The long duration of treatment, toxicity and lack of treatment options, adversely effect the physical and mental well-being of multidrug-resistant tuberculosis (MDR-TB) patient.
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First International Conference on RASopathies in Asia: Advances in RASopathies and Neurofibromatoses and in Identification of New Therapeutic Targets
The Course of the Disease in Patients with Multidrug Resistant Tuberculosis with Depression

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Abstract
Aims: Despite research advances in the microbiological and clinical aspects of MDR-TB, research on the psychosocial context of MDR-TB is limited and less understood and requires more intervention and interpretation. Our study aims to determine the course of the disease in patients with multidrug-resistant tuberculosis with depression.

Methods: The data of 45 patients with chem-drug resistant tuberculosis, who belonged to 4th treatment category were examined. Patients were interviewed using the HADS scale and the reliability of the differences in qualitative indices between groups was determined by Fisher's exact test.

Results: It was determined that the proportion of patients among the persons who were treated in the 4th category for the first time and received anti-tuberculosis drugs for a duration of more than 4 months, was greater in the 1st group 1: 5 patients (62.5%) versus 3 persons (11.1%) in the 2nd group, p<0.01. So, depression mostly affects patients, who treated for a longer time.

Conclusions: From the obtained data it is shown that drug users and patients who treated more than 4 months have psychological problems that complained after specific therapy side effects. In patients with functional disorders, depression is a reason for diseases course severity.

Key Words
Multidrug-Resistant Tuberculosis; Depression; Psychological Stress; Infectious Disease; Microbiology

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Introduction: The long duration of treatment, toxicity and lack of treatment options, adversely affect the physical and mental well-being of multidrug-resistant tuberculosis (MDR-TB) patient. Regardless of advancement in the microbiological and clinical aspects, research on the psychosocial context of MDR-TB is limited and less understood, requiring more intervention and interpretation. The emergence of mental disorders in patients with multidrug-resistant tuberculosis (MDR-TB) are due to the same risk factors for their disease development, namely being stress, family and financial reasons. The impact of tuberculosis as a socially dangerous disease has been progressing due to side effects from the treatment for a longer period of anti-TB medicines and fear of treatment failure, as well as due to the social isolation of patients. Amongst all psychiatric disorders, depression is widely prominent in patients with MDR-TB. The global burden of MDR-TB is estimated to be around 60% in countries like India, China, and Russia. Due to the high transmission rate, illiteracy, poor knowledge and inability to afford the treatment from private practitioners makes the disease contagious especially in high density communities. The perception of psychological stress is obscure but it is largely defined as a state of emotional suffering with a variety of symptoms like anxiety and depression. Psychological stress is the major cause of mortality and individuals having high stress die 25 years earlier than normal population. The poor prognosis is due to the long duration of treatment and drug toxicity, causing resistance and this psychological distress also complicates the treatment of MDR-TB.

Aim
Our study aims to determine the course of the disease in patients with multidrug-resistant tuberculosis with depression.

Material and methods
45 patients with chemo-drug resistant tuberculosis, who belonged to 4th treatment category were
examined. Patients were interviewed using the HADS scale and were divided into 2 groups. The first group included 10 people who scored 8 or more points on HADS scale, who were predisposed to severe depression. The group consisted of 6 men (60.0 %) and 4 women (40.0 %), with a mean age of 39.2 ± 2.3 years. The 2nd group (comparison group) consisted of 35 patients who scored less than 8 points on the HADS scale. The number of men in the comparison group was 27 (77.1 %), women – 8 (22.9 %), the mean average age of patients was 38.5 ± 1.8 years. Both the groups were represented by gender and age (p<0.05).

The statistical analysis and the differences between groups were performed using the STATISTICA® for Windows 6.0 (Stat Soft Inc., AXXR712D833214FAN5). The reliability of the differences in qualitative indices between groups was determined by Fisher’s exact test. The value of the reliability indicator of the difference between groups for the level of statistical significance (p) was taken to be less than 0.05.

**Results and Discussion**

About 1/5th of patients in both groups (20.0 % in the 1st and 22.9 % in the 2nd) were treated repeatedly after the failure of the first course of anti-tuberculosis therapy. It was determined that the proportion of patients among the persons who were treated in the 4th category for the first time and received anti-tuberculosis drugs for a duration of more than 4 months, was greater in the 1st group: 5 patients (62.5 %) versus 3 persons (11.1 %) in the 2nd group, p<0.01. So, depression mostly affects patients, who treated for a longer time. It may be because of drugs side effects, long conversations with other patients who have poor treatment outcomes, or a feeling of total loneliness.

According to the tuberculosis case and their type, the groups of patients did not differ statistically and were not significant (Figure 1).

![Figure 1: Tuberculosis Cases and Their Types in the Patients' Groups](image-url)
So, there were no differences found between the groups in types of tuberculosis cases and in types of drug resistance cases.

4 patients of 1st group (injecting drugs) drug addicts (40.0 %), only 1 patient (2.9 %) in the 2nd group was a drug addict, p<0.01. The proportion of patients with HIV/AIDS co-infection was greater among the patients in the group 1: 4 (40.0 %) patients in the 1st group versus 3 (8.6 %) in the 2nd group, p<0.05. According to the other concomitant diseases (diabetes mellitus, viral hepatitis, bronchitis), the groups did not differ significantly. The higher proportion of drug addicts among MDR-TB patients with depression may be explained because of narcotic drug using and psychological problems, associated with them.

Most patients in both the groups had bacterial secretion: 9 patients (90.0 %) in 1st group and 32 (91.4 %) in the 2nd group. Massive bacterial secretion was observed in 4 (40.0 %) 1st group patients and in 18 (51.4 %) of 2nd group, p>0.05. In 1 patient from the 2nd group, extrapulmonary tuberculosis was diagnosed. All the remaining patients had pulmonary lesions. Disseminated pulmonary tuberculosis occurred in 3 patients from the 1st group (30.0 %) and in 12 (34.3 %) – from the 2nd group, infiltrative – in 6 patients (60.0 %) from the 1st group and in 17 (48.6 %) – from 2nd group. In 1 patient from the 1st group, there was fibrous-cavernous pulmonary tuberculosis, whereas, in 6 patients of the 2nd group there was caseous pneumonia and fibrocavernous tuberculosis, p>0.05.

The proportion of patients with pulmonary destruction was almost the same in both groups: 80.0 % of patients in the 1st group and 85.7 % in the 2nd group, the average size of the cavities in the 1st group patients was 3.3 ± 1.1 cm, in 2nd group patients – 2.8 ± 0.4 cm, p>0.05.

More distinct functional disorders were registered in patients of the 1st group: according to the indicators like external respiration, failure of ventilation of 2nd and 3rd degree were diagnosed in 5 (71.4 %) 1st group of patients and 9 (26.5 %) 2nd group patients, p<0.05.

So, there were not differences in clinical forms and radiological changes, but there were more patients with depression in patients, who had more severe failure of ventilation, because of the impact of functional disorders on quality of life of patients.

Adverse drug reactions took place in 7 patients (70 %) from 1st group and in 22 (62.9 %) – from the 2nd group, p>0.05. Half of them were associated with clinical changes: in 5 patients (50 %) from 1st group and in 17 (48.6 %) – from 2nd, p<0.05. In 5 cases in 1st group (50 %) and in 6 (17.1 %) in 2nd group side effects weren’t cured, p<0.05. So, not cured side effects worsened disease course and quality of patient’s life, that’s why there were more patients with depression among such persons.

Many studies have been conducted to depict the course of the disease in patients with multidrug-resistant tuberculosis with depression.

**Figure 2:** Chemo-Drug Resistant Cases Types in Patient’s Groups
Fentie Ambaw et al 2017\textsuperscript{17}, conducted a cross sectional study on 657 participants. They used PHQ-9 (Patient Health Questionnaires) scale to calculate depression. He suggested that incidence of depressive symptoms is a usual manifestation of tuberculosis. He also stated that female sex, old age are positive aspects and level of education, social support are negative aspects for the occurrence of depression.

Minalini Das et al 2014\textsuperscript{18}, conducted a retrospective cohort study on 45 patients with 7 having depressive symptoms. They specified that routine administration of mental health evaluations by trained staff can help in determining and managing the depression signs during MDR-TB treatment. They also recommended nursing of mental health position by clinical staff.

Arshad Javaid et al 2014\textsuperscript{19}, did a cross sectional study in 289 people of Pakistan. In this study they stated that continuous monitoring of patient’s mental health status is important. Educating patients and their family members helps in proper management of a patient’s condition during entire illness.

In our study we state that Depression affects patients with MDR-TB mostly if they are drug addicts (p<0.01) if they had a ventilatory failure of 2\textsuperscript{nd} and 3\textsuperscript{rd} degree (p<0.05), uncured adverse drug reactions (p<0.05) and if they were treated for more than 4 months (p<0.01). It means that drug users and patients who were treated for more than 4 months have psychological problems that complained after specific therapeutic side effects. In patients with functional psychological problems that complained after specific therapeutic side effects. In patients with functional psychological problems that complained after specific therapeutic side effects.

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