

**Research Article**

## **Tuberculosis relapse and anatomical sites involved**

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### **ABSTRACT**

**Objective** To know anatomical sites involved in relapse of tuberculosis.

**Design** Cohort study

**Place of study:** Outpatient and Inpatient units of Chest and TB ward Bahawal Victoria Hospital Bahawalpur.

**Method:** Patients diagnosed relapse of tuberculosis were interviewed about their prior tuberculosis with documentary record and new area of active tuberculosis was documented.

**Results** There were total 67 patients enrolled in the study and among them 34 (50.7%) males and 33 (49.3%) females. Age ranged from 13-75 years (mean 43.35 years). Time since last ATT taken ranged from 2 months to 30 years (mean 9.42 years). Previously 63 (94%) patients took ATT for pulmonary tuberculosis and 4 (6%) were treated for TB lymphadenitis. The site for which the recurrent tuberculosis was being treated was pulmonary 37 (55.2%), meninges 17 (25.4%), abdominal 12 (17.9%) and pericardial 1 (1.5%).

**Conclusion** pulmonary tuberculosis was main site of reactivation followed by meningeal and abdominal.

**Keywords:** -tuberculosis, tuberculosis relapse, tuberculosis sites, pulmonary tuberculosis, extrapulmonary tuberculosis, lymph node tuberculosis, meningial tuberculosis.

### **INTRODUCTION**

Tuberculosis is chronic granulomatous disease which primarily infects the lungs<sup>1</sup>

It may infect any part of the lung depending upon the immunological state of individual and type of disease with different clinical manifestations. Immunological state is determined by HIV status, diabetes mellitus, smoking, renal failure, chronic

liver disease, any malignancy and immunosuppressive therapy or long term steroid intake<sup>2</sup>.

Different clinical presentations maybe primary TB, tuberculoma, endobronchial TB and laryngeal TB.<sup>3</sup>

These all involve the airway and pulmonary parenchyma thus making it the commonest site. In 90% of cases of primary tuberculosis, the disease enters dormant phase and may get active in 10% of cases when individuals immune response exhausts due to above mentioned reasons<sup>4</sup>. This activation may happen primarily in lungs or if hematogenous spread has happened then any other anatomical location represents 39% and majority in lymph nodes 25% in all tuberculous infections<sup>5</sup>.

Relapse occurs after initial improvement and we studied sites of tuberculosis involved in such cases. We conducted this study at Quaid e azam medical college pulmonary unit where inpatients site of involvement was documented in relapse cases.

## MATERIAL & METHOD

**Study Design:** A retrospective cohort study to determine the site of tuberculosis in relapse cases.

### Study area and Population and Data collection

The study was conducted at Pulmonary unit Quaid e azam medical college Bahawalpur, where study population was cohort of tuberculosis patient who were admitted with relapse. They were interviewed and their past tuberculosis history and documents were read for

previous episode of disease and anatomical location of relapse diagnosed during interview was documented. Only patients who were present during interview and examination were included in the study.

### Data Analysis

Data was analyzed using SPSS software and variables used were site's of tuberculosis, age, gender, time since previous antituberculous therapy.

## RESULTS

Of the cohort of 67 new relapse of tuberculosis patients enrolled in the study, 34 (50.7%) were males and 33 (49.3%) were females with age ranged from 13-75 years (mean 43.35 years) [Table 1]. The age range was 13-75 years (Mean 43 yrs- St Dev + 13.12) [Table 2]. Time since last ATT taken ranged from 2 months to 30 years (mean 9.42 years- St Dev + 7.40)[Table 3]. During previous tuberculosis treatment 63 (94%) patients had pulmonary tuberculosis and 4 (6%) had tuberculous lymphadenitis. Of the 67 patients diagnosed with relapse of tuberculosis 37 (55.2%) had pulmonary tuberculosis, 17 (25.4%) had meninges involvement, 12 (17.9%) had abdominal tuberculosis and 1 (1.5%) had pericardial involvement of tuberculosis [Table 1].

**Table 1-** Site of relapse and previous sites- with gender

Gender	Pulmonary TB		Lymph node TB		Abdominal TB		Meningeal TB		Pericardial TB	
	Previous	Relapse	Previous	Relapse	Previous	Relapse	Previous	Relapse	Previous	Relapse
Male	33(49.25%)	24(35.82%)	1 (1.49%)	Zero	Zero	4(5.97%)	Zero	6(8.95%)	Zero	Zero
Female	30(44.77%)	13(19.40%)	3(4.47%)	Zero	Zero	8(11.94%)	Zero	11(16.41%)	Zero	1(1.49%)

P Value – (Gender to Pulmonary and Extrapulmonary in Relapse Cases)

- Pulmonary TB- 0.105
- Extra-Pulmonary TB- 0.505

**Table 2-** Site of relapse and previous sites- with Age.

Age(yrs)	Pulmonary TB		Lymph node TB		Abdominal TB		Meningeal TB		Pericardial TB	
	Previous	Relapse	Previous	Relapse	Previous	Relapse	Previous	Relapse	Previous	Relapse
13-20	2(2.98%)	2(2.98%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	Zero
21-30	10(14.92%)	9(13.43%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	1(1.49%)
31-40	15(22.38%)	8(11.94%)	2(2.98%)	Zero	Zero	4(5.97%)	Zero	5(7.46%)	Zero	Zero
41-50	19(28.35%)	11(16.41%)	2(2.98%)	Zero	Zero	6(8.95%)	Zero	5(7.46%)	Zero	Zero

<b>51-60</b>	11(16.41%)	3(4.47%)	Zero	Zero	Zero	2(2.98%)	Zero	6(8.95%)	Zero	Zero
<b>61-70</b>	4(5.97%)	3(4.47%)	Zero	Zero	Zero	Zero	Zero	1(1.49%)	Zero	Zero
<b>71-75</b>	1(1.49%)	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	Zero

P Value – (Age to Pulmonary and Extrapulmonary in Relapse Cases)

- **Pulmonary TB- 0.004**
- Extra-Pulmonary TB- 0.261

**Table 3** -Site of relapse and previous sites- with Time since last ATT taken.

Time(yrs)	Pulmonary TB		Lymph node TB		Abdominal TB		Meningeal TB		Pericardial TB	
	Previous	Relapse	Previous	Relapse	Previous	Relapse	Previous	Relapse	Previous	Relapse
<b>2 months</b>	1(1.49%)	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	Zero
<b>5 months</b>	1(1.49%)	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	Zero
<b>8 months</b>	2(2.98%)	2(2.98%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	Zero
<b>1 yr</b>	4(5.97%)	4(5.97%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	Zero
<b>2 yr</b>	5(7.46%)	4(5.97%)	Zero	Zero	Zero	1(1.49%)	Zero	Zero	Zero	Zero
<b>3yr</b>	5(7.46%)	3(4.47%)	Zero	Zero	Zero	1(1.49%)	Zero	1(1.49%)	Zero	Zero
<b>4yr</b>	3(4.47%)	1(1.49%)	Zero	Zero	Zero	1(1.49%)	Zero	1(1.49%)	Zero	Zero
<b>5yr</b>	4(5.97%)	3(4.47%)	Zero	1(1.49%)	Zero	2(2.98%)	Zero	2(2.98%)	Zero	Zero
<b>6yr</b>	5(7.46%)	5(7.46%)	Zero	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero
<b>7yr</b>	1(1.49%)	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero	Zero	Zero
<b>8yr</b>	4(5.97%)	1(1.49%)	Zero	1(1.49%)	Zero	1(1.49%)	Zero	1(1.49%)	Zero	Zero
<b>10yr</b>	4(5.97%)	3(4.47%)	Zero	Zero	Zero	1(1.49%)	Zero	1(1.49%)	Zero	Zero
<b>12yr</b>	5(7.46%)	3(4.47%)	Zero	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero
<b>15yr</b>	7(10.44%)	3(4.47%)	Zero	Zero	Zero	1(1.49%)	Zero	3(4.47%)	Zero	Zero
<b>18yr</b>	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero	1(1.49%)	Zero	Zero
<b>20yr</b>	7(10.44%)	1(1.49%)	Zero	Zero	Zero	1(1.49%)	Zero	4(5.97%)	Zero	1(1.49%)
<b>25yr</b>	3(4.47%)	1(1.49%)	Zero	Zero	Zero	Zero	Zero	2(2.98%)	Zero	Zero
<b>30yr</b>	1(1.49%)	Zero	Zero	Zero	Zero	Zero	Zero	1(1.49%)	Zero	Zero

P Value – (Time since last ATT to Pulmonary and Extrapulmonary in Relapse Cases)

- Pulmonary TB- 0.708
- Extra-Pulmonary TB- 0.261

## DISCUSSION

The finding of this study highlights the preference of body sites involved in tuberculous relapse. The age, gender and time since last ATT completed all determined the involved relapse area.

In males relapse was more seen in lungs but extra-pulmonary involvement was more in females (Table 1). Lung involvement in males was 35.82% in comparison to females of 19.40%. Contrary to this extra-pulmonary areas involved in males were just 5.97% abdominal and 8.95% meninges while in females 11.94% was abdominal TB, 16.41% meninges and 1.49% pericardium. Such a pattern of our community matches with many international researches where more of females show extrapulmonary

involvement. Many factors has been forwarded for such dominance in females for extrapulmonary such as poor access to health facility due to socioeconomic and cultural factors. Others factors for this incongruity are sex hormonal and genetic effects along with poor nutritional status<sup>6,7,8</sup>.

Other important findings for gender discrimination is tumour necrosis factor, CD4 and ineterlukin 10 production differences among gender<sup>9</sup>.

Similarly more extrapulmonary sites were affected by tuberculosis with advancing age and time since last treatment completed after 30 years and 15 years respectively but overall lung involvement was statistical significant change compared to previous disease occurrences (P Value 0.004) as patients age progressed in our

study. This is contrary to the data from Nepal that showed more extrapulmonary involvement in young age<sup>10</sup>. In past too few studies have demonstrated exhausted immune system failure to eliminate dormant mycobacteria of same strain at multisystem sites<sup>11</sup>

The lymph nodes forms a major system involved as extrapulmonary sites. As primary infection after lungs it is the second most common site and mechanism of relapse occurring in this area in priority to lungs is not well understood yet<sup>5</sup>.

. However few postulated factors have been identified as female gender, advancing age, south asian population<sup>12, 13</sup>

This is also an important fact that different genotypes of mycobacteria show variation in virulency thus penetrating the immune barrier of extrapulmonary sites in different way and effecting lymph nodes preferably. Such strain is east African Indian strain<sup>14,15</sup>

However strains identification was beyond the scope of our study.

In western Australian study Asians were found to have 71% prevalence and american multicentral trial showed higher prevalence of lymph nodes involvement thus further signifying Asian gene as a risk factor<sup>16,17</sup>.

It has been well understood that tuberculosis is a disease effecting people with comorbidities that weakens the immune system thus effecting the host. Reduction of TH1 cytokines levels has been found to have key role in this context<sup>18</sup>.

## CONCLUSION

Our study findings matches mostly with the international trials as more involvement of extrapulmonary areas in females. However few conflicting points as seen due to advancing age and time since last treatment have been explained in many studies due to difference in virulence factors among different mycobacterium strains seen in different geographical areas.

## DISCLOSURE

No potential conflicts of interest exist with any company/organization in this study. No funding

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