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Original Research Article

PREDICTORS OF ATYPICAL CHEST IMAGING IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Abstract: *This study aimed to identify the risk factors associated with abnormal chest imaging in patients diagnosed with pulmonary tuberculosis. A retrospective study was conducted between December 2022 and December 2023 in the Radiology Department of Mayo Hospital, Lahore. The study included 100 patients who were diagnosed with smear-positive pulmonary tuberculosis and had undergone chest computed tomography (CT) within two weeks before or after hospital admission. Patients' performance status was assessed on a scale of 0-4. CT scans were performed on all patients, and radiologists were unaware of the patient's data. They examined the scans to determine the presence of lung involvement (upper, middle, and lower) and cavity. Out of 100 patients, 48 (48%) had non-cavity disease. Univariate analysis revealed that patients with non-cavity disease were most likely to be female, older, and have low estimated glomerular filtration rate (eGFR) and C-reactive protein (CRP) levels compared to patients with cavities. In multivariate analysis, low CRP levels were found to be the most potent risk factor for non-cavity disease after adjusting for co-variables. Additionally, 70 patients (70%) presented with non-upper predominant lung disease. Univariate analysis revealed that the majority of patients in this group were women and had high CRP levels, low albumin levels, and poor performance status. Poor performance status was the most potent risk factor for non-upper predominant lung disease. Based on the study findings, low C-reactive protein levels and poor performance status are the most substantial risk factors for non-cavity and non-upper predominant lung disease, respectively, in patients with pulmonary tuberculosis.*

Keywords: Computed Tomography, Imaging, Pulmonary tuberculosis, Radiology

Introduction

Chest computed tomography is the recommended initial imaging to diagnose active tuberculosis (Nel et al., 2022). If the diagnosis of tuberculosis is delayed, the disease can advance rapidly and increase the risk of transmission among individuals. Delay in diagnosis is usually caused by late doctor visits after the presentation of symptoms and delays caused by doctors in diagnosing and treating the disease (Bello et al., 2019; Getnet et al., 2019a). It has been reported that atypical chest images, such as non-cavity disease and unusual lung involvement, were the leading causes of delay in diagnosis by health professionals (Getnet et al., 2019b).

Non-cavity disease on the chest CT is presented in patients with compromised immune systems as a result of advanced age, use of immunosuppressant drugs, and HIV infection. A suppressed immune system can initiate the creation of granulomatous lesions, which can cause cavitation. Secondary tuberculosis usually affects the upper lung lobes, leading to a higher ventilation/perfusion ratio. Advanced-age patients bedridden in usually supine positions have a higher ventilation/perfusion ratio in the ventral lung region, affecting the ventral field (Curry et al., 2022).

Research has evaluated the association between these chest CT abnormalities and tuberculosis patients' underlying conditions (Goto et al., 2019). However, limited research is available to investigate the causes of atypical imaging about confounding factors. Assessment of these risk factors can prevent delay in diagnosis, and doctors will consider these factors in case of ambiguity. We conducted this study to assess the risk factors of atypical chest imaging in patients with pulmonary tuberculosis.

Methodology

A retrospective study was conducted in the Radiology Department of Mayo Hospital, Lahore, from December 2022 to December 2023. A total of 100 patients diagnosed with smear-positive pulmonary tuberculosis who had undergone chest computed tomography within 2 weeks prior to or later hospital admission were included in the study. Patients who tested positive for general bacteria were excluded. All the patients provided informed consent for their information being used for research. The ethical board of the hospital approved the study design.

Patients' demographic, clinical, laboratory, and radiographic data was recorded. We assessed each patient on admission for daily physical activity on a performance status scale by Eastern Cooperative Oncology Group, which describes the patient's activity on a scale of 0 to 4, 0 being fully active and 4 being completely disabled (Honjo et al., 2020). Respiratory failure was also observed in patients upon admission.

A CT scan was performed on all patients, and radiologists unaware of the patient's data examined the scan. They determined the presence of cavity and lung involvement (upper, middle, and lower).

All the data was analyzed using SPSS version 24. The Kappa value determined the extent of agreement between

the two observer radiologists. 95% CI was used for two-tailed analyses. The logistic regression model assessed patients with usual chest imaging after co-variable adjustment. A p-value less than 0.05 defined the statistical significance. Statistically significant variables in univariate analysis were then assessed in multivariate analysis. To study the independent effect of each, BMI and CRP were assessed by multivariate analysis if their p-value was less than in the univariate analysis.

Results

A total of 100 patients were analyzed. Kappa scores were 0.90 and 0.88 for cavity disease and lung involvement, respectively. Forty-eight patients (48%) had non-cavity disease. Univariate analysis revealed that patients with non-cavity disease were most likely female, had low eGFR and CRP, and were older than patients with cavities (Table 1). Low CRP levels were considered the most potent risk factor of non-cavity disease after adjusting co-variables in multi-variate analysis (Table 2).

Upper dominant and diffuse distribution were joint in performance status groups, with diffuse distribution having most PS4 patients (Table 3).

Seventy patients (70%) presented with non-upper predominant lung disease. Univariate analysis revealed the majority of women with high CRP, poor performance status, and low albumin levels in this group (Table 4). Poor performance status was this disease was the most potent risk factor (Table 5).

Table 1: Uni-variate analysis of patients' characteristics in non-cavity disease

Factors	Non-cavity disease (n= 48)	Cavity disease (n=52)	Odds ratio	P- value
Female sex	32 (66.7%)	20 (38.5%)	3.130 (1.350- 7.253)	0.010
Age	85 (78-90)	78 (65-85)	1.032 (1.005-1.054)	0.050
BMI	22 (20-23.6)	21.8 (19.3-23.2)	1.044 (0.919-1.176)	0.552
Performance status				
0	6 (12.5%)	3 (5.8%)		0.931
1	13 (27.1%)	25 (48%)		
2	12 (25%)	8 (15.4%)		
3	12 (25%)	16 (30.8%)		
4	5 (10.5%)	6 (11.5%)		
White blood cells	6700 (5200-7800)	7200 (6200-9800)	0.910 (0.792-1.040)	0.151
Lymphocytes	1200 (770-1600)	950 (640-1400)	1.000 (1.000-1.003)	0.198
C- reactive protein	1.9 (0.3-2.8)	3.0 (1.0-5.2)	0.832 (0.718-0.971)	0.020
Albumin	3.2 (3.3-4.3)	3.0 (2.4-3.6)	1.530 (0.833-2.801)	0.182
Alanine transaminase	17 (13-21)	18 (13-25)	0.990 (0.967-1.017)	0.720
eGFR	68.3 (50.1-85.4)	83.5 (66.7-98.6)	0.977 (0.972-0.994)	0.030
Chronic obstructive pulmonary disease	2 (4.2%)	5 (9.6%)	0.353 (0.037-3.481)	0.375
Cardiac diseases	10 (20.8%)	7 (13.5%)	2.210 (0.684-7.155)	0.195
Diabetes mellitus	9 (18.7%)	13 (25%)	0.642 (0.230-1.820)	0.401
Respiratory failure	5 (10.5%)	9 (17.3%)	0.590 (0.162-2.158)	0.425

Table 2: Multi-variate analysis of patients' characteristics in non-cavity disease

Factors	Adjusted odds ratio	P- value
Female sex	2.310 (0.920- 5.798)	0.080
Age	1.020 (0.088-1.050)	0.215
CRP	0.810 (0.680-0.971)	0.022
eGFR	0.091 (0.972-1.012)	0.310

Table 3: Association between lung distribution and performance status in patients

Performance status	Upper predominant distributions	Middle predominant distribution	Lower predominant distributions	Diffuse distribution
PS0	70%	15%	0%	15%
PS1	43%	0%	3%	54%
PS2	20%	14%	6.5%	64%
PS3	15%	0%	0%	85%
PS4	0%	0%	0%	100%

Table 4: Uni-variate analysis of patients' characteristics in non-upper predominant lung involvement

Factors	Non-upper predominant lung involvement (n=70)	Upper predominant lung involvement (n=30)	Odds ratio	P- value
Female sex	41 (58.5%)	11 (36.7%)	2.631 (1.033-6.680)	0.050

Age	83 (75-88)	73 (62-79)	1.031 (0.993-1.049)	0.090
BMI	21.7 (18.9-22.4)	22.8 (20.3-22.1)	0.890 (0.768-1.025)	0.095
Performance status				
0	2 (2.8%)	6 (20%)	2.597 (1.555-4.335)	<0.001
1	21 (30%)	16 (53.3%)		
2	15 (21.4%)	4 (13.3%)		
3	23 (32.5%)	4 (13.3%)		
4	9 (12.8%)	0 (0%)		
White blood cells	7000 (6000-8800)	7000 (4900-9000)	1.092 (0.933-1.275)	0.322
Lymphocytes	910 (570-1480)	1140 (941-1605)	0.995 (0.994-1.000)	0.075
C- reactive protein	2.9 (1.0-5.0)	1.0 (0.2-2.5)	1.430 (1.079-1.872)	0.009
Albumin	3.2 (2.8-3.8)	3.7 (3.5-4.2)	0.220 (0.095-0.535)	0.001
Alanine transaminase	18 (12-24)	17 (15-24))	1.021 (0.990-0.534)	0.409
eGFR	73.4 (50.0-93.6)	83.3 (68.4-90.0)	0.991 (0.968-1.009)	0.190
Chronic obstructive pulmonary disease	2 (2.8%)	4 (13.3%)	0.118 (0.010-1.219)	0.068
Cardiac diseases	15 (21.4%)	2 (6.7%)	6.266 (0.782-51.460)	0.080
Diabetes mellitus	18 (25.7%)	3 (10%)	3.930 (0.840-19.410)	0.078
Respiratory failure	13 (18.5%)	0 (0%)	-	0.995
Cavity disease	37 (52.8%)	16 (53.3%)	0.835 (0.342-2.033)	0.666

Table 5: Multi-variate analysis of patients' characteristics in non-upper predominant lung involvement

Factors	Adjusted odds ratio	P- value
Female sex	2.850 (0.973-8.401)	0.060
BMI	0.927 (0.790- 1.110)	0.408
Performance status	2.160 (1.262-3.689)	0.007
CRP	1.260 (0.962-1.626)	0.090

Discussion

We conducted this study to assess the predictors of disease in chest imaging in tuberculosis patients. The results revealed that low C-reactive protein is the most potent risk factor for non-cavity disease. Poor performance status is the strongest predictor of non-upper predominant lung disease.
Univariate analysis showed significantly low albumin levels and eGFR levels in non-cavity groups, and these factors were insignificant in the multivariate analysis. These variables may be considered an inflammatory marker by the CRP levels as they both reduce in case of inflammation. Low CRP may signal mild inflammation due to exposure of Mycobacterium tuberculosis to cell-mediated immunological lymphocytes (Abolhassani et al., 2019). Hence, low CRP levels can lead to granulomatous lesions, and the cavity may not develop at the early infection stage.
In our study, patients with non-cavity patients were significantly older than patients with cavity disease. However, advanced age was not a risk factor for non-cavity due to the inclusion of significantly older patients. Other studies support this conclusion (Hikone et al., 2020; Zhang et al., 2019). Diabetes mellitus was not a risk factor (Huangfu et al., 2019). Barreda et al. and Behzadmehr et al. concluded a higher incidence of cavity disease in tuberculosis patients with diabetes (Barreda et al., 2020; Behzadmehr and Rezaie-Keikhaie, 2022). This can be explained by the fact that diabetes mellitus lowers bactericidal activity, increasing the development of cavities. Low immunity might have led to less cavitation in people with diabetes.
Poor performance status strongly predicted non-upper dominant disease after adjusting BMI and CRP (Nakao et al., 2019). This is due to the high ventilation/perfusion ratio in patients with poor performance status in the ventral pulmonary region, affecting the non-upper region. In addition, poor performance status is related to swallowing dysfunction and difficulty in sputum expectoration (Aggarwal, 2019). Gravity-dependent lower lung predominance is standard in tuberculosis patients with swallowing dysfunction. Advanced age is one of the risk factors, but the association between old age and lung distribution was insignificant.
The results of our study are significant as it is the only study in Pakistan to assess the association between CRP levels and performance status and imaging in tuberculosis patients. Our study is also unique as we evaluate chest CT results rather than x-ray results, as in most studies. We eliminated the patients with general bacterial infection to study lung features accurately.
Our study has some limitations. We only included patients with advanced age from a single center, so our results are only helpful for younger patients. We only excluded patients with general bacterial infection, which did not wholly eliminate co-infection risk. Lastly, we did not record the results according to disease duration, which may have altered them.

Conclusion

Low C-reactive protein levels and poor performance status are the most substantial risk factors for non-cavity and non-upper predominant lung disease, respectively.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

Author Contribution

AFSHAN SHAKIR (Consultant)
Coordination of collaborative efforts.
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.
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Manuscript revisions, critical input.
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Data entry and Data analysis, drafting article.
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Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.

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