MAPPING OF ECO-SOCIAL AND GENETIC FACTORS OF SUSCEPTIBILITY TO TUBERCULOSIS AMONG THE POPULATION OF THE REPUBLIC OF KAZAKHSTAN

A. Akhmetova[*], **S. Rakhimova, U. Kairov, Zh. Abilova, A. Askapuli,**
M. Zhabagin, D. Yerezhepov, A. Abilmazhinova,A. Molkenov, A. Akilzhanova

Center for Life Sciences, Nazarbayev University, Astana, Kazakhstan; [*]ainur.akhmetova2@nu.edu.kz

INTRODUCTION.

Tuberculosis (TB) remains a major health problem in Kazakhstan, especially multidrug-resistant TB (MDR-TB). According to various publications, 60-96% of all isoniazid-resistant strains have mutations in *katG* gene, 96-98% of all rifampicin-resistant strains have mutations in “hotspot region” (region between 507 and 533 codons) of *rpoB* gene (1). Polymorphisms of VDR gene (*FokI/rs2228570, ApaI/rs7975232, TaqI/rs731236)* have been reported to be associated with tuberculosis susceptibility in different studies [2].

STUDY DESIGN.

In this study *combined design* was used, which included: 1) Case-control study; 2) Molecular-epidemiological study; and 3) Study of human genetic susceptibility to tuberculosis.

MATERIALS AND METHODS.

Genotyping of 525 samples of venous blood (184 cases and 341 controls) of Kazakh population from Almaty city, Almaty region and Kyzylorda city was carried out using 7900HT (Applied Biosystems) with the set of TaqMan probes for SNP markers by Real-time PCR. Sequencing of genome fragments of 202 culture of *M.tuberculosis* from new TB cases from studied regions of Kazakhstan was done using ABI 3730 GeneticAnalyzer (Applied Biosystems, USA). The Mantel-Haenszel method and Logistic Regression were used to analyze the data obtained from matched case-control study.

RESULTS AND CONCLUSION.

Among clinical isolates of *M.tuberculosis* 39.6% (80 of 202) samples showed a mutation in *katG* (315 Ser→Thr). 4 variants of mutations at codons 531, 516, 533 and 526 were detected in *rpoB* gene. A mutation at codon 531 (Ser → Leu) was the prevalent mutation in *rpoB* gene – 43 (21,5%). Tendency to association of G/A genotype with high risk of tuberculosis development in co-dominant model (OR=1.27; 95% CI: 0.86-1.88 P=0.28) for *FokI* polymorphism, A/A genotype (OR=1.21; 95% CI: 0.72-2.02 P=0.77) for *TaqI* polymorphism was found.

This work is the first case-control study in Kazakhstan where complex factors of TB risk and their effects are estimated. The study confirmed the role of main risk factors of tuberculosis development in Kazakhstan: young age, single relationship status, living in rent apartment, smoking, diabetes and migration.

ACKNOWLEDGEMENTS.

We would like to express special gratitude to our collaborators: National Center of Tuberculosis Problems of the Republic of Kazakhstan, Association of phthisiatricians of Kazakhstan, and The Global Health Research Center of Central Asia, Columbia University.

REFERENCES.

1. Ying Z., Jacobs W.R., Jr. (2005). Mechanisms of Drug Resistance in *Mycobaterium tuberculosis.* Tuberculosis and the Tubercle Bacillus. Chapter 8, pp. 115-140.

2.Kang T.J., *et.al.* (2011). Vitamin D receptor gene *TaqI, BsmI* and *FokI* polymorphisms in Korean patients with tuberculosis. Immune Network, 11 (5): 253-257.