



DRUG RESISTANCE OF MYCOBACTERIUM TUBERCULOSIS CLINICAL ISOLATES FROM NEW TB CASES IN KAZAKHSTAN

**U. Kozhamkulov¹, A. Akhmetova¹, S. Rakhimova¹, A. Daniyarov², A. Molkenov², V. Bismilda³,
L. Chingissova³, U. Kairov², A. Akilzhanova¹**

¹Laboratory of Genomic and Personalized Medicine, National Laboratory Astana, Nazarbayev University, Nur-Sultan City, Kazakhstan

²Laboratory of Bioinformatics and Systems Biology, National Laboratory Astana, Nazarbayev University, Nur-Sultan, Kazakhstan

³National Scientific Center of Phthisiopulmonology the Republic of Kazakhstan, National reference laboratory, Almaty, Kazakhstan

ulan.kozhamkulov@nu.edu.kz

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Introduction: Nowadays and worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent. The global incidence of drug-susceptible TB, multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis in the past decade led to decreased efficiency of chemotherapy. In Kazakhstan, the 2019 WHO report estimates the TB incidence in 2018 to be 68 per 100 000 population and the MDR-TB incidence to be 26/100,000 (WHO, 2019). Therefore, the goal of the study is to analyze clinical isolates from new TB Kazakhstani patients by determining drug resistance, genotyping and whole genome sequencing.

Methods: 192 M. tuberculosis drug resistant strains from new TB cases were analyzed. Resistance to the first-line anti-TB drugs were determined using absolute concentration method on L-J media and BACTEC MGIT-960. Spoligotyping was performed using commercially available kit "Ocimum Biosolutions Inc". The whole genome sequencing was carried out on Roche 454 GS FLX+ platform.

Results: The structure of 192 drug resistant isolates showed that 98 (51.04%) were MDR, 55 (28.65%) – polyresistant, 39 (20.31%) – mono-resistant. Genotyping results showed that W-Beijing family identified in 143 (74.48%) cases, T – 23 (11.98%), LAM – 11 (5.73%), Haarlem – 10 (5.21%), U – in 4 (2.08%) and MANU-2-1 (0.52%) case only. W-Beijing family M. tuberculosis was a dominant genotype and composed more than 50% of two resistant groups: polyresistant – 70.9% and MDR – 87.75% clinical isolates of M. tuberculosis. Missense mutation of rpoB gene at codon 531 with amino acid substitution Ser/Leu was the prevalent among mutations responsible for rifampicin resistance (87.75%). In case of isoniazid resistance, the most prevalent (96.94%) mutation was substitution at codon 315 Ser/Thr including 3 cases (3.06%) with double mutation when replacement simultaneously took place at katG gene and -15 position of promoter mabA (fabG)-inhA operon.

Conclusion: MDR strains are predominant among resistant strains and mostly belong to Beijing family in Kazakhstan. W-Beijing is the most common genotype among all categories of drug resistant M. tuberculosis. As such MDR-TB should be a national priority in National TB Program for Kazakhstan.

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