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Original Research Article

The prevalence of extra spinal skeletal tuberculosis in paediatric population: A pilot study with a review of literature

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Abstract

Background: Tuberculosis affects a significant percentage of the world's population and is responsible for bone and joint infections particularly in the developing world. Skeletal TB is uncommon and it is not very rare. There are no studies to know the prevalence of extra spinal skeletal tuberculosis in children. Therefore present study was done to know the prevalence of extra spinal skeletal tuberculosis in pediatric population who attended orthopedic OPD of Tertiary Health Care Centre and also know the frequency of joints or bones involved in the disease process.
Methods: In this study, all pediatric cases of age less than 12 years and who proven diagnosis of extra-spinal skeletal tuberculosis over the last 6 months were reviewed from the past medical records maintained in the medical records department of the institute.
Results: Total number of children (≤12 years) who attended the Orthopedic OPD over 6 months were 2041, of which 20 children met the inclusion criteria of the study. The prevalence of extra-spinal skeletal tuberculosis in children was calculated to be 0.97%. All had symptoms of pain, swelling, and stiffness. 11 children had involvement of the hip joint, 4 had knee joint, 3 had elbow and 1child each had involvement of lower end of humerus and fourth metatarsal bone.
Conclusion: The diagnosis of pediatric extra spinal skeletal tuberculosis can be made on imaging (X- ray and Magnetic Resonance Imaging) and confirm by BACTEC of synovial fluid or tissue biopsy. Hence, BACTEC of synovial fluid or tissue biopsy are the gold standards in diagnosis.
Keywords: Tuberculosis, Skeletal, Extrapulmonary, Extra spinal, Pediatric, Orthopardic.

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1. Introduction

Tuberculosis (TB) is the leading cause of death from infectious disease in the world. The World Health Organization (WHO) estimated that there were 9.6 million cases of tuberculosis (TB) in the world in 2014 and 1.5 million died from the disease [1]. The incidence of tuberculosis (TB) has increased in recent years in both developed and developing countries [2]. In India 1.8 million new tuberculosis cases is occurring annually [3]. It is estimated that India alone has got one-fifth of the total world population of tuberculous patients. Thus, there are nearly 6 million radiologically proven cases of tuberculosis in India. Of all the patients suffering from tuberculosis, nearly 1-2% has involvement of the skeletal system [4].

Though there are excellent sources of information on the adult disease, but, an accurate description of the burden of tuberculosis in children is very difficult to obtain because in many countries surveillance data are often unreliable because of poor diagnostic facilities and reporting systems [5-10]. It remains one of the major infections affecting children worldwide. Infants and young children are at greatest risk of developing extra pulmonary and severe disseminated disease as they are most likely to develop disease after infection, leading to significant morbidity and mortality [11-14].

Skeletal tuberculosis accounts for only 2% of all cases of tuberculosis and 10–35% of extra pulmonary tuberculosis, [15].

Vertebral tuberculosis is the most common form of skeletal tuberculosis and it constitutes about 50% of all cases of skeletal tuberculosis. While tuberculosis is a major cause of skeletal infection in many developing countries, skeletal tuberculosis in children in the developed world is noted to be rare [16] and extra spinal skeletal tuberculosis is even rarer. There are no studies to know the prevalence of extra spinal skeletal tuberculosis in children. So the present study was carried out to know the prevalence of extra spinal skeletal tuberculosis in children which can in turn help in diagnosis of the disease early. Early diagnosis and early intervention leads to better outcome from this disease process which otherwise can cause disabilities in the patients.

2. Materials and Methods

Following approval from the ethics committee and permission from The In-charge of Medical records department all the pediatric cases of age less than 12 years and who proven diagnosis of extra-spinal skeletal tuberculosis over the last 6 months were reviewed from the past medical records maintained in the medical records department of the institute. All of the clinical notes, laboratory findings, pulmonary evaluations, biopsy results (including BACTEC cultures from the aspirate), and available imaging modalities (X- ray, Magnetic Resonance Imaging, Computed Tomography Scan) were reviewed. The locations of tuberculosis involvement were noted. The data are presented in the next section.

3. Results

During the period of six months, total 20 pediatric patients (<12 years of age) met the inclusion criteria. There were 7 (35%) male and 13(65%) female patients. The mean age was 10 years (range 0–12 years). 60% of children were in the age group of 9-12 years. The age wise distribution of patients was shown in table 1. The prevalence of extra-spinal skeletal tuberculosis in children was calculated to be 0.97%.

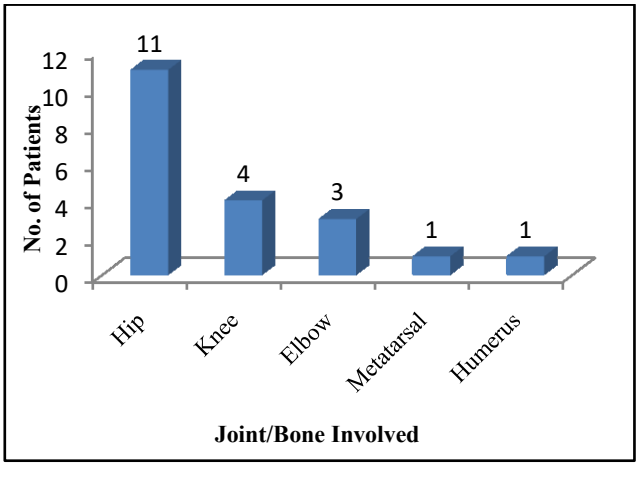
Table 1: Age Wise Distribution of Patients

Age in Years	No. of Patients (N=20)
0-4	1
5-8	7
9-12	12

The presenting symptoms in all of the patients were persistent pain, swelling and stiffness or lack of full motion across the involved joint or location. Children with lower limb involvement presented with a limp. 13 children had constitutional symptoms and 11 children had scar of Bacillus Calmette Guerin. The average duration of symptoms was 4.6 months (range 4 weeks to 16 weeks). Laboratory investigations showed normal total white blood cell counts. The erythrocyte sedimentation rate (ESR) was found to be elevated in all patients and the elevated mean was 74 mm/h with a range of 48 to 112 mm/h. Also C-reactive protein (CRP) was marginally raised in all cases. All patients had sputum testing and/or gastric aspirate testing for tuberculosis. Mantoux test was positive in all the cases. 6 children had history of contact with pulmonary tuberculosis. None of the children had history of pulmonary tuberculosis, active pulmonary or genitourinary tuberculosis.

The frequencies of joints or bones involved in the disease process were shown in figure 1. 11 children had involvement of the hip joint, among them diagnoses of 7 children were based on imaging (X-ray and magnetic resonance imaging) and 4 children underwent hip aspiration which was sent for BACTEC culture for confirmation. 4 children had involvement of knee joint; the diagnosis was confirmed in 2 children with the synovial fluid BACTEC and in 2 children with the synovial biopsy for histopathological examination. X-ray showed no bony lesion, but showed soft tissue swelling. Magnetic resonance imaging showed synovial thickening with effusion. 3 children had involvement of elbow and the diagnosis was confirmed by X-ray, magnetic resonance imaging and synovial biopsy for histopathological confirmation. 1 child had involvement of lower end of humerus and 1 had involvement of fourth metatarsal bone. Diagnoses of both of these were confirmed by histopathological examination and magnetic resonance imaging.

Figure 1: Frequency of Joint/Bone Involved



In terms of imaging studies the most common findings were osteolytic or cystic lesions. Increased soft tissue density attributable to overlying soft tissue swelling was also noted on imaging. There is no question that, given the rarity of this infection in the developed world, all radiologists strongly suspected bone tumors as primary diagnoses.

Figure 2: a) X-ray showing tuberculosis of Hip joint, b) AP X-ray showing tuberculosis elbow joint, c) Lateral X-ray showing tuberculosis elbow joint, d) AP X-ray showing tuberculosis of metatarsal, d1) Oblique X-ray showing tuberculosis of metatarsal, e)AP and lateral X-ray showing tuberculosis of lower end of humerus

4. Discussion

Tuberculosis affects a third of the world's population and each year there are about 20 million prevalent cases and 8million new cases [17]. Tuberculosis remains a major cause of bone and joint infection globally, particularly in the developing world. The developed world however has seen resurgence in the incidence of skeletal tuberculosis. This increase has been attributed to the acquired immune deficiency syndrome (AIDS) epidemic, immigration, homelessness, a decline in TB control programs and intravenous drug abuse [18]. In endemic areas, children are more likely than adults to be affected, often through exposure to adults infected with TB. Skeletal TB is uncommon and represents 10–20% of all extrapulmonary TB and 1–2% of all TB cases [19]. The most common manifestation of skeletal tuberculosis is tuberculous spondylitis or Pott's disease, which is found even in children younger than 5 years of age [20]. The synovial joint is the second most common involvement of skeletal TB. It is typically mono-arthritis with the hip and knee joints frequently affected [21]. In children, the main route of infection in skeletal TB is through haematogenous spread from a primary source. The site of the primary infection is often unknown. It is, therefore, important that clinicians have an increased awareness for this condition and characteristic manifested for early diagnosis. This is especially true for the pediatric population where presentation may not be typical and diagnosis can, therefore, be delayed. Skeletal tuberculosis in pediatrics, therefore, needs to be revisited [16].

In current study, we presented series of pediatric cases with proven diagnosis of extra-spinal skeletal tuberculosis over the last 6 months. We considered total number of children less than 12 years of age who attended the orthopedic OPD over last 6 months as denominator, with total number of proven cases as numerator. Total number of children (≤12 years) who attended the Orthopardic OPD over 6 months were 2041, of which 20 children met the inclusion criteria of the study. Thus, the prevalence of extra-spinal skeletal tuberculosis in children was calculated to be 0.97%. Skeletal TB can occur at any age and almost any site of the body. The mean age of the patients was 10 years (range 0–12 years), this is comparable with the study done by Hosalkar *et al* [16].

The diagnosis of skeletal tuberculosis in children is based mainly on a combination of history of contact with an adult infectious case, clinical signs and symptoms, and investigations based on the 2015 infectious diseases society of America (IDSA) guideline [22]. However, symptoms may often be non specific with over half of children being asymptomatic with early disease [23]. The primary symptoms reported in this study were bone pain, swelling, and stiffness. A similar study in the United States of America demonstrated that the presenting symptoms in all of the patients were persistent pain, swelling, and stiffness or lack of full motion across the involved joint/ location [16]. Systemic symptoms may be rare, particularly in the developed world patient population, where nutritional deficiencies in general are not very common. The differential diagnosis for such symptoms is quite extensive

and the chronicity of symptoms usually demands a thorough work-up to rule out the worst possible scenarios, i.e., bone tumors and sarcomas. Non-disseminated tuberculosis by itself is not life-threatening and can be well controlled and treated if diagnosed early.

The selection of most suitable tests for detection of *M. tuberculosis* infection should be based on the reasons and the context for testing, test availability, and overall cost effectiveness of testing. Currently, there are two methods available for the detection of *M. tuberculosis* infection which is: 1) Mantoux tuberculin skin test (TST) and 2) Interferon-gamma release assays (IGRAs). In present study Mantoux test was used for detection of tuberculosis and which was positive in all the cases. A negative Mantoux test does not preclude a diagnosis of tuberculosis. In the study done by Rasool *et al* [24] Mantoux test was positive in 70% of the children with cystic tuberculosis of bone. In areas where BCG vaccination is routine, it may add to the confusion. Further, bony tuberculosis as a result of Bacille-Calmette-Guerin (BCG) immunization has been reported [25, 26]. It is most often seen in the first five years of life and the interval between vaccination and presentation may vary from five months to five years [25, 26]. In current study, 11 children had scar of Bacillus Calmette Guerin.

Laboratory findings showed normal total white blood cell counts; elevated ESR and marginally increased in CRP; these were seen in all the cases and this may be important markers. But erythrocyte sedimentation rate and C-reactive protein level are non-specific and not reliable for the ultimate diagnosis of skeletal tuberculosis. In the cases presented by Vohra *et al* [27], 88%, had an elevated ESR, which ranged from 31–83 mm/hr (Westergren) whereas Rasool *et al* reported normal ESR in 40% of their patients [24]. The C-reactive protein (CRP) was mentioned by Wang *et al* however in 22 of his 23 patients, the value was negative [26]. So, the radiographic features may suggest the disease, but a negative result does not exclude the disease [28]. Radiographic skeletal survey may help in determining the extent of the disease. It has been reported that only 3–6% patients with bone, joint, or spinal tuberculosis have normal plain radiographs; therefore, this imaging modality is essential and very cost effective[29].

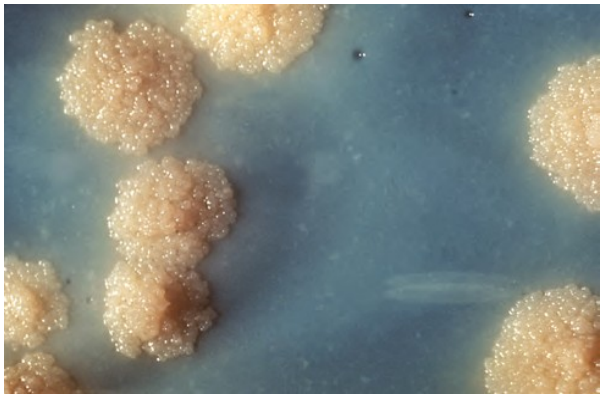
X-rays: The basic imaging analysis includes plain films of bone/joint. The radiological findings include rarefaction, bony deformity, disc space narrowing, anterior vertebral collapse, kyphosis and abscesses. Abscesses may appear as widened paravertebral shadows with soft tissue calcifications and loss of the psoas muscle shadow. Involvement of the disc space resulting in disc space narrowing on radiographs is commonly seen before vertebral body collapse. However with plain radiographs, the extent of the disease is often underestimated and it requires further imaging with CT and MRI with contrast enhancement to fully demonstrate the extent of the disease [30].

CT scan: CT is excellent for defining the anatomy of bony destruction, extension into the spinal canal, posterior element involvement and formation of paravertebral abscess and provides useful information especially for surgical planning. CT-guided needle aspiration of lesion can provide specimens for both culture and histological diagnosis if necessary [31].

MRI: MRI is most useful in delineating soft tissue involvement because of its multiplanar capability and superior resolution, and in evaluating intramedullary lesions. Further administration of gadolinium will help to discriminate between abscesses and granulation tissue and can define a soft tissue mass and the extent of bony destruction [32,33]. Skeletal tuberculosis can appear as joint space narrowing, subchondral erosions, lytic lesions, orarticular osteopenia on plain radiographs. The gold standard in diagnosis, however, is made with microbiological and/or histological techniques [16, 34].

The positive cultures for *M. tuberculosis* confirm the diagnosis of TB disease. Culture examinations should be done on all diagnostic specimens. The commercially available broth culture systems (e.g., BACTEC, MGIT, VersaTREK, and MBBACT) allow detection of most mycobacterial growth in 4 to 14 days compared to 3 to 6 weeks for solid media (Figure 3). Histology/biopsy cultures in skeletal tuberculosis are seldom positive. This is usually because the organism needs to be in specific conditions to be cultured and it sometimes takes a long incubation time for in vitro growth in the laboratory [28]. In present study BACTEC broth culture systems was used for confirmation of diagnosis. Hence, interestingly, is a retrospective case series of all biopsy/culture-positive cases of extra spinal skeletal tuberculosis in the pediatric population. Therefore, in certain ways, this is a biased population of positive cases of skeletal tuberculosis. Hosalkar *et al*. performed a retrospective review of all pediatric biopsy-proven skeletal (extra-spinal) cases of tuberculosis over a five-year period; biopsy and culture are the gold standards in diagnosis [16].

Figure 3: Colonies of M. tuberculosis Grown in Culture



The most common site of skeletal tuberculosis in the adult population is the spine (Pott's disease). An epidemiological study of tuberculosis in the United States reported that the spine was involved in 50% of tuberculosis patients [35]. The current study involved only the pediatric extra-spinal cases, as the nature of clinical practice in our institutions involves spine care as a separate subspecialty. According to the literature the major areas of predilection after spine in order is hip, knee, foot, elbow and others [36, 37]. Current study confirms this fact with as many as 55% of the children had involvement of the hip and 20% of children had involvement of the knee.

The main treatment of skeletal tuberculosis is conservative management with bracing and anti-tuberculosis drugs. Surgery is needed only if there is a neurologic deficit or spinal instability. These lesions respond rapidly to anti-tuberculosis drugs. In the present study, all patients received complete course of anti-tubercular therapy for minimum of 12 months. There was no need of surgery.

5. Conclusion

According to the results, it can be stated that extra spinal skeletal TB should be considered as a differential diagnosis in which patients suffer from bone pain, swelling, and stiffness or lack of full motion across the involved joint or location. Radiography could aid to confirm or reject the diagnosis of extra spinal skeletal TB, but the final diagnosis should be done by Histology/biopsy cultures.

The present study has provided much useful information about the prevalence of extra spinal skeletal tuberculosis in the children; it will help future investigators in determining the sample size for further studies in this subject. Also, it's recommended to conduct supplementary research to include more subjects for more relevant results.

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