# Serum Calcium Levels in Skeletal Tuberculosis

Asadullah Makhdoom, M. Qasim Rahopoto, Pir Abdul Latif Qureshi and Khaleeque Ahmed Siddiqui

# ABSTRACT

OBJECTIVE: To evaluate the serum calcium levels in the patients suffering from tuberculosis of various bones and joints.

**DESIGN:** Observational case series.

PLACE AND DURATION OF THE STUDY: The Department of Orthopedics Unit-I Liaquat University of Medical and Health Sciences Jamshoro from December 2006 to November 2007.

PATIENTS AND METHODS: Forty-one patients, age 06-75 years, of either gender suffering from tuberculosis of various bones and joints were evaluated for the serum calcium levels. There were 14 males and 27 females with male-female ratio of 2:3. The involved bones and joints included knee (19.51%), dorsal spine (17%), elbow (14.63%), ankle (14.63%), wrist (12.19%), hip (9.75%), shoulder (7.31%) and ilium (4.87%).

RESULTS: Serum calcium level range was 1.7-mg/dl, minimum 5.50 mg/dl and maximum was 7.20 mg/dl. Mean±SD calcium level was 7.50±0.92 mg/dl, median 7.50 mg/dl and mode was 7.40 mg/dl.

CONCLUSION: The serum calcium levels in patients suffering from skeletal tuberculosis appear to be low.

KEY WORDS: Skeletal tuberculosis, Serum calcium levels, Bones, Joints.

#### INTRODUCTION

Tuberculosis, a disease caused by Mycobacterium tuberculosis is probably one of the oldest diseases known to mankind. It is commonly seen in the poor populations of the developing countries including Pakistan.<sup>1</sup> Poor nutrition, underprivileged and unhygienic living conditions and low immunity being some of the predisposing factors. However, the developed world is not completely free of its dangers. The United States has seen the resurgence of both the pulmonary and musculoskeletal tuberculosis<sup>2</sup> and patients in old age group and those with AIDS are most vulnerable to the dangers of this disease in other developed countries<sup>3</sup>.

Skeletal tuberculosis is frequently not diagnosed prior to the onset of permanent damage to the joints or spine. Not infrequently an aggressive approach including synovial biopsy or surgical exploration of the back is needed to confirm the diagnosis when there are no other clues. The ability to kill Mycobacterium tuberculosis by macrophages and monocytes is reduced in the absence or in the deficiency of extracellular and intra-extra cellular calcium. It is very interesting to note that persons with low serum calcium level, living in close contact with a tuberculous patient almost always contact the disease.<sup>1</sup> Calcium is one of the most important elements in the diet because it is a structural component of bones, teeth, and soft tissues and is essential in many of the body's metabolic processes. It accounts for 1 to 2 percent of adult body weight, 99 percent of which is stored in bones and teeth.<sup>4</sup> On the cellular level, calcium is used to requlate the permeability and electrical properties of biological membranes (such as cell walls), which in turn control muscle and nerve functions, glandular secretions, and blood vessel dilation and contraction. Calcium is also essential for proper blood clotting.<sup>3</sup> Calcium levels are carefully controlled in various compartments of the body. The three major regulators of blood calcium are parathyroid hormone (PTH), vitamin D, and calcitonin. PTH is normally released by the four parathyroid glands in the neck in response to low calcium levels in the bloodstream (hypocalcemia). PTH acts in three main ways: (1) It causes the gastrointestinal tract to increase calcium absorption from food, (2) it causes the bones to release some of their calcium stores, and (3) it causes the kidneys to excrete more phosphorous, which indirectly raises cal-

cium levels.<sup>3,5</sup> Low serum calcium in these patients is also associated with vitamin D deficiency. This is possibly a cause rather than the effect of the disease; deficiency being due to decreased dietary intake<sup>6</sup>.

If the disease is diagnosed and treated at an early stage, approximately 90% to 95% of patients would achieve healing with near normal function. The mainstay of treatment is multi-drug anti-tuberculous

#### Serum Calcium Levels in Skeletal Tuberculosis

chemotherapy for 12 to 18 months and active-assisted non weight-bearing exercises of the involved joint throughout the period of healing. Operative intervention such as synovectomy and debridement is required only when the patient is not responding after 4 to 5 months of chemotherapy.<sup>7</sup> The outcome of surgical intervention (excisional arthroplasty for the hip or the elbow) is not satisfactory and the healed status (arthrodesis of the ankle, wrist, or knee) has resulted in a painful ankylosis. Second-line and potential antitubercular drug and possible immunomodulations may control the situation.<sup>7</sup>

The aim of this study was to estimate the frequency of skeletal tuberculosis and to evaluate the serum calcium levels in such patients.

#### PATIENTS AND METHODS

This study was an observational case series carried out from December 2006 to November 2007 at the Department of Orthopedics Unit 1, Liaquat University Hospital Jamshoro-Pakistan. All patients were admitted from out patients and emergency departments of Liaquat University Hospital, Jamshoro & Hyderabad.

The diagnosis of skeletal tuberculosis was suspected on the clinical presentation of pain and swelling over the affected joints, particularly the large joints. Swollen joints were assessed radiologically and through joint microb aspiration. Aspirated fluid was sent for culture and sensitivity, detailed report (DR) and acid fast bacilli (AFB). Radiologically, there were increased joint spaces and washout appearance was visible in adjacent bones. Patients' joints were explored and curetted and biopsies were taken from soft tissues as well as from bone. All patients were kept on antituberculous drugs.

All such cases of skeletal tuberculosis diagnosed from their history, clinical examination, investigations and biopsy reports were included in this study to confirm our low calcium levels hypothesis. Their blood samples were taken for serum calcium levels.

The data were collected through a detailed proforma completed for each case and range, mean, median, mode, standard deviation, ratios and percentages were calculated through SPSS program version 10.0 with the help of biostatistician.

#### RESULTS

Total numbers of patients were 41. There were 14 males and 27 females. Male and female ratio was (2:3). Seventeen (41.5%) patients were from urban and 24 (58.5%) were from rural areas. Age ranged from 06 to 75 years, mean age was 30 years, median 25 years and mode was also 25 years. Occupation-wise 18 (43.1%) female patients were housewives, 14 (34.1%) were students, 05 (12.2%) were labors, 02

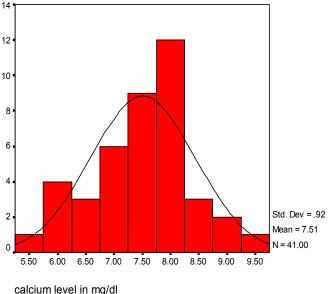
(4.9%) were teachers and 02 (4.9%) were nurses. Most common involved bones and joints were knee with femoral condyles and proximal tibia 08 (19.51%), dorsal spine 07 (17%), elbow with ulna 06 (14.63%), ankle with medial malleolus, lateral malleolus, calcaneum and talus 06 (14.63%), wrist with radius and scaphoid 05 (12.19%), hip with femoral head 04 (9.75%), shoulder with proximal portion of humerus 03 (7.31%) and ilium 02 (4.87%). Serum calcium level range was 1.7-mg/dl, minimum 5.50 mg/dl and maximum was 7.20 mg/dl. Mean±SD calcium level was 7.50±0.92 mg/dl, median 7.50 mg/dl and mode was 7.40 mg/dl.

 TABLE I:

 INVOLVEMENT OF BONE AND JOINTS (n=41)

Bone and Joint	Frequency	Percentage
Knee with femoral condyles and proximal tibia	08	19.51
Dorsal spine	07	17.1
Elbow with ulna	06	14.63
Ankle with medial, lat- eral malleolus, cal- caneum and talus	06	14.63
Wrist with radius and scaphoid	05	12.2
Hip with femoral head	04	9.75
Shoulder with proximal portion of humerus	03	7.31
llium	02	4.87

GRAPH I: CALCIUM LEVELS



#### DISCUSSION

Serum calcium levels are regulated by the action of parathyroid hormone (PTH). Major drivers of PTH hyper-secretion and parathyroid cell proliferation are the hypocalcemia and hyper-phosphatemia that develop in chronic kidney disease patients with secondary hyper-parathyroidism (SHPT) as a result of low calcitriol levels and decreased kidney function.<sup>8</sup>

Vitamin D is an immunoregulatory hormone. The epidemiological evidence suggests a link between vitamin D deficiency and tuberculosis (TB). Patients with active TB have lower serum vitamin D concentrations than controls from similar ethnic and social backgrounds and with comparable dietary intake and sun exposure, and do not show the expected seasonal variation. These observations indicate that some other factor(s) are contributing to vitamin D deficiency in patients with TB and suggest abnormal handling of this vitamin.<sup>9</sup>

Tuberculous disease of bones and joints is becoming uncommon; but it still occurs and may cause devastating sequelae. It is frequently not diagnosed prior to the onset of permanent damage to the joints or spine; the most important reason for this delay may be the fact that it is not generally considered in the differential diagnosis of mono arthritis or back pain until and unless some other evidence pointing to the possibility of tuberculosis is present. The national tuberculosis surveys conducted by the British Thoracic Association in 1965 and 1971 recorded only the main lesion and so provided little information<sup>-</sup>. Bone and joint infection may account for 10 to 35 percent of cases of extrapulmonary tuberculosis and, overall, for almost 2 percent of all cases of TB.<sup>10,11</sup>

Musculoskeletal tuberculosis involves the spine in approximately one-half of patients. The next most common syndrome is tuberculous arthritis followed in frequency by extra-spinal tuberculous osteomyelitis.<sup>12</sup>

Tuberculous arthritis tends to occur in the weightbearing joints, the hip and the knee, and is usually mono articular. However, multi-focal lesions are reported in 10 to 15 percent of cases in developing countries.<sup>13</sup>

The generally non-specific clinical and radiological patterns of skeletal tuberculosis make it similar to other bacterial, fungal, inflammatory and neoplastic diseases of the bones and joints. Physicians must not omit tuberculosis in the differential diagnosis of any osteo-articular inflammatory process so that specific treatment may be initiated as soon as possible.<sup>14</sup>

The present study was aimed to evaluate the serum calcium levels because we found that most of the patients attending our out patient department were from the poor socioeconomic groups. Most of these patients were young age group. The finding of low serum calcium levels in this age group has proved our hypothesis because, otherwise, in this age group usually calcium levels are normal.

Though the local literature is very scanty on this important finding yet our contemporaries abroad have worked on this subject and our results are matching with their results.<sup>15,16</sup>

#### COCLUSION

We conclude that serum calcium levels are low in skeletal tuberculosis, and it is recommended that patients suffering from bone and joint tuberculosis must be evaluated for serum calcium levels and other bone minerals like serum phosphorus and alkaline phosphatase, because therapy with calcium supplements will help to improve the prognosis of disease.

#### REFERENCES

- 1. David Le Vay. The History of Orthopedic. The Parthenon publishing group. 1990; 4-5.
- 2. Enarson DA, Fujii M, Nakielna EM, Grzybowski S. Bone and joint tuberculosis: a continuing problem. Can Med Assoc J 1979;120(2):139-5.
- 3. Shirai M, Sato A, Suda T, Shichi I, Yasuda K, Iwata M, et al. Calcium metabolism in tuberculosis, Kekkaku. 1990 Jun;65(6):415-20.
- Ali-Gombe A, Onadeko BO. Serum calcium levels in patients with active pulmonary tuberculosis. Afr J Med Med Sci. 1997 Mar-Jun;26(1-2):67-8.
- Kalita J, Misra UK, Ranjan P. Tuberculous meningitis with pulmonary miliary tuberculosis: a clinicoradiological study.Neurol India. 2004 Jun;52 (2):194-6.
- MV Palmer, DL Whipple, SC Olsen. Development of a model of natural infection with Mycobacterium bovis in white-tailed deer. J Wildl Dis 1999 35: 450-7.
- Tuli SM. General Principles of Osteoarticular Tuberculosis. Clin Orthopaed Rel Res 2002; 398:11-19.
- 8. Rodriguez M, Nemeth E, Martin D. The calciumsensing receptor: a key factor in the pathogenesis of secondary hyperparathyroidism. Am J Physiol Renal Physiol 2005;288: F253-F264.
- Sita-Lumsden A, Lapthorn G, Swaminathan R, Milburn HJ. Reactivation of tuberculosis and vitamin D deficiency: the contribution of diet and exposure to sunlight. Thorax. 2007;62(11):1003-7.
- Enarson DA, Fujii M, Nakielna EM, Grzybowski S. Bone and joint tuberculosis: a continuing problem. Can Med Ass J 1979;120(2):146-9
- 11. Davies PD, Brown RC, Woodhead JS. Serum concentrations of vitamin D metabolites in untreated tuberculosis. Thorax 1985; 40:187-90
- 12. Fanning A. Tuberculosis: Extra-pulmonary dis-

ease. CMAJ 1999; 160:157-9.

- Vohra R, Kang HS, Dogra S, Saggar RR, Sharma R. Tuberculous osteomyelitis. J Bone Joint Surg Br 1997; 79-B: 562.
- 14. Kumar K, Saxena MBL. Multifocal osteoarticular tuberculosis. Int Orthop 1988; 12:135.
- 15. Paradisi F, Corti G. Skeletal tuberculosis and other granulomatous infections. Best Practice Res Clin Rheumatol 1999;13(1):163-77.
- Baig MA. Low serum calcium associated with tuberculosis. 2nd OASAC, SICOT, ASAMI and 16th Orthocon Karachi Pakistan. 2002 5<sup>th</sup>-8<sup>th</sup> April.



#### AUTHOR AFFILIATION:

**Dr. Asadullah Makhdoom** (*Corresponding Author*) Assistant Professor, Department of Orthopaedics Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Sindh-Pakistan. Email: makhdoomasad@hotmail.com

#### Dr. M. Qasim Rahopoto

Assistant Professor, Department of Medicine LUMHS, Jamshoro, Sindh-Pakistan.

## Dr. Pir Abdul Latif Qureshi

Postgraduate Student Department of Orthopaedics LUMHS, Jamshoro, Sindh-Pakistan.

### Prof. Khaleeque Ahmed Siddiqui

Professor Department of Orthopaedics LUMHS, Jamshoro, Sindh-Pakistan.