

ASSOCIATION OF VITAMIN D RECEPTOR (FOKI, TAQI, APAI & BSMI) AND IF-Y GENES' POLYMORPHISMS WITH RISK OF DEVELOPING PULMONARY TB (PTB) AMONG KAZAKHSTANI POPULATION

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Introduction. Almost one third of the world's population is infected with *Mycobacterium tuberculosis* (MTB) and only 10% of them will develop any active form of the disease. TB is second (1st is HIV/AIDS) greatest killer worldwide due to a single infectious agent. In 2012, 8.6 million people developed active TB and 1.3 million died. Over 95% of TB deaths occur in developing countries. In 2012, an estimated more than half million children became ill with TB and 74 000 of them died. The TB cases are declining annually, but very slowly. Multi-drug resistant TB (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) is present in almost all surveyed countries. Kazakhstan is not highly burdened by TB. Kazakhstan is the list of MDR-TB and XDR-TB burden countries. Our aim is to investigate an association of Vitamin D receptor (FokI, TaqI, ApaI & BsmI) and IF-y genes" polymorphisms with risk of developing pulmonary TB (PTB) among Kazakhstani population.

Materials and methods. Patients and healthy volunteers recruitment from Kostanay, Almaty and Kizilorda regions of Kazakhstan. Data collection by medical cards, interviews and questionnaires for environmental factors and epidemiological data. Genotyping for specific SNPs. Analysis of genotyping data for correlation with PTB susceptibility.

Results and discussion. All required epidemiological data from 1569 participants collected. 560 cases, 489 samples of familial control and 520 samples of external control. 46.6% of all participants were males. Kostanay, Almaty and Kizilorda represented by 415, 648, and 506 samples respectively. Kazakhs were major nationality in group (75.65%). Russians (15.3%) were 2nd, Uighurs (2.93%) were 3rd major nationality. Social factor as employment was main, because income amount will contribute to the health status. Employed/unemployed participants" ratio was approximately equal but 65% of all cases were unemployed. Main risk factor was tobacco smoking (14.5%). Risk factors like diabetes (3.5%), contact with TB (2.0%), alcohol consumption (1.7%) also were included as moderate. Maternity leave, Narcomania and HIV were included but contributed less than 2% in total. Genotyping of all group did not show significant association with PTB ($p > 0.05$) possibly due to heterogeneity of participants. However grouping by covariate "Gender" showed association with susceptibility to PTB among participants in TaqI-C/C genotype (OR=1.27; 95%, CI: 0.93-1.74, $p=0.054$), BsmI-C/T (OR=1.46; 95%, CI: 1.07-1.98, $p=0.049$) of VDR gene, and A/A genotype of IF-y gene (OR=1.95; 95%, CI: 1.07-3.55, $p=0.029$) among females. Analysis inside "Ethnicity" showed strong correlation with susceptibility (OR=2.11; 95%, CI: 1.04-4.27, $p=0.039$) to PTB among Caucasians of research participants. Genotyping results inside Cases revealed very strong association with susceptibility to PTB among Caucasians by 4 polymorphisms. Caucasian population of Kazakhstan are more susceptible in compare to Asians more than 2.5-fold.

Conclusions. Biobank of TB samples is established. e-Database is constructed. Analysis of genetic and epidemiological data revealed susceptibility to PTB among women of Kazakhstan. Results showed strong correlation among Caucasian ethnic group of participants. Results can be used as prerequisites for personalized approaches in PTB treatment. Further investigation is needed to collect more data for understanding whole picture and mechanism of PTB and its elimination.