Original Article

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A Prospective Study of 18F-FDG PET-CT Application in Therapeutic Monitoring of Osteoarticular Tuberculosis

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Abstract:

Objective: Confident diagnosis, identification of occult sites, assessing treatment response, and precisely ascertaining the duration and endpoint of treatment in skeletal tuberculosis is often challenging. magnetic resonance imaging (MRI) and computed tomography (CT) are less dependable owing to low sensitivity and the inability to discern current illness and old changes. 18F-FDG PET/CT utilizes variations in glycolysis rates between healthy and diseased tissue to quantitatively estimate the maximal standard uptake value (SUVmax) of 18F-FDG to assess disease activity.

Material and Methods: 32 patients who presented to the department with a clinicoradiological suspicion and pathologically proven diagnosis of skeletal tuberculosis were prospectively analyzed. All patients underwent a whole body 18F-FDG PET-CT scan before initiation of anti-tubercular therapy (ATT), and then treatment was started as per the Revised National Tuberculosis Control Program (RNTCP) guidelines. All patients were followed up with repeat PET-CT scans and relevant clinical investigations at 2, 6, and 12 months.

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Results: A gradual decrease in SUVmax values, as the treatment courses progressed indicated a decrease in disease activity with treatment. There was an overall mean decrease of 6.5 units in the SUVmax values when compared to the pre-treatment levels, which was statistically significant (p-value<0.001). At 2 months of anti-tubercular treatment, the mean SUVmax values decreased by 39%, and at 6 and 12 months of ATT, they were reduced by 60% and 81%, respectively. **Conclusion:** 18F-FDG PET-CT helps to determine the prevalence of occult multifocal activity elsewhere in the body. The gradual decrease in SUVmax values during the course of ATT is a useful tool to assess disease response and to precisely decide the endpoint of ATT.

Keywords: 18F-Fluoro-deoxy-glucose, latent tuberculosis, positron emission tomography, treatment response, tuberculosis

Introduction

Infection with Mycobacterium tuberculosis remains a major problem worldwide. The global incidence as estimated by the World Health Organization (WHO), is increasing by 0.4% per/annum[1]. In 2021, 82% of global tuberculosis (TB) deaths among human immunodeficiency virus (HIV)-negative people occurred in the WHO African and South-East Asia regions; India alone accounted for 36% of such deaths[2]. India ranks third among the 10 high-burden countries for TB, HIV-associated TB, and Multidrug-resistant TB in the 2015-20 list of WHO[2]. This is largely driven by the HIV-1 pandemic but other causes are poor sanitation, overcrowding, exanthematous fevers, repeated pregnancies, malnutrition, intravenous, drug abuse, alcoholism, cirrhosis, diabetes mellitus, advancing age and transplants may also precipitate activation of latent tuberculosis[3]. TB is a chronic infectious disease caused by the tubercle bacilli. Earlier studies have reported that, skeletal and extra-pulmonary TB accounts for 10 to 15% of all TB infections[4, 5]. Involvement of bones and joints is secondary to pulmonary lesions. TB of bone usually appears two years or longer after the initial pulmonary disease[6]. Hematogenous spread from foci in the lungs, viscera, or lymph nodes causes bone and joint TB. Most of those lesions heal with humoral or cellular immunity but in some cases, bone and joint involvement may manifest. POTT's spine also known as vertebral tuberculosis or tuberculosis of the spine is the commonest form of skeletal tuberculosis, accounting for 50% of all cases of skeletal TB[8]. Tuberculous spondylitis most commonly appears in the lumbar and thoracic spine, especially in the thoracolumbar region. The diagnosis of skeletal tuberculosis is challenging. Due to subtle symptoms and the slow course of the disease, clinical presentations are typically ambiguous and delayed. Preventing deformity and morbidity requires early diagnosis and commencement of treatment. Yet, fewer than 50% of skeletal TB patients have a certain radiographic diagnosis. In addition, the paucibacillary nature of the illness makes pathological confirmation difficult[9] and the management of skeletal TB continues as a subject of debate. Although it is reasonably acceptable that conventional antitubercular drugs shall be the first-line management of uncomplicated osteoarticular tuberculosis, the precise duration of treatment remains controversial. Defining a clear radiological endpoint to halt therapy continues to be challenging[10]. Clinical diagnosis remains the mainstay in diagnosing TB. As TB is a great imitator, practitioners must be acquainted with the disease's diverse characteristics and in case of ambiguity, it is crucial to provide histological evidence to support the diagnosis. Currently, the standard imaging modalities for the assessment of osteoarticular TB are magnetic resonance imaging (MRI) and, to a lesser degree, computed

tomography (CT). Although generally accurate for sampling in histopathological analysis and culture, CT-guided fine needle aspiration is incapable of distinguishing between active disease and old changes. Moreover, compared to 2- (fluorine 18) fluoro-2-deoxy-D-glucose (18F-FDG) Positron emission tomography (PET), it is less sensitive for the diagnosis of early skeletal disease[11,12]. Assessing the disease activity is paramount in deciding the plan of treatment for skeletal tuberculosis. Over X-ray, CT, and MRI, 18F-FDG-PET-CT is a critical modality to evaluate real-time disease activity as 18F-FDG gets collected in neutrophils and activated macrophages at the sites of inflammation[12, 13]. Additionally, preliminary research suggests that measuring quantitative 18F-FDG uptake by evaluating the Standardized Uptake Value Maximum (SUVmax) can be used to track the efficacy of treatment[11, 12]. As a result, compared to diagnostic CT alone, detailing the results of skeletal TB using 18F-FDG PET-CT is necessary. The use of 18F-FDG is essentially based on its detection of increased glucose metabolism, which in TB is mainly due to increased macrophage and neutrophil activity. As the FDG-PET-CT scan is an indicator of the activity of the disease, this could be used to determine the end point of treatment and for deciding duration[13]. This study was therefore designed to evaluate the FDG uptake change in tuberculosis, as a function of time from the start of anti-tubercular therapy (ATT).

Material and Methods

This was a prospective study conducted in the Department of Orthopaedics, St. Stephen's Hospital, Delhi from Nov 2016 to Nov 2018.

Inclusion criteria

1. All patients who presented to St. Stephen's hospital, with osteoarticular tuberculosis, and were willing for PET-CT scanning before, during (at 2 months & 6 months), and after the complete course of ATT.

2. Patients with spinal tuberculosis at one level with or without neurological deficit.

Exclusion criteria

1. Patients who were not willing to undergo PET-CT imaging.

2. Patients who discontinued ATT during the course of the study.

3. Women who were pregnant (because of the hazards of CT radiation and 18-FDG radiation).

4. Patients with uncontrolled diabetes (as Fluorodeoxyglucose is used as a dye).

Based on the inclusion and exclusion criteria, n=32 consecutive patients attending the Department of Orthopaedics at St. Stephen's Hospital, New Delhi, India, were enrolled in the trial. All enrolled patients presented with a clinico-radiological suspicion were confirmed histopathologically as skeletal TB. Basic blood tests were performed on all patients, including complete blood counts and erythrocyte sedimentation rates (ESR). All patients underwent a whole body 18F-FDG PET-CT scan before initiation of ATT, then treatment was started as per the RNTCP guidelines and was followed up with repeat PET-CT scans and relevant clinical investigations at 2 months, 6 months, and 12 months. A specialized PET-CT scanner (Discovery STE with a 16-slice CT system from GE) was employed for all scans. The PET scan was performed as per the standard protocol, with 18-F-FDG administered at a dosage of 0.15 mCi/kg body weight and after waiting for 60 min[14]. Intravenous contrast material was administered for contrast enhancement as part of the PET-CT scan. A maximum standardized uptake value (SUVmax) was determined by mapping a sphere-shaped ROI (region of interest) with a 1.5 cm diameter across the lesion's most metabolically active region and then adjusting for the patient's body weight[14]. Wherever feasible, both the affected soft tissue and bone were included. SUV max values were derived via

The SUV formula:

$$SUV = \frac{\text{radiotracer activity} \times \text{weight of the patient}}{\text{Injected dose}}$$

Patients were maintained nil-oral for a minimum of 4 hours before receiving the 18F-FDG injection for the whole body 18F-FDG PET-CT. A portable capillary glucometer was used to monitor blood glucose levels. The dosage of 18F-FDG given to patients was determined by their body weight. All of the patient 's demographic information, clinical and treatment histories, general and systemic examination results, laboratory parameters, and pertinent radiological imaging findings were documented in a specific format and tabulated. The active tuberculous sites were identified in the acquired 18F-FDG PET-CT images. For quantitative analysis, SUVmax was used. Thus, in this study, we evaluated the activity of TB and the effectiveness of ATT using a PET-CT by observing the presence of FDG uptake. Absence/decrease of FDG uptake up to the desired level (SUVmax<2) in PET was used along with clinical signs to decide when to stop ATT correlating with other relevant parameters.

Availability of data and materials

All data generated or analyzed during this study are included in this published article (and its supplementary information files) and any further requirements will be provided on reasonable request to the corresponding author.

Statistical analysis

All the available data were recorded in an MS Excel spreadsheet and analyzed by Statistical Package for the Social Sciences (SPSS) version 19 in Windows format. The continuous variables were represented as means, standard deviations, and percentages. The categorical variables were calculated with Fischer's exact test p-values of <0.05 and were considered significant.

Results

Out of the 32 cases studied in the trial 15 (47%) were males and n=17 (53%) were females. The most common age group of the study was 21 – 40 years with n=15 (47%) of the total cases as shown in Figure 1. The mean age of the cohort was 40.65±15.66 years. Based on the modified Kuppuswamy scale to assess socio-economic status in urban and rural areas[15], in this study, 38% of the cases were in the lower class, 59% were classified as middle class, and 3% were classified as upper-class. The number of spinal cases was 22 (68.75%) and of extra-spinal cases was 10 (31.25%). The extraspinal cases included hip 2 (6.25%), knee 2 (6.25%), elbow 2 (6.25%), wrist n=2 (6.25%), ankle n=1(3.12%), and ilium n=1 (3.12%), as shown in Figure 2. Hence the majority of cases were of Potts spine. The majority of cases of spinal TB involved the dorso-lumbar region (55%). The total number of vertebrae involved cases was 54, out of which 4 were cervical; 26 were dorsal; 21 were lumbar; and 3 were sacral. Among the dorsal cases, the most common locations were D11 and D12 (7 each), and the most common lumbar site was L1[6]. All the patients (n=32,100%) had the clinical symptom of pain, n=10 (31%) patients had localized swelling when they presented, and n=12 (40%) patients gave a positive history of one or more constitutional symptoms like loss of weight, fever with an evening rise, and loss of appetite. The mean duration of ATT received by the spinal Tuberculosis cases was 9 months, and for the extraspinal tuberculosis cases was 7 months. In the ATT, which consisted of isoniazid+rifampicin+pyrazinamide+ethambutol group with 30 (93.75%) of the cases, the mean duration of treatment was 8 months. Two (6.25%) cases were treated with a second line of ATT because of MDR-TB, bringing their mean duration of treatment to 11 months. ESR was done in all patients. The mean ESR of patients before the start of the ATT was 55±14.9 and at 12 months post-ATT treatment was 12±4.3. There was a gradual decrease in ESR values as the treatment course progressed which indicated a decrease in disease activity

with treatment. The mean decrease in the ESR values of 43 units, which was statistically significant (P-value=<0.001). Two months of anti-tubercular treatment reduced the ESR values by 32%, and 6 and 12 months of ATT reduced it by 58% and 78%, respectively (Table 1). Fluorodeoxyglucose (FDG) PET was done at 4 time points as described in Figures 3, 4. The mean standardized uptake value maximum (SUVmax) of the patients before the start of ATT was 8±3.3 and at 12 months post-ATT, (i.e., post-treatment) was 1.5±1.9. There was a gradual decrease in SUVmax values as the treatment course progressed as shown in Figures 3, 4, which indicated a decrease in disease activity with treatment. There was an overall mean decrease of 6.5 units in the SUVmax values compared to the pre-treatment levels which was statistically significant (p-value=<0.001). Two months of ATT reduced the SUVmax values by 39% and 6 and 12 months of ATT reduced it by 60% and 81%, respectively (Table 2). The treatment course of 32 osteoarticular TB patients was categorized into 4 stages viz. pre-Rx, mid-treatment (2 months), mid-treatment (6 months), and post-treatment. These stages were compared with respect to ESR and SUVmax values by categorizing them into 4 groups – viz categories 1,2,3 and 4 as shown in Table 3. The comparisons between the different categories of ATT courses concerning both ESR and SUVmax values showed a gradual rise in the percentage of decreasing means from categories 1 to 4. Except for category 1 (p-value=0.147), the remaining categories viz. categories 2, 3, and 4 showed statistically significant differences (p-values=0.02, 0.014, 0.042, respectively). As is also evident from Table 3, the changes in ESR and SUVmax values were in parallel and correlated with each other and also with a decrease in disease activity. Among the 32 patients with skeletal TB, the mean pretreatment weight was 59 kg and the mean post-treatment weight was 61 kg which was a significant difference (p-value=<0.001). Table 4 shows the presence of FDG activity on the PET scans in 22 patients with spinal TB at various sites, other than the primary diagnosed site of Pott's spine, which were confirmed as tuberculosis by the progressive decrease in SUVmax in the successive PET-CTs following the ATT. It was found that of the different spinal TB regions, the dorsolumbar region showed activity at the maximum number of sites. Activity at the hilar LN, peripancreatic LN, and sacrum was found in both cervical as well as dorso-lumbar TB patients. However, all patients were asymptomatic at sites of activity other than the primary diagnosed site.

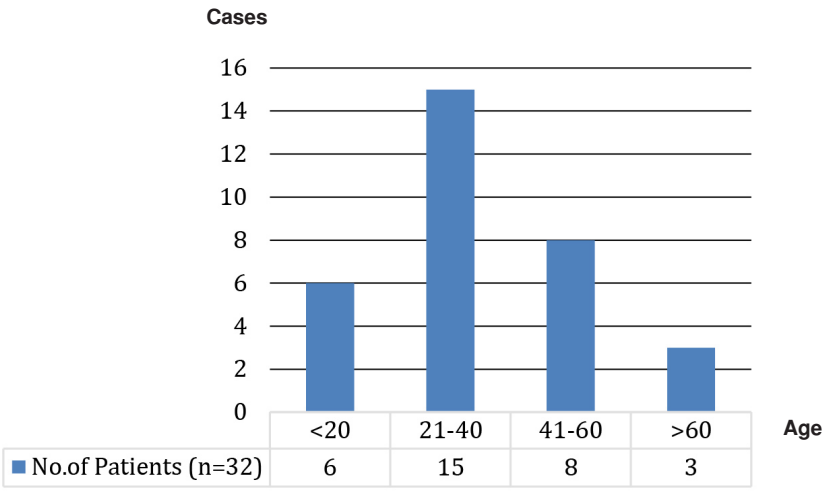

Figure 1 Age distribution of No. of cases in the study

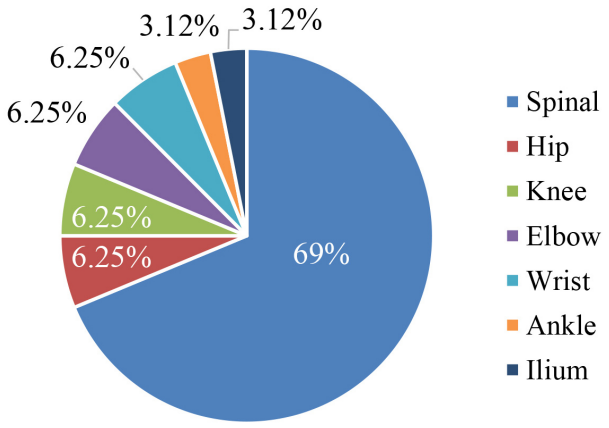

Figure 2 Anatomical distribution of the lesions

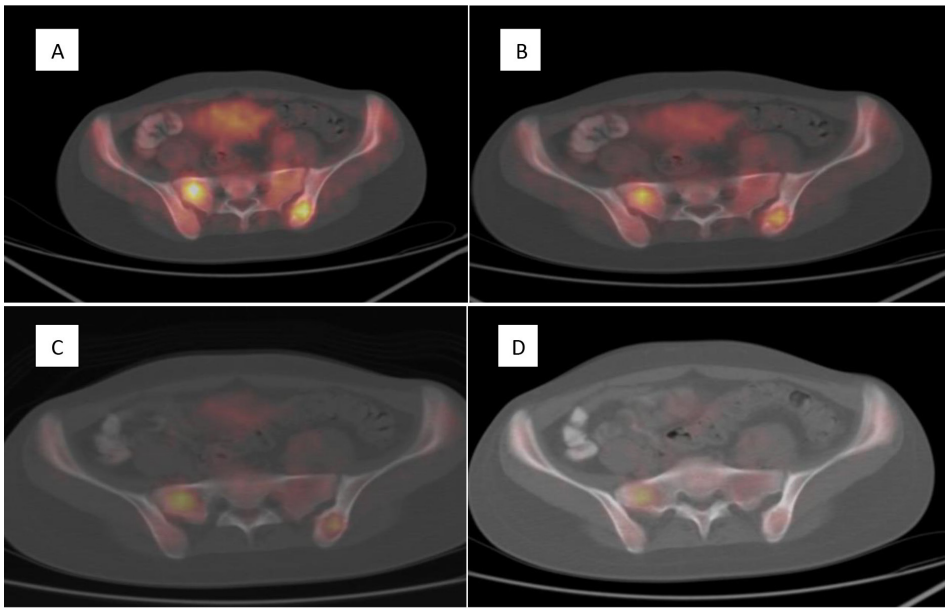

Figure 3 18F-FDG-PET-CT in a 20-year-old woman who presented with pain in the right groin and loin for 3 months and was diagnosed with tuberculosis of the left ilium and right sacrum showing (A) increased uptake before the start of ATT [SUVmax 10.4] and (B) decreased uptake at 2 months [SUVmax 2.8], (C) 6 months [SUVmax1.6], and (D) after completion of ATT at 12 months with SUVmax 0.6

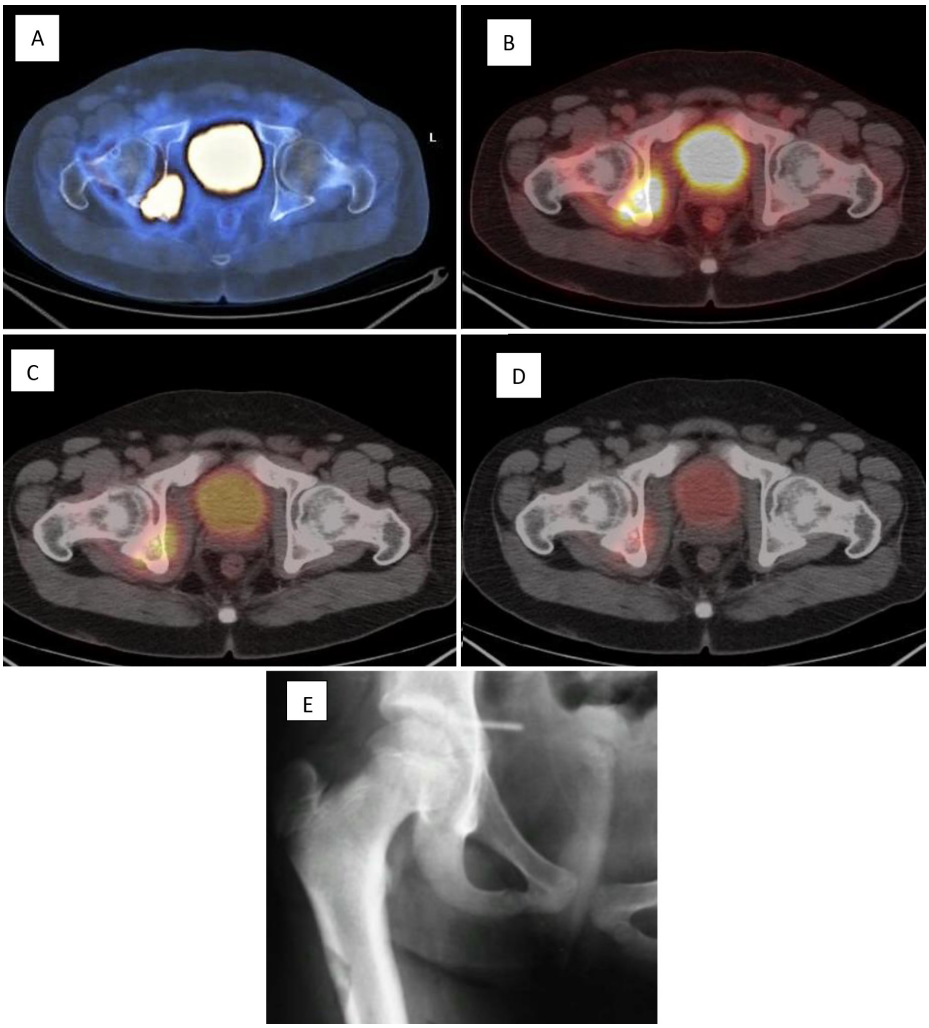

Figure 4 18F-FDG-PET-CT images of a 30yrs old male who presented with pain in the right hip for 2 months without any fixed deformity and was diagnosed as tuberculosis of right acetabulum showing (A) increased uptake before the start of ATT [SUVmax 5.8] and gradual decrease in uptake (B) at 2 months [SUVmax 4.2], (C) 6 months [SUVmax 2.1] and (D) after completion of ATT at 12 months with SUVmax of 0.9. Image (E) is the radiograph of the patient before the start of ATT showing sclerosis in the acetabulum

Table 1 Mean changes in ESR during the ATT course

	ESR	ESR (Mean±S.D.)	% Decrease in ESR during treatment
	Pre-Treatment	55±14.9	-
	Mid-Treatment (2 months)	36±10.3	32%
	Mid-Treatment (6 months)	23±5.9	58%
	Post-treatment (12 months)	12±4.3	77%

ESR=erythrocyte sedimentation rates, ATT=anti-tubercular therapy, S.D= standard deviation

Table 2 Mean changes in SUVmax during the ATT course

	SUVmax	SUVmax (Mean±S.D.)	% Decrease in SUVmax during treatment
	Pre-Treatment	8±3.3	-
	Mid-Treatment (2 months)	5±2.8	39%
	Mid-Treatment (6 months)	3±2.3	60%
	Post-treatment (12 months)	1.5±1.9	85%

SUVmax=maximal standard uptake value, ATT=anti-tubercular therapy, S.D.=standard deviation

Table 3 Correlation between ESR and SUVmax values

		No of Patients	% Mean change	S.D.	Mean difference	p-value
Category 1	ESR Pretreatment -Mid-treatment (2 months)	32	32	17.1	-6.6	0.147
	SUVmax Pretreatment - Mid-treatment (2 months)	32	39	17.2		
Category 2	ESR Mid-treatment (2 months – 6 months)	32	35	9.6	-9.4	0.027
	SUVmax Mid-treatment (2 month-6 months)	32	44	20.7		
Category 3	ESR Mid-treatment (6 month-posttreatment)	31	49.5	10	-14.7	0.014
	SUVmax Mid treatment (6 month-Post treatment)	31	64	26.7		
Category 4	ESR Pre Rx – Post Rx	32	77	9.5	-7.7	0.042
	SUVmax (Pretreatment -Post Rx)	32	85	16.3		

ESR=erythrocyte sedimentation rate, ATT=anti-tubercular therapy, S.D.=standard deviation

Table 4 Prevalence of occult multifocal lesions in the 22 spinal tuberculosis patients

Occult multifocal lesions site	Site of primary spinal TB diagnosis			
	Cervical spine	Dorsal spine	Dorsolumbar spine	Lumbar spine
Bones				
Odontoid process	Yes	No	No	No
Sternum	Yes	No	No	No
L2 vertebrae	Yes	No	No	No
S-I joint	No	No	Yes	No
Ilium	Yes	No	No	No
Sacrum	Yes	No	Yes	No
Lymph Nodes				
Cervical and mediastinal LN	No	No	Yes	No
Peripancreatic LN	Yes	No	Yes	No
Mesenteric LN	No	No	Yes	No
Inguinal LN	No	No	Yes	No
Hilar LN	No	Yes	Yes	No
Soft Tissue				
Upper or lower lung lobes	No	No	Yes	Yes
Iliopsoas muscle	No	No	Yes	No

**Lumbosacral region showed no multifocal lesions elsewhere*
TB=tuberculosis

Discussion

Skeletal TB refers to TB involving bones and/or joints. Based on statistics, osteoarticular TB accounts for 1- 4.3% of all TB cases and 10-15% of extrapulmonary TB cases[16-20]. In our present study, it was found that the maximum number of osteoarticular TB patients were in the age group of 21-40 years and the highest percentage was of females (53%). This higher incidence of osteoarticular TB in females can be attributed to the relatively poorer health and nutritional status of Indian women and their greater stress levels. Chopra et al[21]. showed a similar finding of a higher percentage of skeletal tuberculosis in females, although in their study the most common age group affected was the 11-30 yrs group. However, both their and our study findings were contrary to a study conducted by Sinan et al.[22], which found a higher percentage of osteoarticular TB in males. In Western countries, patients with osteoarticular tuberculosis are much older. This is possible because there is a demographical difference between our country and the Western world. Moreover, TB is endemic in our country, and therefore younger age groups are commonly exposed, A study by Watts et al[23]. found that the age distribution of tuberculosis was associated with the endemicity of the disease. In our study, the spine was the most commonly involved site (69%) as compared to extraspinal sites (31%). Chopra et al[21]. also found spine involvement in 63% of the cases, followed by hip and knee involvement at 13%. Among the 22 spinal tuberculosis patients in our study, the most common region involved was the dorsolumbar spine, followed by the dorsal vertebrae (18%), and 9% in the lumbar, lumbosacral and cervical regions. In the dorsolumbar region, the D11 and D12 vertebrae were most commonly involved followed by the L2 vertebrae, in agreement with SM Tuli's study which found that spinal tuberculosis was most commonly found in the lower thoracic and upper lumbar regions[6]. In our study,

all patients presented with pain. Which is in agreement with Watts et al[23]. and Sinan et al[22]. found pain to be the most common presenting symptom. 43% of the patients had a positive history of constitutional symptoms, and another symptom found was localized swelling (31%) or abscess on presentation; therefore, healing of the abscess can be a useful tool to assess recovery of tuberculous infection.

The erythrocyte sedimentation rate is considered to be a nonspecific marker of inflammation in the body. Vaughan et al[24]. reported an elevated ESR at the time of presentation of tuberculosis. However, Watts et al[22]. and Rasool et al[25]. also found that ESR may remain low and non-specific in TB. The mean ESR of the patients in our study at the time of presentation was 55±14.9 S.D. and at 12 months post-ATT was 12±4.3 S.D. There was a gradual decrease in ESR values as the treatment course progressed (Table 1). Hence ESR can be used as a reliable indicator in monitoring disease activity. Martins et al[26], in their study on 51 tuberculosis patients found that, in the ESR analysis, this marker was above the reference value before the start of anti-TB treatment, and then gradually decreased over the course of treatment, with (p-value<0.0001) showing it to be a good marker in diagnosis and monitoring of cases. Spinal tuberculosis is indolent and slow-growing and it is very difficult to recognize radiologically in the early stages[6]. The changes of healing appear late in X-rays (in the form of sclerosis) and thus if radiographic findings are taken as a marker for cure, ATT will be administered for a longer time and the chances of affect of adverse effects are more. The lesions are better seen by MRI than by radiography. MRI is particularly beneficial for diagnosing tubercular infection[27]. MRI scans can detect early joint effusion and soft tissue swelling. The overall sensitivity and specificity for diagnosis are 100% and 88.2%, respectively[26]. An MRI scan can detect a tubercular lesion before it can be seen on a plain radiograph[26]. Some surgeons have utilized MRI with contrast to assess TB disease activity. Nevertheless, MRI cannot detect bacteriological sterilization, it can only show the area's vascularity or fluid content. The restoration of normal signal patterns may take a long time. A paradoxical worsening of lesions following effective TB therapy may also occur. Paradoxical response or immunological reconstitution inflammatory syndrome (IRIS) are terms used to describe this condition[28]. Being merely an immunological reaction to the tubercular protein, it might cause the surgeon to assume that the patient is not responding to therapy. Thus, MRI is non-specific in monitoring disease activity. Current results on the application of PET/CT to measure disease activity are encouraging. With the use of PET/CT technology, it is possible to analyze in great detail how specific tuberculous lesions evolve over time and to keep track of how they respond to therapy[29]. Based on the level of inflammatory activity, studies have found that active tuberculous lesions frequently have a significant degree of FDG absorption[7,12,13,14,30]. In the current study, standard uptake values were used to quantify the variability of FDG uptake in TB during ATT therapy. The mean SUVmax of the 32 patients before the start of ATT was 8±3.3 S.D. (range 2.8-13.8) and at 12 months post-ATT was 1.5±1.9 S.D. (range 0 – 7.2). There was a gradual decrease in SUVmax values (Figures 3, 4) as the treatment course progressed, which indicated a decrease in disease activity with treatment (Table 2). There was a mean decrease of 6.5 units in the SUVmax values which was statistically significant. The mean changes in SUVmax at baseline, 2 months, 6 months, and 12 months were shown to be extremely significant (Figures 3, 4). This progressive decrease in the activity on PET scans can help to decide when ATT can be stopped, making FDG PET-CT a useful tool to decide the end point of chemotherapy. The mean SUVmax values decreased by 38.9% from baseline to 2 months of ATT, by 44.6% from 2 months to 6 months of ATT, and by 64 % from 6 months to 12 months of ATT (Figures 3, 4). The overall decrease in mean SUVmax from pre to post-treatment was 85 %. Dureja et al's study on 33 patients with spinal TB resulted in the identical finding that SUVmax may be used as a

valid marker for serial assessment of metabolic activity in spinal TB, which might open up the prospect of employing FDG as an imaging biomarker for noninvasive response assessment in skeletal TB[14]. In our study, the Revised National TB Control Program (RNTCP) guidelines were followed 4 drugs HRZE were used in the intensive phase, and 3 drugs (HRE) in the continuation phase[31]. Among the spinal TB patients who received the HRZE regime (20 patients) most (11 patients) received ATT for 9 months, while among the extra-spinal TB patients who received the HRZE regime (10 patients) most (6 patients) received ATT for 6 months. The American Thoracic Society recommends 6 months of chemotherapy for spinal tuberculosis in adults and 12 months in children[32]. The British Thoracic Society recommends 6 months of treatment, irrespective of age[33]. However, many experts still prefer a duration of 12–24 months or until there is radiological or pathological evidence of regression of disease[34]. In this study, the response to ATT was evaluated using activity on FDG-PET scans along with the resolution of clinical symptoms, and the significant improvement in these metrics guided us in deciding the duration of chemotherapy. Though it might not seem prudent to perform repeated PET-CTs, certainly it has its merits over the needless continuing of ATT for several months after healing, especially in fragile patients. Besides, it provides insight to prevent the deleterious effects of ATT in high-risk patients.

Limitations of the study

Being a single-center study, the increased sensitivity of FDG PET-CT to identify lesions may be the explanation for our study's higher rate of occult lesion detection. FDG PET-CT scan cannot reliably differentiate between malignant lesions from active tuberculosis. Also, our study reported follow-up for a period of 6 months only, whereas a prolonged follow-up period of 5-10 years is essential to ascertain the actual rate of relapse.

Conclusion

18F-FDG PET-CT can help us to determine the prevalence of occult multifocal activity apart from the primary diagnosed site of tuberculosis. A gradual decrease in its SUVmax values (in scanning at 4 different time points) during the course of ATT highlighted this modality as a useful tool to assess the course of disease response and to precisely decide the duration and end point of ATT as well. There were no cases of relapse during the course and for up to 6 months post-completion of ATT. However, this system is expensive and linked to radiation risks, therefore it might not always be practical.

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