ORIGINAL ARTICLE Tuberculosis of Bones and Joints in Orthopedic

ABDUL HANNAN¹, MUHAMMAD BILAL², MUHAMMAD SHAKEEL BASIT³, ASIFA KARAMAT⁴, MUHAMMAD ADEEL ABBAS⁵ ¹Assistant Professor, University College of Medicine & Dentistry, The University of Lahore

²Assistant Professor, Al-Aleem Medical College Lahore

³Assistant Professor, Al-Aleem Medical College Lahore

⁴Assistant Professor, Pulmonology Al-Aleem Medical College Lahore

⁵Senior Registrar, Al-Aleem Medical College Lahore

Correspondence to: Muhammad Bilal, Email: drbilalfrcs@yahoo.com, Cell: 03370444482

ABSTRACT

Background: Mycobacterium Tuberculosis (TB) is a major global health concern and burden on developing countries economy. Pakistan ranks in top 10 countries of the world with high load of TB and a big chunk of this disease process is extra pulmonary TB (EPTB). Among extra pulmonary sites, is bone and joint TB is very common yet under reported. Recent literature has found up to 35% of all extra pulmonary cases are bone and joint TB.

Purpose: We aim to do an analysis of frequency of bone and joint TB in our institution in all new patients getting registered for treatment of TB.

Methodology: This was retrospective analysis 8 years of Data collected in Gulab Devi Hospital Lahore. Data was analyzed using Microsoft excel software and results are tabulated.

Findings: Total number of new registered patients of Extra-pulmonary Tuberculosis (EPTB) were 13000 (20%). Out of these EPTB patients, bone and joint TB diagnosis was made in 690(5.3%) patients. Out of these 690 patients, 400 (58%) cases were recorded in Indoor facility and 290 (42%) cases were seen in outdoor facility. Most common site is Spine 340 cases (85%) followed by Hip joint 16 cases (4%), knee joint 12 cases (3%) and upper limb 16 cases (4%).

Practical Implication: Regarding management of newly registered cases, Gulab Devi hospital is working in collaboration with world Health Organization TB control program and Provincial TB control Program Punjab (PTP). All new cases are managed by multi-disciplinary team and after initial registration are referred to their relevant specialties.

Conclusion: Axial skeleton remains the most common site in al literature and so is the conclusion of our analysis. Detailed research work is still needed in several aspects of this ancient disease to reduce the morbidity and mortality associated with it. **Keywords:** Bone and joint TB, Pulmonary Tuberculosis, Extra pulmonary Tuberculosis

INTRODUCTION

Mycobacterium Tuberculosis has been known to mankind since ancient times and still causing a lot of morbidity and mortality especially in developing countries. Annually more than 10 million new tuberculosis (TB) cases are reported worldwide and this burden is increasing.1. 95% of worldwide TB cases are being reported in developing countries with 99% of worldwide TB mortality but recently a peak in incidence of TB has been seen in developed countries as well².Pakistan ranks 5th amongst the TB prevalent countries in the world. The prevalence, incidence, and mortality per 100,000 population per year from TB in Pakistan are 340, 259 and 20 respectively.²⁴TB was declared as national emergency in Pakistan in 2001 and national TB control Program (NTP) was launched. Now it has been made mandatory to report TB infections in three out of four provinces of Pakistan.

TB can involve virtually any part of body and TB of bones and joints is up to 3%. Amongst the extra pulmonary manifestation of tuberculosis (EPTB), previously this was under reported but recent studies have reported the incidence of bone and joints involvement in 27- 35% of all EPTB cases and this makes it the most common system to be involved of extra pulmonary TB.³ Frequency of EPTB cases in Pakistan have been reported from up-to 25% to 33% of all TB patients reported in Rawalpindi and outdoor clinics in Karachi. Regarding involvement of body part byEPTB, most common site is lymph nodes (36%), and axial skeleton (26%), Nervous System (18%), abdomen (18%), bones and joints (18%), pericardial tissues (3%), breast (3%), pleural membrane (2%) and others.² Among total cases of bones and joint TB, the spine includes 50% cases while remaining half is distributed in remaining musculoskeletal system.Clinical presentation of TB in bones and joints is more often nonspecific with overlapping poly microbial infection. Inflammatory arthropathies such as rheumatoid arthritis, hyper uricemia, nontuberculous joint infections, and chronic osteomyelitis and bone tumors can also complicate clinical picture and make accurate diagnosis more challenging. Once contracted low virulent infections such as TB can do sub clinical pathology for unknown clinical periodsand patients remain asymptomatic of any pulmonary involvement. Late presentation is the result of this sub-clinical activity and very often patients present with advance features of spinal cord compression, vertebral collapse, and joint ankyloses and pathological fractures.Post TB paralysis in TB spine has poor clinical outcomes⁴. Early diagnosis is only possible by patient education, a low threshold to suspect tuberculous infection work up and prompt referral to a specialist facility.As per WHO recommendation tissue diagnosis through fine needle aspiration cytology, true cut biopsy or histopathology is strongly recommended before starting anti tuberculous therapy (ATT). Current studies show a successful outcome in 90-95% of patients when ATT is started in timely fashion and patient compliance is good⁵.

In developing countries like Pakistan incidence of pulmonary TB and EPTB is increasing due to overcrowding, poor living condition, poor dietary status, late diagnosis and low compliance from patients. Late diagnosis with advance bone and joints destruction in TB infection is associated with significant morbidity and mortality. Delay in presentation and diagnosis is often due to social stigmas related to TB, non-availability of specialist healthcare facilities, missed clinical findings and laboratory results could be misleading. A significant research work has been done into diagnosis and treatment of PTB but bones and joints TB has been under reported. In this study we aim to look into frequency of bones and joint TB in patient population presenting to our hospital. **Objective:** To measure the ratio of bone and joints TB in our institution, and compare it with local / international studies.

MATERIAL AND METHODS

This is a retrospective study of 8 years duration in a tertiary care facility in Lahore with well established pulmonary and TB units. Patients are referred to our institution from a wide catchment area surrounding Lahore. Data was collected on the designated proforma which included: patient demographics age, gender. Clinical site of disease involvement, laboratory test especially complete blood count, and erythrocyte sedimentation rate (ESR), C-reactive protein, gene X-pert of joint fluid / pus / discharge materials if available, and tissue diagnosis such as FNAC, True-cut or open biopsy. In case of discharge from wound microbiology culture and AFB cultures were also conducted.

All patients in our institution diagnosed with EPTB, in our study bones and joint TB are enrolled into Provincial TB control Program Punjab (PTP). This comprises of a multidisciplinary approach including specialist from orthopedics, medicine, physical therapy and dedicated TB control program team. PTP team is responsible for disease surveillance, drug resistance and sharing of data to the national and international stakeholders. Data collection on our proforma was for all bone and joint TB patients (irrespective of site).

Data analysis: All collected data was reviewed and analyzed using Microsoft office and excel software to determine disease frequency and age / gender / site distribution. Data was also compared with previous literature for purposes of discussion.

Inclusion criteria: Bone and joint TB diagnosed for first time with no previous history was included in our study.

Exclusion criteria: Previous history of non-tuberculous bone and joint infection, recurrent TB infection, multi drug resistance (MDR) and poor patient compliance was excluded from study.

Operational definitions: Bone and Joint TB; mycobacterium tuberculosis infection affecting any bone or joint in non-axial skeleton and axial skeleton (Spine) will be considered as bone and joint TB excluding skull, and maxillofacial bones.

Multi Drug Resistance: MDR TB is defined as TB disease caused by bacteria that are resistant to at least isoniazid and rifampicin.

RESULTS

We reviewed and analyzed 8 years data of new bone and joint TB cases registered from 2014-2021 at Gulab Devi Hospital Lahore. Total number of new registered patients of Extra-pulmonary

Table-1: Demographic Profile of Patients Presented Indoor since 2014-2021

2018 2014 2015 2016 2017 2019 2020 2021 2014-21 (n=20) (n=58) (n=65) (n=63) (n=67) (n=65) (N = 400) (n=26) (n=36) Age (Average) 34 15-70 34 15-74 Mean Age 35±1.8 Years 34 35 37 35 36 15-74 15-70 15-70 15-75 15-74 13-74 Range Gender n (%) Male 28 (45%) 30 (45%) 31 180 (45%) 07 (35%) 26 (45%) 27 (42%) 14 (54%) 17 (47%) 35 (55%) 37 (55%) (47%)13 (65%) 32 (55%) 38 (58%) 12 (46%) 19 (53%) 220 (55%) Female 34 (53%)

Table-2: Demographic Profile of Patients Presented to OPD Since 2014-18

| Table-2: Demographic Profile of Patients Presented to OPD Since 2014-18 | | | | | | | | | |
|---|-----------|------------|------------|-----------|-----------|----------------------|----------------------|----------------------|----------------|
| | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2014-18 |
| | (n=58) | (n=23) | (n=14) | (n=19) | (n=37) | (n=48) | (n=45) | (n=46) | (N = 290) |
| Age (Average) | 36 | 37 | 37 | 38 | 40 | 36 | 38 | 39 | Mean Age |
| Range | 16-60 | 19-72 | 15-68 | 19-74 | 15-75 | 19-72 | 18-73 | 19-75 | 37.6±2.6 Years |
| Gender n (%) Male Female | 26 (45%) | 10 (43%) | 13 (93%) | 12 (63%) | 21 (57%) | 29 (62%) 19 (38%) | 25 (57%) 21 (43%) | 24 (57%) 22 (43%) | 157 (54%) |
| 1 emaie | 32 (3370) | 10 (01 /0) | 02 (01 /0) | 07 (0770) | 10 (4370) | | | | 133 (46%) |



Figure-1: Frequency Distribution of bone and joint TB as per Site in Indoor Patients 2014-2021



Figure-2: Frequency Distribution of bone and joint TB as per site in Outdoor Patients 2014-2021

With a high volume unit, accurate reporting and differentiation of new and old cases of TB is difficult task. PTP team has dedicated personal in registering of all TB data but considerable variations have been observed on year to year basis in frequency of bone and joint TB and one factor could be data entry errors Table 1. Highest number of Osteoarticular TB was recorded in 2020 (n=67) followed by 2016 (n=65). Average age at the time of presentation was 36 year, minimum age reported was 13 and maximum age reported was 75. Incidence of bone and joint TB was higher in females (55%) and males (44%). Table 1

We recorded involvement of bone and joint TB site and among our admitted indoor patient population (n=400), most common site is Spine 340 cases (85%) followed by Hip joint 16 cases (4%), knee joint 12 cases (3%) and upper limb 16 cases (4%). Unfortunately 16 cases (4%) were not specified for site involvement Figure 1.

Among the patient presenting in orthopedic clinic with diagnosis of bone and joint Tb total patients were 290 (42%), and most common site was axial skeleton 255 patients (88%), upper limb involvement n=15 (5%), Knee Joint n= 12 (4%), Hip and ankle joints were n= 8 (3%) Figure 2. Among outdoor presentation the male to female ratio was reverse with 54% male patients and 46% female patients. Table 2

DISCUSSION

We performed an analysis of frequency of bone and joint TB in new patients presenting at Gulab Devi Hospital. Recent studies across the world report an upwards trend of EPTB including bone and joint TB [3-5]. South Asian countries including Pakistan, India and Bangladesh, females, younger population have shown increase exposure to EPTB $^{\rm [6,\ 7]}.$ Our analysis results have revealed EPTB rate of 20%, a one percent increase from previous analysis. Bone and joint TB comprised 5% of this EPTB population⁸. Some literature in TB prevalent areas have shown bone and joint TB of up to 25% [1,8], and an estimated worldwide prevalence of 20-39 million patients [9]. One study revealed average patient age of contracting the disease of bone and joint TB from 45 years, this is different from our analysis where peak age is 37years [7]. This age range shows that a majority of young population is being affected which has a domino effect on their work, family life and leads to poor economic conditions in already low income families. Literature has also mentioned a bimodal age pattern of disease frequency ^[10]. Another fact about patient presentation, is increased number of hospital admissions among female patients (56%). On the other hand among outdoor patient presentation, male patients were in majority (54%). This is in line with other studies ^[4, 8]. A reversal in the patient presentation ad hospital admission between male to female could mean that female population has increased tendency of serious complications after bone and joints TB. This fact need further dedicated studies and is beyond the scope of our current study.

In line with other literature most frequent involvement is of axial skeleton (up to 80%) followed by non-axil skeleton the hip, upper limb, knee, and ankle/foot ^[7]. Among children, TB arthritis of large synovial joints is more prevalent according to one study ^[11]. Increased incidence of bone and joint TB has been attributed to host related elements in addition to other factors and plays a role in the particular site involvement, according to European surveillance data ^[12]. As late presentation and diagnosis is very common among TB spine patients, a majority of literature (53%) focussed on early diagnosis and management of TB spine ^[13]. Among the axial skeleton involvement, thoracic spine comprises up to 50% cases, Lumbar and cervical regions are next in line in order of frequency ^[14, 15]. Complications of cervical spine involvement are most severe. In this analysis we did not recorded frequency of individual spinal region involvement.

Regarding management of newly registered cases, Gulab Devi hospital is working in collaboration with world Health Organization TB control program and Provincial TB control Program Punjab (PTP). All new cases are managed by multidisciplinary team and after initial registration are referred to their relevant specialties. Bone and joint TB patients are under care of orthopedic department. To improve patient compliance with long course of anti-tuberculous therapy (ATT), TB Directly Observed Therapy (DOTS) program has been implements all across Pakistan which means trained health care worker or other designated individual (excluding a family member) provides the prescribed TB drugs and watches the patient swallow every dose. This program has proven highest compliance and disease eradication ^[17, 18, 19, 26 and 27] Tuberculosis was declared a National Emergency in 2001 by the Government of Pakistan and in 2002 the National Tuberculosis Control Program (NTP) was initiated ministry of Health (MOH).

TB remains a high prevalence disease in subcontinent and Pakistan is among top 10 countries of world dealing with this challenging disease. Our study shows a reflection of bone and joint TB load in our society and measure to curb the spread and improve the cure. Several factors play a role in successful management. Better equipped hospitals with latest technology, staff training and patient education are of paramount importance for successful outcome in this disease process ^[20, 21, 22, and 23].

CONCLUSION

Purpose of our study was to look at the frequency of bone and joint TB with most common affected areas of skeletal system. Axial skeleton remains the most common site in al literature and so is the conclusion of our analysis. Detailed research work is still needed in several aspects of this ancient disease to reduce the morbidity and mortality associated with it.

REFERENCES

- Global tuberculosis report 2017. Geneva: World Health Organization; 2017. ISBN 978-92-4-156551-6. License: CC BY-NCSA 3.0 IGO. https://www.who.int/tb/publications/global_report/MainText_13N ov2017.pdf
- Chandir S, Hussain H, Salahuddin N, Amir M, Ali F, Lotia I, et al. Extrapulmonary Tuberculosis: A retrospective review of 194 cases at a tertiary care hospital in Karachi, Pakistan. J Pak Med Assoc 2010; 60: 105-8.
- Incidence of tuberculosis (per 100,000 people) [Internet]. Worldbank.org. [cited 2022 Dec 9]. Available from: https://data.worldbank.org/indicator/SH.TBS.INCD
- Zhou Z, Zheng Y, Wang L. Diagnostic accuracy of the Xpert MTB/RIF assay for bone and joint tuberculosis using tissue specimens. Int J Infect Dis [Internet]. 2021;105:224–9.
- Lin YS, Huang YC, Chang LY, Lin TY, Wong KS. Clinical characteristics of tuberculosis in children in the north of Taiwan. J MicrobiolImmunol Infect 2005; 38: 41-6.
- Musharrafich UM, Araj GF, Zaatari GS, Musharrafich RS. Tuberculosis of the Knee. Saudi Med J 2002; 23: 1130-5.
- Sambri A, Spinnato P, Tedeschi S, Zamparini E, Fiore M, Zucchini R, et al. Bone and joint infections: The role of imaging in tailoring diagnosis to improve patients' care. J Pers Med [Internet]. 2021 [cited 2022 Dec 8];11(12):1317
- Broderick C, Hopkins S, Mack DJF, Aston W, Pollock R, Skinner JA, Warren S. Delays in the diagnosis and treatment of bone and joint tuberculosis in the United Kingdom.Bone Joint J. 2018 Jan;100-B(1):119-124.
- Faroug R, Psyllakis P, Gulati A, Makvana S, Pareek M, MangwaniDiagnosis and treatment of tuberculosis of the foot and ankle-A literature review.J.Foot (Edinb). 2018 Dec;37:105-112.
- Saurabh, Sharma BP, Kumar A, Das S, Prasad S. Prospective study of immunomodulation in osteoarticular tuberculosis non responsive to anti tubercular therapy.J Clin Orthop Trauma. 2018 Mar;9(Suppl 1):S1-S9.
- Dhillon MS, Agashe V, Patil SDRole of Surgery in Management of Osteo-Articular Tuberculosis of the Foot and Ankle.Open Orthop J. 2017 Jul 31;11:633-650.
- Barik S, Choudhury AK, Singh V, Bali S. Extra-Spinal Osteoarticular Tuberculosis: A Retrospective Analysis of 103 Cases.Curr Health Sci J. 2019 Apr-Jun;45(2):142-147.
- Wang L, Yang Z, Wang C, Zhu X, Shi J, Niu N. Isolated tuberculosis of the lumbar facet joint: A case report: A case report. Medicine (Baltimore) [Internet]. 2021;100(51):e28268.
- Sotgiu G, Falzon D, Hollo V, Ködmön C, Lefebvre N, Dadu A, van der Werf M. Determinants of site of tuberculosis disease: An analysis of European surveillance data from 2003 to 2014.PLoS One. 2017 Nov 20;12(11)
- Panigrahi S, Jain M, Panda R, Karaniveed Puthiyapura L. Patient with tuberculous flexor tenosynovitis of the hand. BMJ Case Rep [Internet]. 2021;14(5):e243091.
- Held M, Bruins MF, Castelein S, Laubscher M, Dunn R, Hoppe S. A neglected infection in literature: Childhood musculoskeletal tuberculosis - A bibliometric analysis of the most influential papers. Int J Mycobacteriol. 2017 Jul-Sep;6(3):229-238.
- Procopie I, Popescu EL, Huplea V, Pleşea RM, Ghelase ŞM, Stoica GA, Mureşan RF, Onțică V, Pleşea IE, Anuşca DN. Osteoraticular Tuberculosis-Brief Review of Clinical Morphological and Therapeutic Profiles.Curr Health Sci J. 2017 Jul-Sep;43(3):171-190.
- Everden A, Mamo JP, Somasunderam D, McKee A, Brij SO, Enoch DA.Bone and joint mycobacterial infection: a retrospective review of cases presenting to a UK district hospital.J Med Microbiol. 2018 Dec;67(12):1698-1705.
- Chopra R, Bhatt R, Biswas SK, Bhalla R. Efficacy of alternate day Directly Observed Treatment Short-course (DOTS) in skeletal tuberculosis - A retrospective study.Indian J Tuberc. 2018 Jan;65(1):70-75.
- Global tuberculosis report 2019. Geneva: World Health Organization; 2019. ISBN 978-92-4-156571-4. License: CC BY-NC-SA 3.0 IGO https://www.who.int/tb/publications/global_report/en/

- 21. Ahuja K, Ifthekar S, Mittal S, Yadav G, Sarkar B, Kandwal P. Defining mechanical instability in tuberculosis of the spine: a systematic review. EFORT Open Rev [Internet]. 2021 [cited 2022 Dec 8];6(3):202–10.
- 22. Procopie I, Anușca DN, Onțică V, Mureșan R. Diagnosis and Treatment Particularities in Osteoarticuar Tuberculosis.Curr Health Sci J. 2017 Apr-Jun;43(2):153-158
- 23. Tahseen S, Khanzada FM, Baloch AQ, Abbas Q, Bhutto MM, Alizai AW, Zaman S, Qasim Z, Durrani MN, Farough MK, Ambreen A, Safdar N, Mustafa T. Extrapulmonary tuberculosis in Pakistan- A nation-wide multicenter retrospective study.PLoS One. 2020 Apr 28;15(4):e0232134.
- Hegazy WAH, Al Mamari R, Almazroui K, Al Habsi A, Kamona A, AlHarthi H, et al. Retrospective study of bone-TB in Oman: 2002-24. 2019. J Epidemiol Glob Health [Internet]. 2021;11(2):238-45.
- 25. Pollett S, Banner P, O'Sullivan MVN, Ralph AP. Epidemiology, diagnosis and management of extra-pulmonary tuberculosis in a lowprevalence country: A four-year retrospective study in an Australian Tertiary Infectious Diseases Unit. PLoS One. 2016; 11(3):1-15.
- 26. Ohene SA, Bakker M., Ojo J, Toonstra A, Awudi D, Klatser P. Extrapulmonary tuberculosis: A retrospective study of patients in Accra, Ghana. PLoS ONE. 2019;14(1), 1–13.
- Kim JH, Kim ES, Jun KI, Jung H, Bang JH, Choe PG, et al. Delayed diagnosis of extrapulmonary tuberculosis presenting as fever of 27. unknown origin in an intermediate-burden country. BMC Infectious Diseases.2018; 18(1), 1–8 10.1186/s12879-018-3349-5
- 28.
- National TB Control Programme Pakistan. National TB Programme; 2020 [cited 2022 Dec 3]. Available from: https://ntp.gov.pk/about-us/ Directly observed therapy (DOT) for the treatment of tuberculosis [Internet]. State.mn.us. [cited 2022 Dec 8]. Available from: https://usu.bacib.ettac.mp.ud/diseases/tb/lb/dk.tbtml 29. https://www.health.state.mn.us/diseases/tb/lph/dot.html