

# Atypical Imaging Features of Tuberculosis on Computed Tomography That Presented As a Diagnostic Dilemma and To Suggest Possible Factors Responsible For the Unusual Presentation

ANIQUA SALEEM,<sup>1</sup> HUZAIFA SALEEM,<sup>2</sup> SHARJEEL SARFRAZ AHMED SHEIKH,<sup>3</sup> SABA AKRAM,<sup>4</sup> SADIA ALI,<sup>4</sup> SABA MAQSOOD<sup>4</sup>

<sup>1</sup>Radiology Department, District Head Quarter (DHQ) Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan.

<sup>2</sup>Pathology Department, Holy Family Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan.

<sup>3</sup>Surgery Department, District Head Quarter (DHQ) Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan.

<sup>4</sup>Radiology Department, Avicenna Medical and Dental College and Hospital, Lahore, Pakistan.

Correspondence to Dr Aniqua Saleem; Email: aneeqa\_068@hotmail.com, Cell: 0300-2731833

## ABSTRACT

**Aim:** To identify the atypical imaging features of tuberculosis on CT that presented as a diagnostic dilemma and to suggest possible factors responsible for the unusual presentation.

**Methodology:** Descriptive study conducted through collaboration of the Radiology Department and General Medicine department for a period of 12 months from October 2017 to October 2018. Patients with clinical suspicion of tuberculosis (TB), or patients who had TB as a valid differential, showing typical and atypical radiological features on CT were included in the study and were further followed up in medicine department. Patients with subsequent diagnosis of TB via clinical, radiological and pathological assessment were studied.

**Results:** A total of 300 patients were included in the study. 54 of 300 patients (18 %) showed atypical radiological features which presented with diagnostic difficulty. 33 of 54 (61%) patients with atypical imaging features were within the age group of 21 to 50 years. Socioeconomically patients either belonged to low class 261 of 300 (87.2%) or lower middle class 39 of 300 (13%). There were 45 cases of disseminated TB and 26 of these 45 cases (57.7%) were females. All females with disseminated disease were less than 40 years. 37 of 300 TB patients (12.3%) had concurrent diabetes. 3 patients simultaneously were diagnosed to have HIV co infection and 2 patients had pneumocystis co-infection with TB.

**Conclusions:** TB with atypical imaging is not uncommon and radiologists should be aware of these imaging features so they may not be misdiagnosed.

**Keywords:** Tuberculosis, Radiologist, Computed Tomography, Pneumocystis, HIV Coinfection, Diabetes, Socioeconomically.

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## INTRODUCTION

TB is one of the top ten leading causes of death worldwide and it is the top cause of death due to an infectious disease<sup>1</sup>. In 2017, 6.4 million new cases of TB were reported worldwide out of which 80% were reported from the top 10 countries with highest TB burden<sup>1</sup>. The annual incidence rate of TB cases in 2017 was estimated to be approximately 150-400/100000 persons in 30 high TB burden countries<sup>1</sup>. Pakistan is ranked 5th amongst 22 extremely TB burdened countries with approximately 413,450 TB cases per year<sup>2</sup>. Pakistan is also included in World health organization (WHO) list of 30 high TB burden countries accounting for 87% of TB cases all over the world<sup>1</sup>. In 1993 WHO declared TB as a global emergency and directly observed treatment strategy (DOTS) was implemented, resulting in reduced TB incidence and its associated morbidity and mortality. In Asia and Sub-Sahara Africa effective DOTS strategy could not be implemented due to multiple factors like lack of awareness, poverty, limited resources and funds, religious myths. Variable non classic presentations of TB also emerged which presented not only therapeutic but diagnostic challenges. Some of these challenges include TB / HIV/ pneumocystis co-infection, superimposed TB on the background of interstitial lung disease, diabetes concurrent with tuberculosis and extra pulmonary TB (EPTB) in atypical and rare locations involving body parts such as pancreas, sternum, ribs, thymus, thyroid or breast. These rarer atypical clinical

presentations created additional hurdles in the process of tuberculosis control. The rationale of this study is to identify and recognize atypical imaging features of tuberculosis encountered by radiologists, which will facilitate in timely diagnosis reducing the morbidity and mortality associated with the disease.

## METHODOLOGY

Descriptive prospective cross sectional type of study was conducted in the Radiology Department in collaboration with the medicine department at Rawalpindi Medical University and Allied Hospitals. The study was conducted for 12 months, from October 2017 to October 2018. All patients with clinical suspicion of TB were referred to the radiology department for computed tomography scan by Toshiba Aquilion 16 slice and were further followed up in hospital. Only those patients who were identified to have TB by positive AFB smear microscopy, culture and cytology or positive TB geneXpert (MTB/RIF) as indicated in EPTB guidelines<sup>3</sup>, were included in the study and the frequency of patients with atypical imaging features of TB was calculated. All the patients also underwent serological testing for HIV. Patients were also assessed for presence of co-morbid diabetes mellitus and interstitial lung disease, and in terms of demographic characters like age, gender and socioeconomic status.

All patients with suspected TB referred for CT scan to radiology department, showing typical or atypical

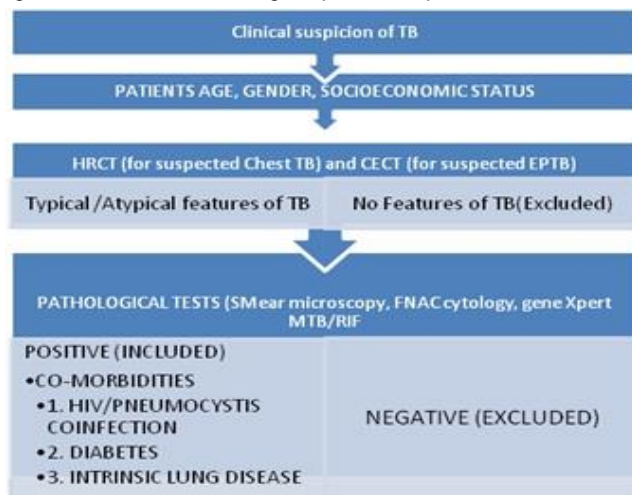
radiological features of active tuberculosis along with pathological evidence of TB were included in the study. Patients found negative for tuberculosis pathologically, irrespective of clinical or radiological features were excluded from the study. (Figure1.) Flow chart indicates the process of patient selection.

**Sample size calculation::** Sample size was calculated by using Raosoft sample size calculator with confidence interval of 95%, taking margin of error as 5.62%, using population size as 20000 and response distribution as 50%. Sample size is 300 <sup>4</sup>.

**Definitions and classifications:** Typical pulmonary TB was identified as parenchymal consolidation in the lower and middle lobes with lymphadenopathy or nodules with or without cavitations, usually involving upper zones 5, 6. Typical Musculoskeletal TB involves anterior segments of spine localized joint and adjacent bone <sup>6</sup>. Typical abdominal TB involves cecum and distal ileum, particularly medial wall of cecum with abdominal lymph nodes with or without ascites and smooth peritoneal thickening <sup>6</sup>. Atypical imaging features of TB were identified as pattern of involvement different from typical pattern as mentioned above or involvement of sites other than lungs, cecum or bone. Pathological diagnosis of pulmonary and extra-pulmonary TB was done by conventional smear microscopy, culture and cytology in FNAC specimen, and pathological test Xpert MTB/RIF were used to confirm diagnosis of pulmonary or extra pulmonary TB, as per EPTB guidelines <sup>3</sup>.

Patients were classified into four socioeconomic classes taking account of per capita income which is based on the criteria provided by the World Bank. It was simplified by converting U.S Dollar into Pakistani Rupee (PKR) and rounding it off to nearest thousand (U.S Dollar in 2017 was 103.938 PKR). Patients were classified into high (> PKR 103,000), upper middle (PKR 35,001 to 103,000), lower middle (9001 to 35,000 PKR) and low class (< PKR 9000). Patient educational status was also considered <sup>7</sup>.

Figure 1. Flow chart indicating the process of patient selection.



**Statistical analysis:** Consecutive non probability convenience sampling was used for data analysis. All variables included in Performa were entered in computer

program SPSS (version 20.0). Descriptive statistics for numerical data was calculated as mean with SD, while categorical data was analyzed as frequencies and percentages. Chi square test was applied to calculate the p value, and to know the significant difference, if any, in atypical presentation of radiological finding in different age groups and the two genders.

**RESULTS**

A total of 300 patients of tuberculosis were included in the study. The mean age of patients was 40.9 years with +/- standard deviation variation of 17.27. Out of 300 patients, 155(51.67%) were male and 145(48.33%) were female, 72 (24%) were less than 25 years of age and 133 (44.3%) were above 25 years of age at the time of diagnosis.

Atypical radiological features were seen in 54 of 300 patients (18%). Out of these 54 patients, 33 (61%) were within the age group of 26 to 50 years. Chi square test revealed that there was significant difference (P=0.002) between occurrences of typical and atypical TB imaging features in different age groups. Atypical imaging features were more frequently seen in the age group of 26 to 50 years. Difference of occurrence of typical and atypical imaging features between two genders was insignificant (P=0.337). Table 1 summarizes the demographic characteristics of the study.

Table 1: Demographic Characteristics of Tuberculosis

No.	Characteristics	n	%age	Mean/Median (SD)
I	Age (Years)	300		40.9 ± 17.277
	Age Group (Years)			
II	< 25	72	24	
	26-50	133	44.3	
	51-75	78	26	
	75>	17	5.7	
III	Gender			
	Male	155	51.7	
IV	Female	145	48.3	
	Socio Economic Status			
	Low	261	87	
	Lower Middle	39	13	

There were 45 cases of disseminated TB, out of which 28 (75.6%) patients were less than 50 years of age, and 26 (57.7%) were females, all young aged less than 40 years. There were 37 of 300(12.3%) cases of concurrent diabetes with TB. All diabetic patients were above the age of 25 years. We observed 32 of 37 (86%) diabetic patients belonged to low class having poor nutritional status, unhealthy life styles and were illiterate. Furthermore, 16 of 37 (43.2%) diabetic tuberculous patients showed atypical imaging findings and 20 of 37 (54%) diabetic tuberculous patients had disseminated disease.

Amongst 300 patients, 261 (87.2%) belonged to low class and 39 (12.8%) patients belonged to lower middle class.

Table 2 summarizes the comparison between typical and atypical imaging feature of tuberculosis and Table 3

indicates frequencies of presence of co-morbidities along with tuberculosis in different age groups and genders.

Table 2: Comparison between typical and atypical imaging feature of tuberculosis

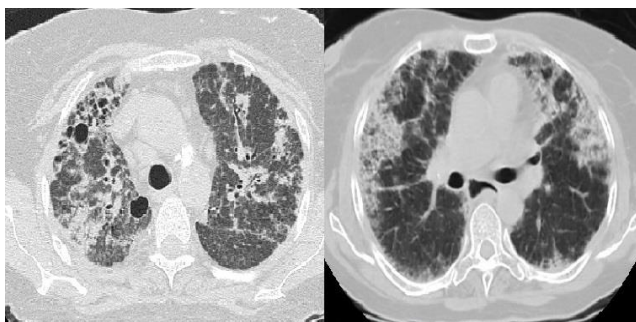
No.	Characteristics	Typical TB imaging features (n)	%age	Atypical TB imaging features (n)	%age
I	All patients	246	82	54	18
II	Age Group (Years)				
	< 25	69	95.8	3	4.2
	26-50	100	75.2	33	24.8
	51-75	65	83.3	13	16.7
	75>	12	70.6	5	29.4
III	Gender				
	Male	129	83.2	26	16.8
IV	Female	117	80.7	28	19.3
	Diabetes	21	56.8	16	43.2

Table 3: Frequency of presence of co-morbidities along with tuberculosis in different age groups and genders

No.	Characteristics	Number of patients with Tuberculosis and studied Co-morbidities		
		Interstitial Lung Disease	Co Infection with HIV/Pneumocystis	Concurrent Diabetes
I	Age Group (Years)			
	1 to 25	1	0	0
	26-50	4	1	13
	51-75	4	2	15
	76 & above	3	2	9
III	Sex			
	Male	5	4	22
	Female	7	1	15
	Total	12	5	37

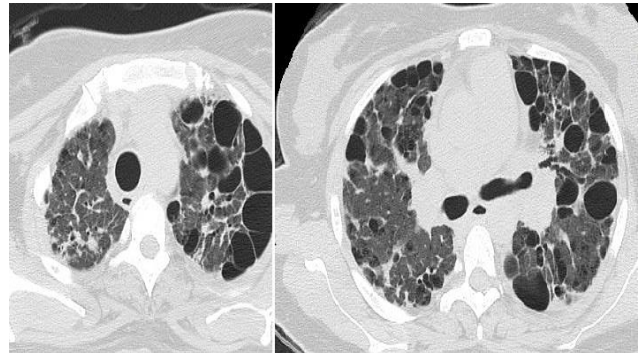
The atypical imaging features observed in 54 patients included 29 patients with abnormal findings in chest, 11 of them had coexisting nonspecific interstitial pneumonitis (NSIP) and 1 had coexisting usual interstitial pneumonitis (UIP). Cellular type of NSIP has ground glass opacities as a predominating imaging feature along with centrilobular nodules, consolidations and sub pleural reticulations and concurrent TB may be overlooked (figure 2).

Figure 2: Consolidations and nodules with sub pleural reticulations and honey combing.



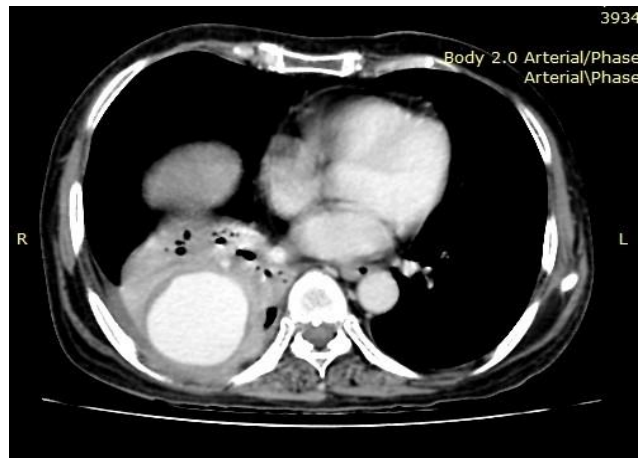
There were 2 sputum AFB positive teenager females who on HRCT showed multiple lung cysts with ground glass haze. One of these girls had complete architectural distortion of the left lung and the right lung showed evenly distributed cysts suggesting lymphangioleiomyomatosis (LAM) with tuberculosis (Figure 3).

Figure 3: Scattered nodules along with lung cysts Patient was reported to be positive for AFB on sputum examination.



There were 2 patients above 75 years, on HRCT demonstrated consolidations with few cysts, bronchio-alveolar lavage revealed tuberculosis and pneumocystis co-infection. A patient with positive TB geneXpert test had extensive centrilobular emphysema and scattered randomly distributed nodules, and 1 patient had transbronchial biopsy proven left hilar mass with miliary pulmonary TB and disseminated abdominal TB. One of the patients, showed multiple cavities in bilateral upper lobes and apical segment of bilateral lower lobes along with a rare formation of a pseudo aneurysm invading bronchial artery "Rasmussen" aneurysm in apical segment of right lower lobe (figure 4).

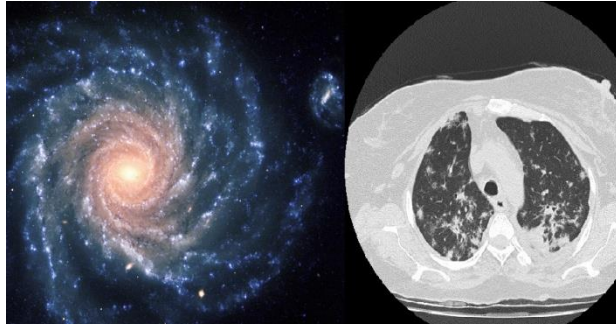
Figure 4: Rasmussen Aneurysm.



Few patients developed nodular thickening with effusions mimicking neoplasia. A patient with positive TB geneXpert (MTB/RIF), showed nodules surrounded by ground glass opacities (galaxy sign) which represent a granulomatous mass "the central core of galaxy" surrounded by small granulomas "the peripheral planetary bodies" (figure 5).

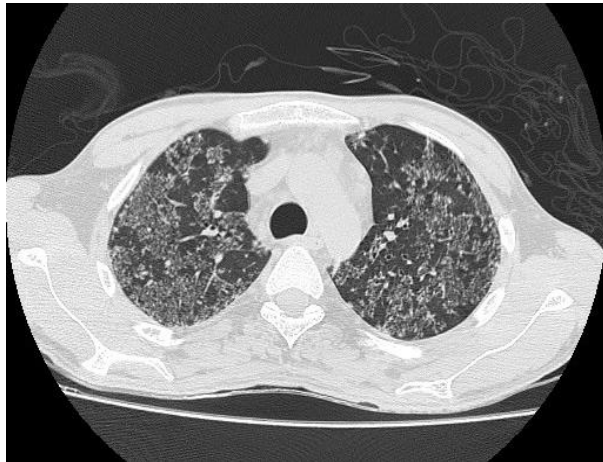


Figure 5: Galaxy sign depicting granulomatous lesion.



This radiological sign is considered to be specific for granulomatous etiology including sarcoidosis and tuberculosis. A patient with clinical features of TB and positive sputum AFB showed randomly distributed clustered nodules along with interstitial septal thickening, mimicking appearance of crazy paving (Fig. 6).

Figure 6: Sputum AFB positive patient showing clustered nodules, randomly distributed with interstitial septal thickening mimicking crazy paving pattern.



Then we had 2 young female patients 30 and 34 year old, who were reported to have a well defined breast lesion and one 12 year old boy, who had a well defined hypodense lesion in thymus. On histopathology, these lesions were diagnosed as caseous tuberculomas. Breast and thymus are rare sites to be involved by tuberculosis <sup>3, 8</sup>.

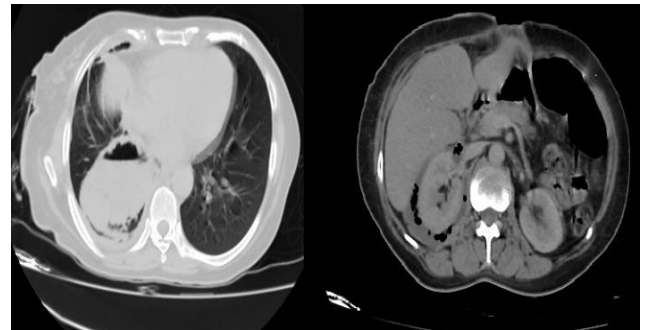
Out of 54 patients, 21 had atypical imaging findings in abdomen and pelvis which included 4 patients with bulky lymphoid masses mimicking neoplastic involvement (lymphoma or metastasis) 6. There were 47 patients of TB with typical cecal and distal ileal loop involvement 6, however 2 patients had atypical involvement, 1 young male had splenic flexure thickness which was radiologically reported as neoplastic and other 65 year old male showed long segment narrowing of descending colon (Fig. 7), which was reported radiologically as ischemic versus infective colitis.

Figure 7: Long segment narrowing of descending colon with past history of tuberculosis.



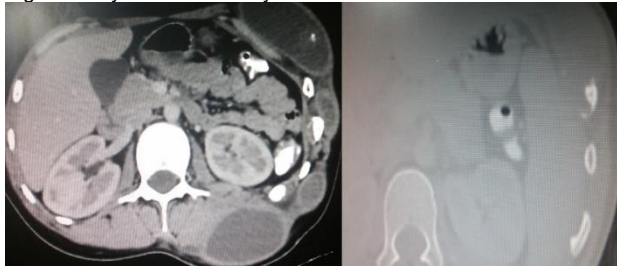
We noted that 7 patients with disseminated TB had homogenous bulky pancreas and mildly raised pancreatic enzymes. Psoas abscesses are typically bacterial in origin but 7 of patients who had psoas abscess with retroperitoneal collections on CT came out to be TB gene PCR positive 8, 9. A young girl with lung abscess and right perinephric abscess (Fig. 8).

Figure 8: Tuberculous lung abscess with perinephric tuberculous abscess.



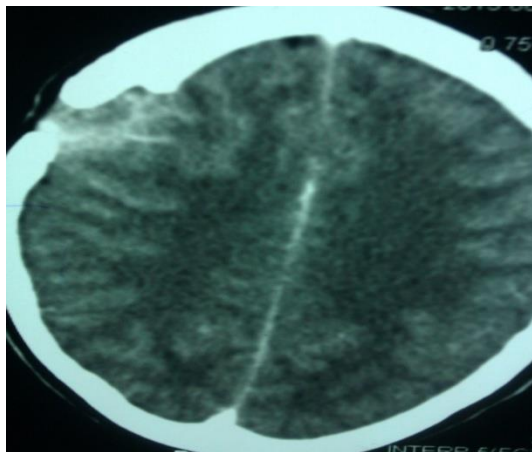
Out of 54 patients, 4 had atypical musculoskeletal system manifestation. Two of these TB patients had concurrent HIV co-infection, on CT showed aggressive looking soft tissue lesion causing destruction of all of the lumbar vertebral bodies and their posterior vertebral elements mimicking aggressive neoplastic lesion. Patients with concurrent HIV infection, uncontrolled aggressive looking Pott's disease may be encountered due to impaired T4 cell immune response, which may confuse the radiologist to report them as malignancy 10. A young 16 year old gene Xpert MTB/RIF positive TB patient, developed multiple soft tissue swellings along left lateral chest wall, on CT scan; these lesions appeared cystic with peripheral enhancement arising from left sided ribs causing expansile lytic lesions of these ribs (figure 9). This is a rare form of cystic bone tuberculosis, also studied and discussed by Burillet all <sup>6</sup>.

Figure 9: Cystic TB osteomyelitis with rib involvement



An elderly male patient with immunocompromised status and uncontrolled blood sugar levels, presented with multiple scalp ulcers with destruction of underlying skull vault (figure 10), mimicking multiple metastatic deposits but histopathologically these lesions were tuberculouscaseous granulomas.

Figure 10: TB scalp, granulomatous lesion mimicking metastasis



## DISCUSSIONS

Tuberculosis (TB) is endemic in Pakistan with variable clinical presentations and imaging findings which pose diagnostic difficulties for radiologists. It is vital for radiologists to be familiar with these atypical imaging features for timely.

Interstitial infiltrates and fibrosis in interstitial lung disease (ILD) obscures the typical picture of pulmonary TB presenting a diagnostic challenge 11. Patients with ILD use immune modulating drugs hence they have increased risk of acquiring TB and other opportunistic infections 12. Our study revealed that, 13 of 300 TB patients (4.3%) had co existing ILD. In >76 years age group, ratio of atypical imaging findings of tuberculosis was 5 out of 17 (29.4 %). All these patients were immuno-compromised; either had co infection with pneumocystis or had ILD along with TB. In a study by Park et al. percentage of patients with pulmonary tuberculosis was 4.4 % in patients with pre existing ILD, which was higher than in general population, likely due to decreased immune status secondary to steroid and immunosuppressant use 13.

Another factor contributing for atypical imaging features of tuberculosis was co-infection with another organism. We

had 3 patients of HIV co infection, and of them 2 had disseminated TB and 1 had destructive spinal involvement. Anley et al reported that patients with TB/HIV co infection usually show less tuberculous destruction in spine which is explained by reduced autoimmune response of Type 4 hypersensitivity reaction caused by HIV 14. However in our study we observed that patients with TB/HIV co-infection showed aggressive tuberculous destruction mimicking malignancy, the reason being advanced HIV infection causing severe immune compromise leading to uncontrolled tuberculous destruction. We had 2 elderly chronically ill patients pathologically proven to have pulmonary TB with pneumocystis co- infection.

We observed 12.3% prevalence of diabetes in TB patients and amongst them 43.2% showed atypical radiological features. Majority of patients were more than 50 years. Previous study by Tahir et al revealed a prevalence of 14.8% of diabetes amongst TB patients which was associated with increased age, poor socioeconomic development and poor immune status 15.

Our study also demonstrated that young females belonging to low socioeconomic class, illiterate and having poor nutritional status presented to us in tertiary care with disseminated disease, multiple organ infection and infection of body parts rarely involved by TB, which resulted in unusual imaging features presenting a diagnostic query. There were 45 cases of disseminated TB and amongst these, 26 (57.7%) were females and all these patients were less than 40 years. Avdeeva et al showed that TB is twice more common in men than in women, and the maximum incidence was observed in women aged 25–34, peaks reported between 18–24 and 25–34 years of age, occurring mostly during the fertile age group 16.

Our study analysis showed that TB is clearly a socially determined disease, amongst 300 patients, 261 (87.2%) belonged to low class and the 39(13%) belonged to lower middle class. According to Avdeeva et al, the social risk factors including poor housing, low income, single-parent family, migrants, not only influences clinical form of the disease, but these factors increase the risk of complicated tuberculosis 16.

We came across one case of thymic tuberculosis. There have been very few case reports of mediastinal tuberculosis in literature. Only fifteen cases of thymic tuberculosis have been reported in literature in the past seven decades, worldwide. A study by Pillai et al suggested that thymic tuberculosis in children was most likely primary tuberculosis unlike adults where it represents post primary localized mediastinal tuberculosis 17.

We had 2 cases of breast masses diagnosed as breast malignancy but pathologically they were found to be tuberculous. Literature review reveals that pregnancy, HIV co-infection and an exacerbating breast cancer increases the propensity to get inflicted with breast TB. Modupeola et al studied and classified breast TB into five clinical entities. Commonest clinical presentation is the nodular variant which mimics malignancy, is seen in 60% of patients 18.

There were several limitations of the study. First, patients were not randomly selected but consecutive patients were selected by convenience sampling. In our study we excluded all patients who showed negative pathology for tuberculosis but according to EPTB guidelines patients

clinically suspicious for tuberculosis should be given ATT as a clinical trial 3. Studies suggest that patients with chronic kidney disease may also have unusual imaging findings if they get tuberculous infection however frequency of patients with concurrent TB and chronic kidney disease could not be studied because per CECT protocol, all patients with deranged RFTs could not be given contrast and hence were excluded from the study.

## CONCLUSIONS

Atypical imaging is not an uncommon occurrence in TB therefore radiologists should be aware of these unusual imaging features so that a misdiagnosis can be avoided. Disseminated disease may present diagnostic dilemma due to involvement of body organs otherwise rarely infected by TB like pancreas, thymus and breast. Young females belonging to very low and low developed socioeconomic status, likely owing to poor nutritional status had particularly come up with disseminated form of tuberculosis with typical clinical features and with typical or atypical imaging findings. In case of atypical features pathological evaluation of patient should be prompt so as to timely diagnose this treatable endemic disease. Factors like diabetes, HIV co-infection and preexisting ILDs confuse radiologist resulting in atypical imaging picture and delayed diagnosis of tuberculosis.

**Data availability:** The radiological CT images used to support the findings of this study are included within the article. However other demographic data used to support the findings of this study are restricted by the Institutional Review Board Rawalpindi Medical University, in order to protect patient privacy. Data are available from corresponding author for researchers who meet the criteria for access to confidential data.

**Conflicts of interest:** The study was conducted in public sector hospital attached to medical university. There were no sponsors involved in the study. Authors state that they have no conflicts of interest to disclose.

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