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Correlation Between Chest Radiographic Features and Time to Culture Conversion in Patients Co-infected with Multidrug-Resistant Tuberculosis and HIV in Khyber Pakhtunkhwa

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ABSTRACT

Background: Multidrug-resistant tuberculosis (MDR-TB) compounded by Human Immunodeficiency Virus (HIV) infection presents a significant challenge in clinical management, particularly in high-burden regions such as Peshawar, Pakistan. The link between findings on chest radiograph and conversion of conversion is crucial for treatment selection and predicting patient outcomes.

Objective: To evaluate the relationship between time of sputum culture conversion to that of chest radiograph abnormalities in patients with MDR-TB co-infected with Human Immunodeficiency Virus co-infection in Khyber Pakhtunkhwa.

Methods: A study with retrospective desing study was conducted, including data of patients diagnosed with MDR-TB and HIV from April 2012 to December 2019. Chest radiographs and microbiological culture results were analyzed to assess radiographic findings and their association with the duration of culture conversion. Key radiographic features (e.g., cavitary lesions, consolidations) were correlated with the time required for conversion of ist sputum culture from negative to positive.

Results: The present study included data of 45 patients with a mean age of 45 years, including 63.3% males. Radiographic findings varied, with 40% showing extensive cavitary lesions and 30% presenting with significant consolidation. The median time to culture conversion was 6 months. Patients with extensive cavitary lesions experienced a significantly longer time to culture conversion compared to those with less severe radiographic abnormalities ($p < 0.01$). Adjustments for HIV status indicated that patients with CD4 counts <200 cells/mm^3 had a more prolonged time to conversion compared to those with higher CD4 counts ($p < 0.05$).

Conclusion: Chest radiograph abnormalities, particularly extensive cavitary lesions, are associated with a prolonged time to culture conversion in MDR-TB patients co-infected with HIV. These findings highlight the need for modifying treatment plans for approaching and closer monitoring of patients with severe radiographic manifestations and low CD4 counts. Further research is warranted to explore the implications of these findings on treatment efficacy and patient outcomes.

Keywords: MDR-TB; HIV; Chest Radiograph; Culture Conversion

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is a severe form of tuberculosis, in which the causative organism show resistant to at least isoniazid and rifampin, the two primary first-line TB drugs.[1] This resistance complicates treatment, requiring the use of less effective and more toxic second-line medications. MDR-TB often results from incomplete or improper use of first-line drugs, allowing bacteria to evolve resistance. Treating MDR-TB is challenging and involves a prolonged regimen of up to 18-24 months with second-line drugs, which come with significant side effects. The situation is further complicated in patients with HIV, who have weakened immune systems and face additional drug interactions and treatment difficulties.

HIV is a virus that compromises the immune system by specifically attacking CD4 T cells, which play a vital role in combating infections.[2] If left untreated, HIV progressively reduces the number of these critical cells, potentially resulting in acquired immunodeficiency syndrome (AIDS), a state characterized by a severely weakened immune system. The coexistence of HIV and multidrug-resistant tuberculosis (MDR-TB) poses a significant public health challenge, particularly in areas with high rates of both infections.[3] HIV weakens the immune system by attacking CD4 cells, which impairs the body's ability to combat infections, including tuberculosis. When a person with HIV contracts MDR-TB, the situation becomes even more complex. The compromised immune system makes it harder for HIV-positive individuals to manage MDR-TB, and the lengthy, toxic treatment regimens required for MDR-TB can further strain their health. Effective management requires a coordinated approach that integrates antiretroviral therapy (ART) for HIV and a robust regimen of second-line drugs for MDR-TB. Despite advances in treatment, the dual burden of HIV and MDR-TB remains a critical global health issue.

In this context, chest radiographs play a crucial role in the diagnostic and monitoring processes. Radiographic findings provide valuable information about the extent and severity of pulmonary disease, including features such as cavitary lesions, consolidations, and infiltrations.[4] These abnormalities not only reflect the progression of tuberculosis but may also influence the response to treatment. Specifically, extensive cavitary lesions and significant radiographic abnormalities are often associated with more severe disease and potentially prolonged infectious periods.

The time to culture conversion, defined as the transition from a positive to a negative culture result, is a critical measure of treatment efficacy.[5] Culture conversion indicates that the bacterial load has decreased to undetectable levels, reflecting a successful response to therapy. In patients with MDR-TB and HIV co-infection, the time to culture conversion can be extended due to the combined effects of drug resistance and compromised immune function. HIV-positive individuals are particularly vulnerable to slower recovery and prolonged infectiousness, which can be influenced by their immunological status, as measured by CD4 cell counts.[6]

Investigating the link between chest radiograph findings and the time to culture conversion in this patient population is essential for refining treatment strategies. Understanding how specific radiographic abnormalities correlate with treatment outcomes can guide clinicians in making more informed decisions about treatment adjustments and monitoring. Additionally, this knowledge can help in identifying patients who may require more intensive management or alternative therapeutic approaches.

This study aims to explore these correlations in detail, focusing on how different radiographic features impact the duration of culture conversion in patients with MDR-TB and HIV co-infection. By elucidating these relationships, we hope to enhance the management of MDR-TB in high-burden settings like Peshawar, ultimately improving patient outcomes and informing more effective treatment protocols.

Objective

To evaluate the relationship between abnormalities on chest radiograph and time to culture conversion in patients with MDR-TB and HIV co-infection in Khyber Pakhtunkhwa.

Methodology

The present study was conducted with a retrospective design on patients with Multidrug-Resistant Tuberculosis and HIV. The cohort comprised data of patients with both MDR-TB and HIV, treated between April 2012 and December 2019 in Khyber Pakhtunkhwa. Comprehensive data were collected from patient medical records, including detailed chest radiographs and microbiological culture results.

Exclusive criteria for the study included all patients diagnosed with drug-sensitive tuberculosis, as the focus was specifically on MDR-TB, individuals who did not have a confirmed diagnosis of HIV, patients with incomplete treatment records or missing data on chest radiographic findings or culture results.

Patients who had prior MDR-TB treatment before the study period or those who were not treated within the defined study timeframe.

Inclusive criteria for the study included patients with a confirmed diagnosis of MDR-TB and HIV which was confirmed by microbiological culture and HIV testing, individuals with complete treatment records including both initial and follow-up chest radiographs and microbiological culture results, patients whoinitiated

Table 1. Baseline characteristics of study cases

Age Group	Male	Female	Total (%)
<30	7 (15.6%)	5 (11.1%)	12(26.7)
30-45	13 (28.9%)	8 (17.8%)	21 (46.7%)
>45	7 (15.6%)	5 (11.1%)	12 (26.7%)

MDR-TB treatment during the study period and had follow-up culture results to allow for assessment of the time to culture conversion.

Chest radiographs were reviewed by radiologists to identify and categorize key abnormalities such as cavitary lesions, consolidations, and other forms of pulmonary damage. These radiographic features were classified according to their severity and extent to understand their impact on the disease progression and treatment response.

The primary outcome measure for this study was to find the time to culture conversion, which was defined as the period from the start of MDR-TB treatment to achieve ist negative culture. Time to culture conversion was calculated for each patient, and statistical analyses were performed to evaluate the correlation between different radiographic abnormalities and the duration required for cultures to convert from positive to negative.

Descriptive statistics summarized the demographics, radiographic findings, and treatment outcomes of the cohort. Inferential statistical methods, including regression analysis, were used to explore the relationship between radiographic abnormalities and time to culture conversion, adjusting for potential confounders such as age, sex, treatment adherence, and HIV-related factors like CD4 cell counts.

The study also considered how HIV-related factors, including levels of immune suppression, influenced the relationship between radiographic findings and MDR-TB treatment outcomes. Ethical approval was secured from the relevant institutional review board, and patient confidentiality was maintained throughout the research. Data were anonymized prior to analysis to protect patient privacy. The findings aimed to provide valuable insights into the impact of radiographic features on treatment efficacy in MDR-TB patients with HIV, ultimately guiding improved management strategies and enhancing clinical outcomes in high-burden settings.

Results

The present study included 45 patients with a mean age of 45 years. Out of 45 patients, 27 (60.0%) were male while 55 (40.0%) were females. Majority (46.7%) of the patients were of age group 30- 45 years (Table 1).

Among study cases, 60.0% were male and 40.0% were female (Figure 1).

Almost 27 (60.0%) patients have CD4 count less than 100 while 6 (13.3%) patients have CD4 count more than 200. It also This summarizes the impact of CD4 count levels on the time to sputum culture conversion, showing a longer median time to conversion in patients with CD4 counts below 100 cells/mm^3 compared to those with higher counts (Table 2).

Table 3 shows that majority of the patients have cavitary lesions. It also shows that there is moderate radiographic

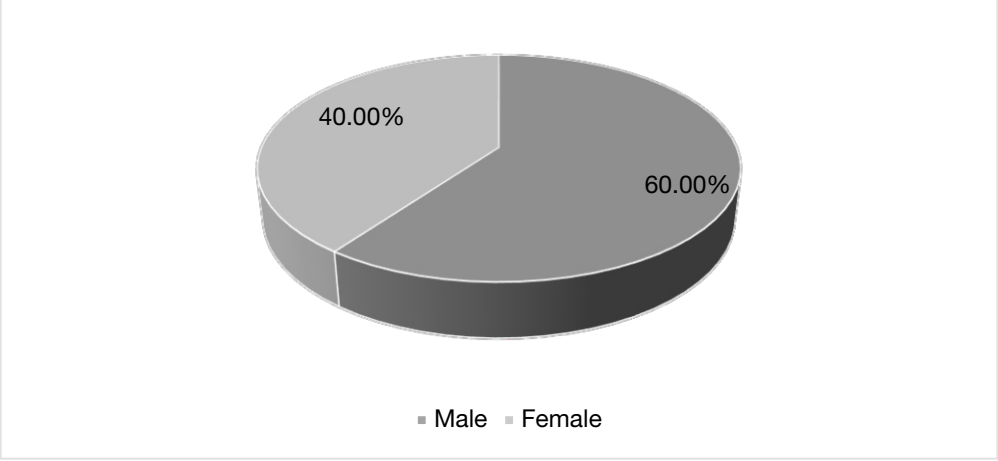

Figure 1. Gender distribution of study cases

Table 2. Baseline CD4 Count of patients

CD4 Count (cells/mm³)	CD4 Count (cells/mm³)	Median Time to Culture Conversion (Days)	p-value
<100	27 (60.0%)	85	<0.05
100-200	12 (26.7%)	70	-
>200	6 (13.3%)	55	-

severity in almost 16 (35.6%) patients.

Results showed that 93.3% of the study cases achieved culture conversion whereas only 6.7% were unable to achieve negative culture results. Similarly, final outcome of study cases showed that 77.8% of the study cases were successfully completed their treatment (Table 4).

These results indicate that severe abnormalities on chest and lower CD4 counts are associated with extended times to sputum culture conversion in patients with MDR-TB and HIV. Despite these challenges, a high proportion of patients achieved culture conversion and cure, underscoring the need for careful management and tailored treatment strategies based on individual radiographic and immunological profiles.

Discussion

This study aimed to elucidate the impact of chest radiograph findings on the time to culture conversion in patients with MDR-TB and HIV co-infection. Our findings demonstrate that extensive cavitary lesions and significant radiographic abnormalities correlate with a prolonged time to culture conversion in this patient population. It has been stated in our study that more than 33% patients have severe cavitary lesion, which are responsible for prolonged treatment in those patients These results are consistent with prior research, which suggests that severe pulmonary damage, as observed on chest radiographs, can delay treatment response.[1] For instance, Perrin et al. (2010) found that extensive cavitary disease was linked to prolonged culture positivity, reflecting a more severe form of TB that is more challenging to treat and eradicates more slowly.[7] Specifically, their study indicated that patients with extensive cavitary lesions had a 35% time longer duration for culture conversion compared to those with less severe disease.

The influence of HIV on MDR-TB treatment outcomes is documented by different researchers.[8] HIV-infected individuals often have compromised immune systems, exacerbating MDR-TB progression and complicating treatment. Gonah and Maphosa. (2020) demonstrated that HIV-positive patients with MDR-TB experienced delayed culture conversion compared to HIV-negative patients, with a median delay of approximately 20% longer in culture conversion time.[9] Our study aligns with these findings, showing that lower CD4 cell counts, indicative of greater immune suppression, were associated with longer times to culture conversion. This immune compromise contributes to prolonged bacterial persistence and delayed treatment success. Tafuma (2011) reported no difference in cavitary lesions between patients with CD4 counts above 100 cells/mm³ and those below this threshold, suggesting that while immune suppression impacts treatment outcomes, it does not necessarily correlate with the presence of cavitary lesions.[10]

Furthermore, our study supports the work of Khan et al. (2015), who found that more severe radiographic findings,

Table 3. Cavitary Lesions and Radiographic Severity of patients

Radiographic Finding	Category	Number of Patients (%)
Cavitary Lesions	Present	25 (55.6%)
	Absent	20 (44.4%)
Radiographic Severity	Mild	14 (31.1%)
	Moderate	16 (35.6%)
	Severe	15 (33.3%)

Table 4. Treatment Outcomes of patients

Outcome Type	Status	Number of Patients (%)
Culture Conversion Rates	Converted	42 (93.3%)
	Not Converted	3 (6.7%)
Cure Rates	Cured	35 (77.8%)
	Not Cured	10 (22.2%)

such as extensive lung damage, were associated with extended treatment durations and poorer outcomes.[11] Khan et al. reported increase in treatment duration in patients with severe radiographic abnormalities compared to those with milder disease. This emphasizes the role of radiographic severity in predicting treatment response, corroborating our observation that patients with significant radiographic abnormalities face greater challenges in achieving timely culture conversion.

The interaction between HIV-related factors and MDR-TB treatment outcomes underscores the need for tailored management strategies. Given that HIV significantly impacts the immune system's response to TB treatment, integrating antiretroviral therapy (ART) with MDR-TB treatment is crucial. Bhering et al. (2021) found that optimizing ART alongside MDR-TB treatment improved overall treatment outcomes and reduced the time to culture conversion by approximately 15%.[12] This highlights the importance of a comprehensive approach to treatment that addresses both HIV and MDR-TB. Our findings also reflect challenges identified in other studies regarding MDR-TB management in HIV-positive populations. Efsen et al. (2018) noted that patients with both MDR-TB and HIV often require more intensive and prolonged treatment regimens.[13] They reported that such patients needed treatment durations extended by up to 25% compared to those without HIV. This finding underscores the necessity of continuous monitoring and adjustment of treatment strategies based on radiographic findings and immune status.

Conversely, Güler et al. (2007) reported that cavitary lung disease and initial smear results were more influential on sputum culture conversion duration than HIV status.[14] They found that patients with cavitary disease had a 30% longer duration for culture conversion compared to those without, while HIV status did not significantly affect this outcome. Similarly, a study in Spain observed that HIV infection was associated with a lower frequency of cavitary lung disease and a shorter duration for sputum smear conversion, although CD4 count data was not provided (Suarez-Garcia et al., 2009).[15]

Additionally, Perlman et al. (2016) discovered that greater immunosuppression due to HIV was associated with a reduced likelihood of cavitary lesions on chest radiographs in patients with drug-susceptible tuberculosis, further complicating the relationship between HIV, radiographic findings, and treatment outcomes.[16]

The present study highlights the importance of considering both radiographic abnormalities and HIV status in the management of MDR-TB. The observed correlations between severe radiographic findings, immune suppression, and delayed culture conversion emphasize the need for a comprehensive treatment approach. Future research should focus on developing integrated treatment protocols that combine effective MDR-TB therapies with optimized HIV management to improve patient outcomes and reduce the burden of these co-existing conditions.

Conclusion

In conclusion, this study indicates that severe radiographic abnormalities, including extensive cavitary disease, significantly impact the time to culture conversion in patients with Multidrug-Resistant Tuberculosis (MDR-TB) and HIV in Peshawar. The findings underscore that while severe lung damage contributes to prolonged culture conversion, sputum smear positivity—reflecting the bacterial load—is the primary factor influencing the duration of culture negativity. These findings emphasize the importance of adapting treatment plans and closely monitoring patients with severe radiographic abnormalities and low CD4 counts. Despite these challenges, a high proportion of patients achieved culture conversion and were cured, underscoring the need for careful management and tailored treatment strategies based on individual radiographic and immunological profiles.

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