982–1991	1	14
Leibert et al. [38]	1996	EEUU	1988–1995	1	7
Pertuiset et al. [25]	1999	France	1980–1994	7	103
Barrière et al. [10]	1999	France	1990–1997	2	16
Alothman et al. [39]	2000	Saudi Arabia	1985–1998	1	69
Solagberu et al. [40]	2001	Nigeria	1990–1999	1	50
Garcia-Lechuz et al. [41]	2001	Spain	1993–1999	1	14
Rasit et al. [11]	2001	Malaysia	1994–1998	1	53
Rodriguez-Gómez et al. [42]	2002	Spain	1986–1999	2	37
Meddeb et al. [43]	2002	Tunisia	1989–1999	1	29
Sakho et al. [44]	2003	Senegal	1986–1998	3	255
Dharmalingam et al.[45]	2003	Malaysia	2000–2002	1	33
Colmenero et al.[12]	2004	Spain	1983–2002	2	78
Schlesinger et al.[13]	2005	EEUU	1994–1999	1	12
López Cordoba et al. [46]	2005	Colombia	1994–2004	1	35
Mulleman et al. [3]	2005	France	1986–2003	1	24
Sharifi-Mood et al. [47]	2006	Iran	1996–2005	2	118
Tasova et al. [48]	2006	Turkey	1997–2003	1	40
Kotil et al. [49]	2007	Turkey	1990–2005	1	44
Park et al. [14]	2007	Korea	1994–2003	7	137
Godlwana et al. [50]	2008	South Africa	2005–2006	1	104
Maeda et al. [15]	2008	Japan	1990–2002	1	23
Kenyon et al. [51]	2009	UK	1999–2009	1	17
Polley et al. [5]	2009	South Africa	2001–2006	1	16
Owolabi et al. [21]	2010	Nigeria	2005–2009	4	87
Su et al. [16]	2010	Taiwan	2002–2008	1	48
Weng et al. [17]	2010	Taiwan	1998–2007	1	38
Benzagmout et al. [52]	2010	Morocco	2001–2006	1	37
Kim et al. [53]	2010	Seoul	2003–2007	1	47
Mwachaka et al. [54]	2010	Kenya	2004–2009	1	129
Alavi et al. [55]	2010	Iran	1999–2008	1	69
Lozano et al. [56]	2010	Spain	2000–2009	1	6
Fedoul et al. [57]	2011	Morocco	2002–2006	1	82

95%. A total of 29 (78.3%) studies performed microbiological diagnosis. The culture test results were positive above 70% in 45.4% of the cases (Table 3).

Clinical features

The most common symptom was back pain reported in up to 80% of patients in 86.6% of the studies while cough, fever, night sweats and weight loss were less frequently reported. Neurological deficit presented a wide range from 12.5 to 100%. The thoracic segment was the most frequent spinal segment affected, followed by lumbar spine. On the other hand, lumbosacral and cervical spine were less involved (Table 4). Only eight studies showed data about the mean number of vertebrae affected; the means and ranges, respectively, were as follows: 4.7, 1–15 [10]; 3.0, 1–9 [11]; 2.6, 1-7[12]; 3.4, 1–7 [13]; 2[14]; 2.3, 1–4 [15]; 2.5, 1–7 [16]; 3.5, 2–5 [17].

Table 2 Epidemiological features of included articles

Author	Age (years), mean (SD)	Age (years), range	Sex (males), *n* (%)	Time to diagnosis (months), mean (SD)	Time to diagnosis (months), range	HIV infection, *n* (%)[a]	Previous pulmonary TB, *n* (%)
Prazuck et al. [33]	34 (−)	1–78	26 (58)	-	-	-	-
Campos et al. [34]	-	0.5–14	14 (52)	8 (−)	0–84	-	-
Richter et al. [35]	-	-	-	-	-	-	-
Fam et al. [36]	52 (−)	26–74	2 (29)	12[b]	5–30	0/2 (0)	1 (14)
Puigdengolas et al. [37]	58 (−)	21–85	10 (71)	6 (4)	-	-	8 (57)
Leibert et al. [38]	43 (15)	24–63	5 (71)	3 (−)	0–24	7/7 (100)	-
Pertuiset et al. [25]	41[b]	17–84	68 (66)	4 (−)	0–36	0/54 (0)	19 (18)
Barrière et al. [10]	42 (−)	20–76	9 (56)	3 (−)	1–6	0/16 (0)	-
Alothman et al. [39]	53 (−)	15–80	37 (53)	-	-	-	5 (7)
Solagberu et al. [40]	27 (23)	2–70	24 (48)	-	-	-	-
Garcia-Lechuz et al. [41]	58 (−)	-	9 (64)	-	1 – 36	1/14 (7)	-
Rasit et al. [11]	40 (−)	-	37 (70)	7 (−)	-	-	-
Rodriguez-Gómez et al. [42]	60 (14)	24–82	19 (51)	7 (7)	1–32	Excluded	8 (22)
Meddeb et al. [43]	49 (−)	-	14 (48)	7 (−)	-	-	-
Sakho et al. [44]	35 (−)	1–80	136 (53)	11 (−)	1–120	1/37 (3)	-
Dharmalingam et al. [45]	34 (−)	3–76	24 (73)	-	-	-	-
Colmenero et al. [12]	49 (19)	14–84	40 (51)	6 (−)	0–7	6 (8)	-
Schlesinger et al. [13]	40 (−)	19–67	7 (58)	-	2–48	1/12 (8)	-
López Cordoba et al. [46]	-	1–71	23 (49)	9 (−)	1–60	0/24 (0)	-
Mulleman et al. [3]	61 (−)	-	9 (38)	4 (−)	1–12	0 (0)	4/24 (17)
Sharifi-Mood et al. [47]	29 (24)	4–73	82 (70)	-	-	-	-
Tasova et al. [48]	45 (19)	18–80	20 (50)	12 (12)	1–28	-	-
Kotil et al. [49]	42 (−)	10–70	21 (48)	-	-	-	-
Park et al. [14]	44 (17)	-	69 (50)	-	-	-	-
Godlwana et al. [50]	28 (−)[c]	-	43 (42)	-	-	29/104 (28)	104 (100)
Maeda et al. [15]	76 (−)	70–92	10 (44)	5 (−)	1–24	-	-
Kenyon et al. [51]	29 (−)	14–65	8 (47)	7[b] (−)	0–24	-	-
Polley et al. [5]	34 (21)	12–68	7 (44)	-	-	1/12 (8)	-
Owolabi et al. [21]	41 (15)	15–70	57 (66)	75 %>2 months	-	15/87 (17)	10 (12)
Su et al. [16]	64 (16)	10–88	24 (50)	7 (6)	1–24	1 (2)	4 (8)
Weng et al. [17]	68 (−)	36–86	23 (61)	3 (−)	0–24	Excluded	2 (5)
Benzagmout et al. [52]	9 (−)	4–15	24 (64)	9 (−)	0–48	-	0 (0)
Kim et al. [53]	56 (−)	-	17 (36)	4 (−)	-	-	6 (13)
Mwachaka et al. [54]	34 (16)	3–81	68 (53)	-	-	0 (0)	-
Alavi et al. [55]	44 (18)	-	42 (61)	7 (4)	-	12/69 (17)	-
Lozano et al. [56]	54 (−)	-	2 (33)	7 (−)	1–20	2/6 (33)	-
Fedoul et al. [57]	43 (−)	4–73	38 (46)	10 (−)	-	-	-

HIV human immunodeficiency virus, *TB* tuberculosis, *SD* standard deviation

[a] Percentage over realised test

[b] Data are expressed by median

[c] Mean age for adults ≥18 years

Treatment

The duration of drug treatment varied from six to 18 months, and it was not specified in 43.2% of the articles. Patients' drug treatment resistances were only recorded in four studies. In 28 of the 37 studies, patients received surgical treatment. The percentage of patients treated by surgical techniques varied between 8.7 and 100%. In 24 (64.8%) articles clinical improvement during follow-up was evaluated. In 62.5% (15) of the studies, at least 80% of patients improved (Table 5).

Table 3 Diagnosis features of included articles

Author	Negative spinal plain radiograph, *n* (%)	Positive MRI, *n* (%)	Positive CT-scan, *n* (%)	Positive TB skin test, *n* (%)	Positive culture TB, *n* (%)	Positive histological, *n* (%)
Prazuck et al. [33]	0/45 (0)	-	-	-	-	-
Campos et al. [34]	0/27 (0)	-	-	14/27 (52)	4/4 (100)	-
Richter et al. [35]	-	-	-	-	-	-
Fam et al. [36]	2/7 (29)	1/1 (100)	7/7 (100)	6/6 (100)	5/5 (100)	4/5 (80)
Puigdengolas et al. [37]	-	-	-	8/8 (100)	-	-
Leibert et al. [38]	2/7 (29)	-	3/7 (43)	6/7 (86)	7/7 (100)	5/7 (71)
Pertuiset et al. [25]	6/103 (6)	44/44 (100)	63/63 (100)	66/70 (94)	86/103 (84)	51/73 (70)
Barrière et al. [10]	2/15 (13)	-	5/5 (100)	-	11/14 (79)	6/14 (43)
Alothman et al. [39]	1/69 (1.4)	69/69 (100)	69/69 (100)	-	25/50 (50)	35/50 (70)
Solagberu et al. [40]	6/25 (24)	-	-	18/27 (67)	-	-
Garcia-Lechuz et al. [41]	-	-	-	7/14 (50)	5/8 (63)	11/15 (73)
Rasit et al. [11]	0/53 (0)	-	-	53/53 (100)	-	-
Rodriguez-Gómez et al. [42]	6/37 (16)	18/18 (100)	8/8 (100)	28/37 (76)	29/37 (78)	7/16 (44)
Meddeb et al. [43]	0/29 (0)	-	26/26 (100)	17/29 (59)	-	1/17 (6)
Sakho et al. [44]	12/255 (5)	-	2/2 (100)	72/91 (82)	-	3/8 (38)
Dharmalingam et al. [45]	-	-	-	-	-	10/13 (77)
Colmenero et al. [12]	11/78 (14)	42/44 (96)	58/61 (95)	54/65 (83)	35/37 (56)	-
Schlesinger et al. [13]	-	12/12 (100)	-	5/12 (42)	9/11 (82)	3/12 (25)
López Cordoba et al. [46]	-	17/17 (100)	5/19 (26)	-	13/35 (37)	14/35 (40)
Mulleman et al. [3]	-	10/24 (42)	8/12 (67)	14/15 (93)	8/20 (40)	3/20 (15)
Sharifi-Mood et al. [47]	-	-	-	78/118 (66)	-	-
Tasova et al. [48]	-	-	-	12/22 (55)	13/22 (59)	26/34 (76)
Kotil et al. [49]	-	35/44 (80)	35/44 (80)	-	19/44 (43)	-
Park et al. [14]	-	75/128 (59)	75/128 (59)	-	-	-
Godlwana et al. [50]	-	-	-	-	-	-
Maeda et al. [15]	0/23 (0)	23/23 (100)	-	-	-	23/23 (100)
Kenyon et al. [51]	-	17/17 (100)	-	-	13/17 (77)	-
Polley et al. [5]	1/16 (6)	16/16 (100)	-	1/3 (33.3)	8/15 (53)	11/15 (73)
Owolabi et al. [21]	20/87 (23)	16/16 (100)	-	58/67 (87)	-	-
Su et al. [16]	-	-	-	-	19/45 (42)	11/45 (24)
Weng et al. [17]	-	35/35 (100)	-	-	24/38 (63)	32/38 (84)
Benzagmout et al. [52]	-	10/10 (100)	-	28/37 (76)	-	7/7 (100)
Kim et al. [53]	-	-	-	-	41/45 (91)	41/45 (91)
Mwachaka et al. [54]	-	-	-	13/129 (10)	-	-
Alavi et al. [55]	13/69 (19)	13/13 (100)	-	-	6/69 (9)	27/69 (39)
Lozano et al. [56]	0/6 (0)	4/6 (67)	-	3/6 (50)	6/6 (100)	4/6 (67)
Fedoul et al. [57]	-	-	-	26/70 (37)	4/30 (13)	6/14 (43)

TB tuberculosis, *MRI* magnetic resonance imaging, *CT* computed tomography

Percentage values are over realized test

Discussion

It is estimated that almost six billon people are infected with TB and over nine million new cases of active TB occur annually with two to three million deaths [4]. Extra pulmonary TB accounts for about 15–20% of all cases and nearly 1–3% of patients suffering from TB have involvement of the skeletal system [1]. In our review the proportion of spinal TB to all TB cases varied from 1% to 5%, which corresponded with the literature findings.

The HIV pandemic is a risk factor for acquired TB. It is upsetting that less than half of the studies searched for HIV among their patients; moreover, the World Health Organisation (WHO) has suggested exploring the association between TB and HIV [18].

Table 4 Clinical features of included studies

Author	Back pain, *n* (%)	Neurological deficits, *n* (%)	Cough, *n* (%)	Fever, *n* (%)	Night sweats, *n* (%)	Weight loss, *n* (%)	Back swelling, *n* (%)	Cervical, *n* (%)	Thoracic, *n* (%)	Thoracolum bar, *n* (%)	Lumbar, *n* (%)	Lumbo sacral, *n* (%)
Prazuck et al. [33]	-	-	-	-	-	-	-	1 (2)	11 (24)	26 (58)	6 (13)	1 (2)
Campos et al. [34]	3 (11)	-	-	7 (26)	-	-	-	2 (7)	17 (63)	-	8 (30)	-
Richter et al. [35]	40 (85)	-	11 (23)	17 (36)	6 (13)	11 (23)	-	6 (13)	40 (87)	-	40 (87)	-
Fam et al. [36]	7 (100)	3 (43)	-	2 (29)	2 (29)	5 (71)	-	1 (14)	0 (0)	2 (29)	2 (29)	1 (14)
Puigdengolas et al. [37]	14 (100)	7 (50)	-	-	-	-	-	2 (14)	2 (14)	2 (14)	7 (50)	-
Leibert et al. [38]	7 (100)	2 (29)	-	5 (71)	-	4 (57)	-	0 (0)	5 (71)	-	2 (29)	-
Pertuiset et al. [25]	100 (97)	51 (50)	-	32 (31)	19 (18)	49 (48)	-	12 (12)	48 (47)	0 (0)	68 (66)	5 (5)
Barrière et al. [10]	13 (81)	2 (13)	-	7 (44)	-	-	-	6 (21)	14 (48)	0 (0)	6 (21)	3 (10)
Alothman et al. [39]	58 (84)	-	-	22 (32)	15 (22)	19 (28)	31 (45)	4 (6)	38 (55)	-	25 (36)	-
Solagberu et al. [40]	-	12 (44)	-	-	-	-	-	2 (8)	6 (24)	6 (24)	11 (44)	0 (0)
Garcia-Lechuz et al. [41]	14 (100)	-	-	1 (7)	-	-	-	1 (7)	7 (50)	1 (7)	3 (21)	2 (14)
Rasit et al. [11]	50 (94)	28 (53)	-	20 (38)	20 (38)	-	-	13 (8)	93 (57)	-	53 (33)	4 (2)
Rodriguez-Gómez et al. [42]	33 (89)	11 (30)	-	7 (19)	-	18 (49)	-	1 (3)	31 (84)	0 (0)	8 (22)	11 (30)
Meddeb et al. [43]	29 (100)	24 (83)	-	17 (59)	-	-	-	-	-	-	-	-
Sakho et al. [44]	232 (91)	202 (80)	-	236 (93)	236 (93)	236 (93)	153 (60)	13 (5)	132 (54)	36 (14)	53 (22)	9 (4)
Dharmalingam et al. [45]	-	-	-	-	-	-	-	-	-	-	-	-
Colmenero et al. [12]	65 (83)	35 (45)	-	27 (35)	-	-	-	3 (4)	32 (41)	11 (14)	25 (32)	5 (6)
Schlesinger et al. [13]	9 (75)	4 (33)	6 (50)	-	-	-	-	1 (8)	3 (25)	4 (33)	3 (25)	1 (8)
López Cordoba et al. [46]	27 (77)	-	-	9 (26)	-	8 (23)	-	1 (3)	10 (29)	-	7 (20)	3 (9)
Mulleman et al. [3]	24 (100)	-	-	9 (38)	-	10 (42)	-	2 (8)	12 (50)	-	13 (54)	-
Sharifi-Mood et al. [47]	107 (90)	-	36 (31)	83 (71)	-	83 (71)	-	4 (3)	69 (51)	0 (0)	45 (46)	0 (0)
Tasova et al. [48]	37 (93)	-	2 (5)	18 (45)	11 (28)	13 (33)	22 (55)	4 (10)	20 (50)	-	33 (83)	-
Kotil et al. [49]	44 (100)	-	-	-	-	-	-	-	16 (36)	18 (41)	10 (23)	-
Park et al. [14]	-	-	-	-	-	-	-	2 (2)	31 (78)	9 (11)	37 (45)	2 (2)
Godlwana et al. [50]	-	-	-	-	-	-	-	11(11)	44 (42)	10 (10)	31 (30)	5 (5)
Maeda et al. [15]	19 (83)	13 (57)	-	7 (30)	-	-	-	1 (4)	11 (48)	7 (30)	5 (22)	-
Kenyon et al. [51]	13 (76)	4 (24)	-	6 (35)	6 (35)	-	-	3 (18)	11 (65)	-	7 (41)	-
Polley et al. [5]	-	12 (75)	-	-	-	-	-	-	16 (100)	14 (81)	-	-
Owolabi et al. [21]	79 (91)	87 (100)	20 (23)	40 (46)	-	18 (21)	29 (33)	0 (0)	39 (58)	0 (0)	19 (28)	9 (13)
Su et al. [16]	46 (96)	37 (77)	-	19 (40)	-	4 (8)	-	2 (4)	16 (33)	8 (17)	20 (42)	2 (4)
Weng et al. [17]	38 (100)	-	-	6 (16)	-	3 (8)	-	1 (2)	14 (37)	3 (8)	15 (39)	4 (11)
Benzagmout et al. [52]	-	-	-	37 (100)	37 (100)	37 (100)	-	2 (5)	5 (14)	-	23 (62)	-
Kim et al. [53]	41 (87)	13 (28)	-	8 (17)	-	-	-	4 (9)	18 (38)	-	25 (53)	-
Mwachaka et al. [54]	100 (78)	-	9 (7)	-	24 (19)	9 (7)	-	7 (6)	49 (43)	10 (9)	42 (37)	3 (3)
Alavi et al. [55]	68 (99)	18 (26)	-	18 (26)	12 (17)	10 (15)	-	-	10 (15)	-	-	-
Lozano et al. [56]	6 (100)	1 (17)	-	2 (33)	-	-	-	0 (0)	3 (50)	0 (0)	3 (50)	0 (0)
Fedoul et al. [57]	81 (9)	34 (41)	-	-	-	81 (99)	-	-	34 (41)	-	43 (52)	-

Table 5 Treatment features of included articles

Author	Duration of chemotherapy, (months) mean (SD)	Surgical treatment, *n* (%)	Follow-up evaluation (months), mean (SD)	Clinical improvement, *n* (%)[a]	Lost follow-up, *n* (%)
Prazuck et al. [33]	8 (minimum)	-	-	45/45 (100)	0 (0)
Campos et al. [34]	-	6 (22)	-	-	-
Richter et al. [35]	-	-	3 (–)	-	-
Fam et al. [36]	12 (minimum)	5 (71)	50 (–)	5/5 (100)	2 (29)
Puigdengolas et al. [37]	-	5 (36)	-	-	-
Leibert et al. [38]	12 (–)	2 (29)	12 (–)	6/7 (86)	0 (0)
Pertuiset et al. [25]	14[b]	25 (24)	10[b]	46/47 (98)	56 (54)
Barrière et al. [10]	-	3 (19)	-	14/14 (100)	2 (13)
Alothman et al. [39]	-	32 (46)	6 (minimum)	32/33 (96)	-
Solagberu et al. [40]	5 (6)		-	-	4 (85)
Garcia-Lechuz et al. [41]	9 (–)	9 (64)	22 (–)	-	-
Rasit et al. [11]	12 (–)	30 (57)	60 (–)	50/53 (94)	0 (0)
Rodriguez-Gómez et al. [42]	11 (4)	12 (32)	7 (–)	13/36 (36)	1 (3)
Meddeb et al. [43]	15 (–)	-	16 (–)	26/29 (90)	0 (0)
Sakho et al. [44]	-	39 (15)	5 (–)	118/148 (80)	107 (42)
Dharmalingam et al. [45]	9 (minimum)	20 (61)	-	-	-
Colmenero et al. [12]	-	55 (71)	12 (–)	-	-
Schlesinger et al. [13]	12 (–)	10 (83)	-	12/12 (100)	0 (0)
López Cordoba et al. [46]	-	29 (83)	-	-	-
Mulleman et al. [3]	-	-	-	-	-
Sharifi-Mood et al. [47]	-	-	-	-	-
Tasova et al. [48]	-	34 (85)	-	27/40 (68)	-
Kotil et al. [49]	-	-	-	42/44 (95)	-
Park et al. [14]	6–12	98 (72)	-	94/116 (81)	-
Godlwana et al. [50]	-	-	-	-	-
Maeda et al. [15]	12 (–)	2 (9)	-	-	-
Kenyon et al. [51]	12 (–)	-	2	13/17 (77)	-
Polley et al. [5]	9 (minimum)	16 (100)	-	15/16 (94)	0 (0)
Owolabi et al. [21]	8 (minimum)	-	6 (minimum)	20/67 (30)	20 (23)
Su et al. [16]	11 (4)	30 (63)	11	26/37 (70)	11 (23)
Weng et al. [17]	11[b]	32 (84)	11	24/34 (71)	4 (11)
Benzagmout et al. [52]	12 (–)	7 (19)	3	37/37 (100)	-
Kim et al. [53]	-	40 (85)	-	-	-
Mwachaka et al. [54]	9 (–)	33 (26)	6	91/129 (70)	12 (9)
Alavi et al. [55]	-	22 (32)	-	53/69 (77)	0 (0)
Lozano et al. [56]	12 (–)	3 (50)	12	5/6 (83)	0 (0)
Fedoul et al. [57]	-	59 (72)	-	78/82 (95)	-

SD standard deviation

[a] Percentage over followed patients

[b] Data are expressed as median

Although the incidence of TB has increased around the world, it is higher in low income countries [3, 19].

In our review there is not a big difference between the proportion of spinal TB in men and women; however, some studies have reported a male predominance [3]. Spinal TB occurs mostly during the first three decades of life. In developed countries the disease is reported more frequently in the elderly [6].

The clinical features of TB spine are varied and depend on either systemic or local disease. General symptoms may include fever, loss of appetite, loss of weight and night sweats. Back pain often occurs, although it is less intense

than in pyogenic infection. Local pain, swelling, and limitation of joint movement may precede discernible radiological changes by four to eight weeks. Pain usually is localised to the joint but can be referred to other areas. In our review pain is also the most frequent symptom reported.

The time from symptom onset to diagnosis varied widely in all of the included studies. The primary infection is not evident, almost always it results from an arterial haematogenous seeding of the mycobacterium, staring from a pulmonary focus [8]. Radiological findings such as narrowing of the disc, reduction in disc space and loss of definition of the paradiscal margins of the vertebrae suggestive of TB are usually evident after three to six months [6]. Moreover, doctors are unfamiliar with the skeletal manifestations of the disease. These factors could explain the delay of the diagnosis.

Plain radiographs of the spine constitute the first image procedure for diagnosis. These image techniques were not performed in two articles. The thoracic and lumbar spine are the most frequently affected sites. MRI and CT are actually the most useful methods for detection of spinal lesions, especially in early stages of the disease [20]. In many developing countries MRI and CT are often reserved for cases where findings on spinal radiography were non specific [21]. Early diagnosis allows rapid therapeutic intervention and prevention of possible complications. In the studies included in the review that conducted MRI and/or CT, most showed positive results in 100% of the patients evaluated.

Due to the high contrast resolution and the ability to detect spinal cord infiltration, MRI has proved to yield a higher diagnostic accuracy than CT scan in incipient TS lesions [22]. No single imaging characteristic exclusively gives the diagnosis of TB spondylitis. However, several simultaneous imaging features can strongly support its diagnosis. Radiologists should be familiar with these characteristics to enable a more rapid diagnosis and to facilitate the prevention of potentially life-limiting consequences [23].

Although the imaging study findings of spinal TB are highly characteristic, they are not fully specific to differentiate spinal TB from other infections or neoplasms [12]. Laboratory signs such as elevated sedimentation rate, C-reactive protein, leucocytosis, lymphopenia and anaemia may be helpful, but are not diagnosis of TB [24]. Microbiological diagnosis based on culture and/or histology techniques are indicated for definitive diagnosis [25]. In this review 80% of the studies performed microbiological tests (culture or histological tests).

Regarding histological analysis, TB has characteristic lesions that may be useful in diagnosis when biopsies or surgical specimens are available. The typical TB tissue lesion is a granulomatous inflammation with central necrosis [26]. This is considered a highly specific finding justifying the start of TB treatment.

For microbiological diagnosis in spinal TB we can obtain samples through surgery biopsy or either CT-guided needle biopsy or CT-guided drainage. Bacteriological and histological yields have been reported to be similar for surgical biopsy and for percutaneous needle aspiration [17, 25]. If surgery is not immediately indicated in patients with a suspicion of spinal TB from clinical features and image findings, CT guided needle aspiration is a reliable and relatively inexpensive diagnostic procedure. The main limitation of the culture test is its slowness in revealing positive results determined by the metabolic characteristics of the pathogen and the number of bacteria present in the sample [27].

The objectives of treatment are to confirm the diagnosis, achieve a bacteriological cure of the lesion, treat compression of the spine and treat spinal deformity and its sequelae such as late onset paraplegia [28]. The optimal duration of chemotherapy TB treatment was assessed by the British Medical Research Council [29] in a series of international studies conducted in India, Korea and Hong Kong. The patterns were studied at six, nine and 18 months with different durations of follow-up. The studies have important methodological limitations, loss to follow-up and without intent to treat analysis [29]. Only the trial conducted in Madras, India with a follow-up period of ten years including a total of 304 patients, adults and children, showed no significant differences in the percentage of patients with a clinical and radiological improvement between six and nine months chemotherapy pattern [30, 31]. In the articles reviewed, there are few studies that specify the average duration of chemotherapy treatment. In the series where this information is provided most of the studies use patterns over eight months.

There is controversy in the literature about the necessity of additional surgical intervention to spinal TB treatments. A Cochrane review of randomised controlled trials comparing the chemotherapy plus surgery with chemotherapy alone for treating active TB of the spine concluded no statistically significant difference for any of the outcome measures [32]. Only two trials were enrolled in the meta-analysis and data are insufficient to be clear as to which of the two treatment policies is better. Future trials need to assess routine surgery and also address subgroups of patients with spinal TB to establish the role of surgery for specific indications [32]. In 75% of the evaluated studies the patients received both chemotherapy and surgical treatment, and in more than half of the studies, the percentage of surgically treated patients was higher than 56%. The indications for the surgical interventions varied across the studies.

Our review has limitations, particularly due to the lack of homogeneity among the included studies. First, all of the case series of spinal TB are retrospective with different samples sizes. Many of the studies are not comparable due to the presence of heterogeneity in the information obtained in the variables of interest and the absence of information on many of them. This makes comparison and interpretation of the results difficult.

The language selection criteria could introduce a selection bias. Only one article was excluded due to the language. Additionally, we could not obtain the full texts in eight articles.

In conclusion, spinal TB is still an important infectious disease and should be considered as a differential diagnosis in patients with chronic back pain and neurological symptoms. Imaging tests such as MRI and CT help diagnose the disease but, to confirm it, a microbiological diagnosis is necessary. It should establish specific indications for surgical treatment.

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