



Impact of Viral Hepatitis “C” and “B” on the Course and Effectiveness of Therapy in Patients with MDR-TB

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Abstract

Dual infections of multidrug-resistant tuberculosis (MDR-TB) or rifampicin-resistant tuberculosis (RR-TB) and hepatitis C virus (HCV) have resulted in nearly half a million cases of MDR-TB annually worldwide and 71 million people living with HCV. Aim of the study to analyze the features of the course of MDR-TB when combined with viral hepatitis “C” and “B”. We examined 354 MDR-TB patients aged from 20 to 70 years who were undergoing inpatient treatment in the 2-therapeutic department of the Tashkent City Clinical Hospital of Phthysiology and Pulmonology (TCCHPhP) in the city of Tashkent in 2021-2023. It was found that out of 354 patients, 86 (24.3%) were diagnosed with viral hepatitis. Accordingly, the development included 86 patients with co-infection with MDR-TB and viral hepatitis. Of these, 21 (24.4%) were newly diagnosed patients, 65 (75.6%) were previously treated. The spectrum of viral hepatitis was as follows: 75 patients had viral hepatitis C (87.2%), 5 patients had a combination of viral hepatitis “C” and “B” (5.8%) and 6 had viral hepatitis “B” (7%). Among those examined, the social characteristics of the patients played an important role. Thus, the bulk were unemployed—77 (89.5%). Workers and employees account for only 9 (10.5%) people. 53 people had a criminal record, which accounted for 61.6% of patients. Persons without a fixed place of residence made up 17 (19.7%) patients. Almost all patients had secondary education - 77 (89.5%), 9 (10.5%) patients had higher education. All patients had bad habits: smoking was noted in 60 (69.7%) patients, alcohol abuse - in 52 (60.4%), injecting drugs - 16 (18.6%) and nasvay use - in 6 (6.9%). Moreover, more than half of the patients had two or three bad habits - 49 (56.9%). In conclusion the study of medical and social characteristics made it possible to establish that patients with MDR/RR tuberculosis in combination with viral hepatitis belong in most cases to a socially maladjusted contingent (76.2%). The presence of bad habits, and in more than half of the cases two or three, as well as the presence of a criminal record (61.6%), persons without a fixed place of residence (19.7%), alcohol abuse (60.4%), injection drugs use (18.6%) significantly affects the treatment process.

Keywords: MDR-TB, Viral hepatitis “C” and “B”, TB treatment outcome

Introduction

Globally, an estimated 10.6 million tuberculosis (TB) cases occurred in 2021 and TB is the second leading cause of death from a single infection after SARS-CoV2 [1]. Chronic hepatitis B (HBV) and hepatitis C virus (HCV) infections are major causes of morbidity and mortality worldwide. Globally, an estimated 328 million people are chronically infected with HBV or HCV with the vast majority of people undiagnosed and untreated [2,3]. Despite the availability of interventions to prevent transmission, an estimated 3 million new chronic HBV and HCV infections occurred in 2019 and 1.1 million people died primarily due to HBV/HCV-induced chronic liver disease and liver cancer [2]. There is an overlap in the epidemiology of HBV, HCV infections, and TB due to an overlap in some of the risk factors for these infections (socio-economic factors, risk behaviours, etc.). Additionally, there is some geographical overlap with settings having a high burden for both TB and chronic viral hepatitis. Sub-Saharan Africa has the highest TB burden fuelled primarily by HIV followed by South-East Asia [1]. For multidrug-resistant (MDR)-TB, countries in the Former Soviet Union are most severely affected [1]. The African and Western Pacific WHO Regions account for two thirds of HBV infections with the African Region having the largest proportion of individuals who are unaware of their infection [2,3]. Routine testing of the general population for HBV in settings with moderate and high HBsAg prevalence can be considered, and has been shown to be cost-effective [4], however testing is frequently hampered in low-resource settings by test availability and out of pocket patient costs. New HCV infections are mainly due to unsafe practices during healthcare procedures and intravenous drug use. The highest estimated prevalence

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of chronic HCV infection in the general population can be found in the WHO Eastern Mediterranean Region at 2.3%, mainly related to unsafe injections, followed by the European Region with 1.5% with transmissions linked primarily to intravenous drug use [5].

The combination of tuberculosis and HBV/HCV co-infection is important for patient management, affects the choice of anti-tuberculosis drugs and poses a higher risk of treatment-related side effects. In addition, diagnosis of viral hepatitis when patients seek medical care can lead to initiation of treatment for viral hepatitis C and B, which will prevent future complications associated with chronic viral hepatitis.

Aim of the Study

To study the features of the course and treatment outcome of MDR-TB when combined with viral hepatitis “C” and “B”.

Materials and Methods

Study design

This was a cohort study using secondary data from medical charts and TB forms of patients with MDR-TB combined with viral hepatitis “C” and/or “B” Tashkent City Clinical Hospital of Phthisiology and Pulmonology (TCCHPhP) in Tashkent, Uzbekistan, from 2021 to 2022.

Study setting

In Uzbekistan, the commendable task of delivering comprehensive care for tuberculosis (TB) patients is entrusted to the National TB Program, which operates in seamless coordination with the Republican specialized scientific-practical medical center for phthisiology and pulmonology (RSSPMCPP). This collaboration enables the efficient implementation of various crucial activities pertaining to TB diagnosis and treatment, all of which are delivered to patients without any financial burden.

The provision of top-notch TB care spans across the entirety of Uzbekistan's robust healthcare system, catering to patients at every level of medical assistance. At the primary level, individuals seeking care for presumptive TB can easily access a network of primary healthcare facilities, commonly known as polyclinics. These polyclinics serve as the initial point of contact for patients, offering a gateway into the comprehensive TB care services available. The delivery of tuberculosis (TB) care in Uzbekistan follows a well-structured framework involving multiple levels of care. At the district level, TB clinics act as the second level of care, where patients undergo initial examinations, including a range of laboratory tests such as microscopy, XpertMTB/RIF assays, and X-rays. Based on the results, patients may be referred to higher levels of care for additional laboratory examinations, such as mycobacterial culture and the Mycobacteria Growth Indicator Tube (MGIT). Additionally, patients requiring inpatient care are also directed to the third level of TB care. For more complex cases and patients with advanced co-morbidities, the fourth level of TB care is provided at the RSSPMCPP. This level of care is dedicated to managing patients with complicated diagnoses and ensuring the highest standards of treatment.

Patients with presumptive TB typically enter the first and second levels of TB care, where they undergo initial assessments and examinations. Depending on the need for a more precise diagnosis and treatment, they may be further referred to the third and fourth levels of care. If sputum smear-positive, these patients are classified as

pulmonary TB cases and receive inpatient TB care tailored specifically for pulmonary TB. It is important to note that the national TB treatment protocols implemented in Uzbekistan strictly adhere to the guidelines provided by the World Health Organization (WHO). This adherence ensures the highest quality of care and standardization in the management of TB cases throughout the country.

Study population

The study included all patients admitted to the inpatient department of TCCHPhP from 2021 to 2022, who were diagnosed with multi-drug resistant tuberculosis (MDR-TB). The final diagnosis of MDR-TB was determined by considering various factors, including clinical symptoms, radiological evaluations such as chest X-ray or chest CT scan, and sputum examinations. These sputum examinations included bacteriological tests like smear microscopy for acid-fast bacilli (AFB), Xpert MTB/RIF, and mycobacterial culture, as well as biochemical examinations. These diagnostic tools were used to confirm the presence of MDR-TB and guide appropriate treatment approaches for the patients.

Data collection and validation

The information taken from patients' medical charts and TB forms was recorded in electronic records that were created using the EpiData application (version 3.1, EpiData Association, Odense, Denmark). To ensure accuracy, the data underwent thorough checks for errors and discrepancies through cross-tabulation and analysis of extreme values. In case any inconsistencies were identified, the source documents were consulted to resolve them. This meticulous process helped maintain the integrity and reliability of the collected data.

Data variables

To meet the study objectives, several demographic, socio-economic, and medical history-related variables were taken into consideration. These included age, sex, education level, tobacco use, alcohol consumption, and the presence of co-morbidities such as diabetes mellitus, human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV). Additionally, information pertaining to the treatment received and its outcome was noted. Detailed data on sputum examination, including microscopy, Xpert MTB/RIF, and mycobacterial culture, were also recorded. By considering these variables, a comprehensive analysis of the relevant factors influencing the study outcomes was made possible.

Definitions

Data on smoking and alcohol use were obtained based on patient self-reports. Tuberculosis treatment outcomes were classified according to the WHO recommended definitions: successful outcome (including cure and treatment completion) and unsuccessful treatment outcome comprising failure, loss to follow-up, and death [2,5-10].

Results and Discussions

We examined 354 MDR-TB patients aged from 20 to 70 years who were undergoing inpatient treatment in the 2-therapeutic department of the TCCHPhP in the city of Tashkent in 2021-2023. It was found that out of 354 patients, 86 (24.3%) were diagnosed with viral hepatitis. Accordingly, the development included 86 patients with co-infection with MDR-TB and viral hepatitis. Of these, 21 (24.4%) were newly diagnosed patients, 65 (75.6%) were previously treated. The spectrum of viral hepatitis was as follows: 75 patients had viral hepatitis C (87.2%), 5 patients had a combination of viral hepatitis

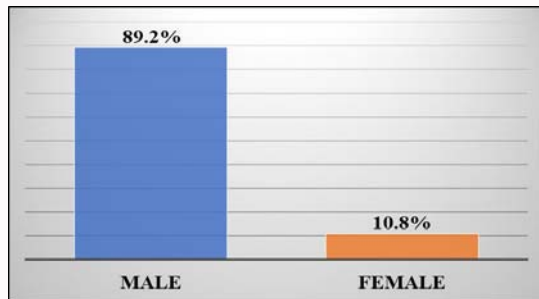


Figure 1: Distribution of patients by gender.

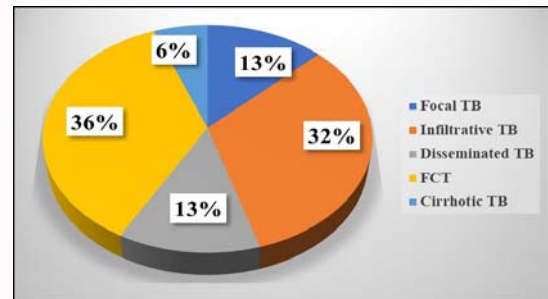


Figure 3: Distribution of patients by clinical forms.

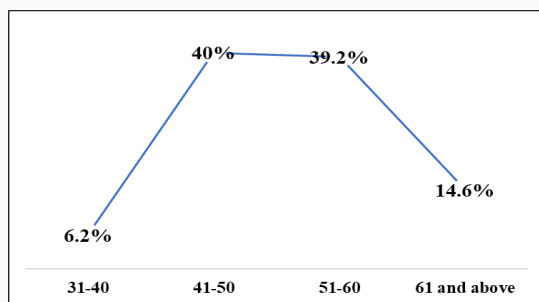


Figure 2: Distribution of patients by age.

“C” and “B” (5.8%) and 6 had viral hepatitis “B” (7%). All patients underwent a comprehensive clinical and radiological examination in a hospital setting . Mandatory (radiation research methods, bacterioscopic analysis of sputum for Mycobacterium tuberculosis , general blood test, biochemical blood test and general urine analysis) and additional research methods (advanced bacteriological diagnostics, bronchoscopy, study of liver, kidney, cardiovascular system function) were used.

It was found that among 86 patients the proportion of men was 89.2% - women 10.8%. The characteristics of patients by gender and age are presented in Figures 1 and 2.

Among the patients, the prevailing age groups were: 41-50 and 51-60 years old, accounting for 40% and 39.2%, respectively. (Figure 2)

Among those examined, the social characteristics of the patients played an important role. Thus, the bulk were unemployed—77 (89.5%). Workers and employees account for only 9 (10.5 %) people. 53 people had a criminal record, which accounted for 61.6% of patients. Persons without a fixed place of residence made up 17 (19.7%) patients. Almost all patients had secondary education - 77 (89.5%), 9 (10.5%) patients had higher education.

All patients had bad habits: smoking was noted in 60 (69.7%) patients, alcohol abuse - in 52 (60.4%), injecting drugs - 16 (18.6%) and nasvay use - in 6 (6.9%). Moreover, more than half of the patients had two or three bad habits - 49 (56.9%).

From the medical history, 41 (47.6%) patients had contact with bacillary patients. Of these, in 19 (46.3%) cases there was contact during their stay in penitentiary institutions and 22 (53.7%) - with close relatives (brother, husband, father).

According to clinical forms (Figure 3), patients are distributed as follows: focal tuberculosis - in 11 (12.8%), infiltrative pulmonary

tuberculosis - in 28 (32.5%), disseminated - in 11 (12.8%), fibrocavernous TB (FCT) - in 31 (36.1%) and cirrhotic pulmonary tuberculosis - in 5 (5.8%) patients.

Radiologically, a unilateral process was diagnosed in 33 (38.4%) patients, and in 53 (61.6%) the process was bilateral.

Upon admission to the hospital, Mycobacterium tuberculosis was detected in the sputum by various methods in 55 (63.9%) patients. Of these, MBT was found in 21 (38.2%) cases in newly diagnosed cases, and in 34 (61.8%) among previously treated cases.

All patients showed symptoms of intoxication upon admission to the hospital. 65 (75.6%) patients were admitted in a state of moderate severity, in a serious condition - 12 (13.9%) and in a relatively satisfactory condition - 9 (10.5%) patients. MDR-TB of the lungs in combination with hepatitis was characterized by a fairly clear clinical picture. Thus, an increase in body temperature was noted in 59 (68.6%) patients, complaints of general weakness were found in almost all patients. Body weight loss of 5 kg or more was detected in 69 (80.2%) patients, loss of appetite - in 83 (96.5%). In 2 (2.3%) patients, hoarseness was noted as a sign of generalization of the process (Figure 4).

All patients had various clinical manifestations of the respiratory system. As can be seen from Figure 5, the leading clinical symptom in 84 (97.6%) cases is cough, mainly with sputum - in 61 (71%). Chest pain occurred in 16 (18.6%) patients, which is a sign of involvement of the parietal pleura in the process.

Changes in the hemogram were detected in 91.8% of cases (79 out of 86 people). Most often, an acceleration of ESR was observed (more than 32 mm per hour) - in 88.1% of cases. Changes in red blood showed that: 54 patients (62.7%) had anemia of degrees 1,2 and 3. Lymphopenia was detected in 32 (37.2%) patients and leukocytosis - in 16 (18.6%).

Of the 86 patients with tuberculosis with concomitant hepatitis, 59

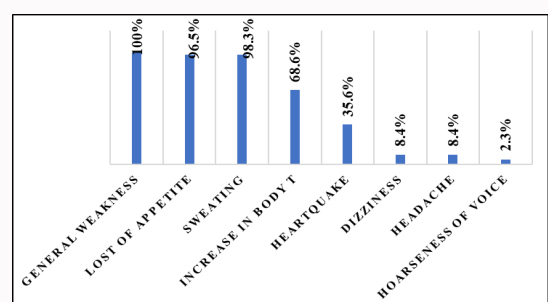


Figure 4: Distribution of patients according to symptoms of intoxication.

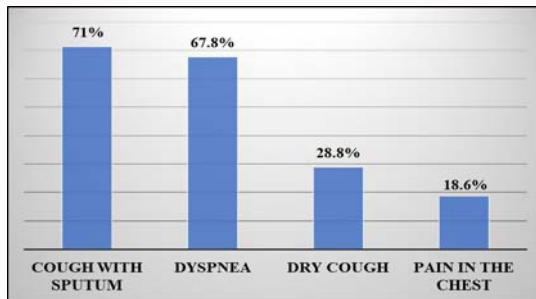


Figure 5: Distribution of patients by bronchopulmonary symptoms.

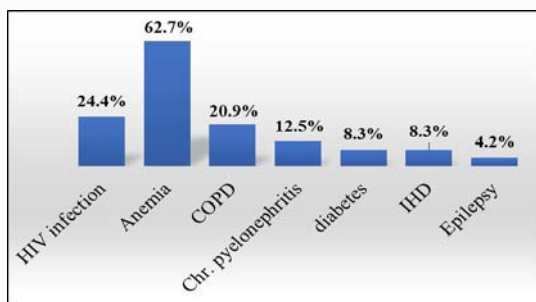


Figure 6: Distribution of patients by concomitant diseases.

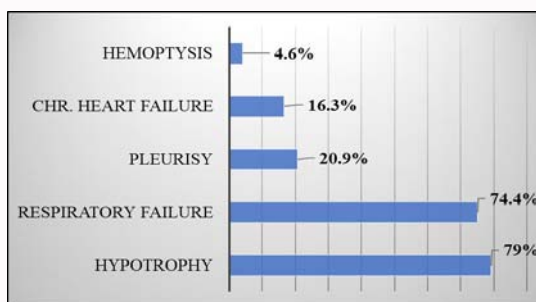


Figure 7: Distribution of patients by complications.

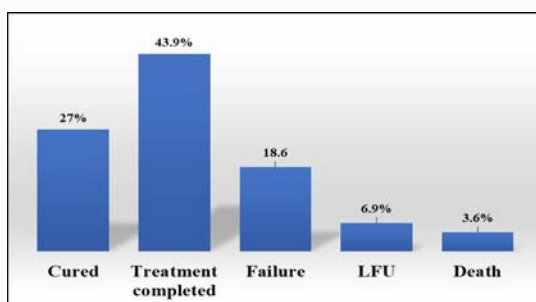


Figure 8: Treatment outcome.

(68.6%) had the following other concomitant diseases. Of these, more than half of the patients had two, three or more concomitant diseases, 23 (26.7%) and 21 (24.4%), respectively. Only 42 (48.8%) patients had one concomitant pathology. Information on the frequency and nature of concomitant diseases is presented in Figures 6-8.

When analyzing the structure of concomitant diseases, a predominance of anemia was noted - in 54 (62.7%), followed by frequency of occurrence: HIV infection - in 21 (24.4%) and COPD -

in 18 (20.9%). Other pathologies occur in isolated cases.

According to our data, various complications were identified in almost all patients against the background of the tuberculosis process in combination with viral hepatitis. When studying the structure of complications, it was established that hypotrophy of 1, 2, 3 degrees was noted in 68 (79%) patients, respiratory failure - in 64 (74.4%), chronic heart failure (CHF) - in 14 (16.3%) patients. A combination of two or more complications was observed in 57 (66.3%) patients. Hemoptysis was observed in 4 (4.6%) patients, exudative pleurisy - in 18 (20.9%). This group consisted mainly of patients with destructive forms of pulmonary tuberculosis.

Anti-tuberculosis therapy was carried out taking into account the presence of resistance to antibacterial drugs. All patients received anti-tuberculosis treatment according to the standards of the national clinical protocol for the treatment of patients with MDR/RR-TB with drugs of the second group.

As a result of treatment, successful treatment was achieved (cured, treatment completed) in 61 (70.9%) patients, failure of treatment in 16 (18.6%), lost to follow-up in 6 (6.9%) and death due to complex treatment was observed in 3 (3.6%) cases [10-16].

Conclusions

1. The conducted analysis of medical and social characteristics demonstrated that patients with MDR/RR tuberculosis combined with viral hepatitis predominantly represent a socially maladjusted group, reaching 76.2%. This category of patients is characterized by a high prevalence of negative behavioral and social factors, which considerably complicate the treatment process and reduce adherence to therapy. More than half of the patients simultaneously have two or even three harmful habits, among which alcohol abuse (60.4%) and injection drug use (18.6%) are most prominent. Additionally, a significant proportion of individuals have a criminal record (61.6%) and lack stable housing (19.7%), which further aggravates their social vulnerability. The combination of these unfavorable conditions underscores the necessity of developing comprehensive medical, psychological, and social support strategies to enhance treatment outcomes in this particularly complex patient population.

2. The results of the study clearly demonstrate that the presence of viral hepatitis significantly worsens the clinical course of tuberculosis, leading to more severe manifestations of the disease and contributing to a decrease in the overall effectiveness of anti-tuberculosis therapy. According to the obtained data, in 29.1% of patient's treatment outcomes were assessed as unsuccessful, which reflects the pronounced negative impact of concomitant hepatic pathology on therapeutic efficacy. It was also established that the success of treatment largely depends on the timeliness of initiating hepatoprotective therapy in parallel with anti-tuberculosis treatment. The earlier such supportive therapy is started, the higher the likelihood of achieving stable clinical and bacteriological improvement. At the same time, when prescribing therapy, it is critically important to take into account the individual sensitivity of the pathogen to antibacterial drugs, which makes it possible to reduce hepatotoxic risks and increase the chances of favorable outcomes. These findings emphasize the necessity of an integrated treatment approach for patients with tuberculosis and viral hepatitis, involving early hepatoprotective support and individualized selection of anti-tuberculosis regimens.

Author Contributions

Conceptualization and methodology L.M., F.A.; data collection L.M., D.O.; data analysis and interpretations— L.M.; writing— original draft preparation L.M.; final review and approval L.M., F.A., D.O. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author, [L.M.], upon reasonable request.

Informed Consent Statement

A waiver of informed consent was granted by ethics review bodies, as the study collected and analyzed de-identified routine recording and reporting data.

Ethics Statement

his research did not involve human participants, animal subjects, or any material that requires ethical approval.

Clinical Trial Registration

This research does not involve any clinical trials.

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