

² *Chiril Draganiuc* Pneumophthysiology Institute of the Republic of Moldova

Introduction. Isoniazid monoresistance is the most common type of single TB drug resistance worldwide. There is no strong evidence regarding the best treatment regimens in this group of patients.

Aim of the study. To assess the impact of HR tuberculosis (TB) on treatment outcomes and survival among pulmonary TB patients treated under TB control program in the Republic of Moldova.

Materials and methods. We have performed a comparative retrospective analysis of treatment outcomes in all pulmonary TB patients registered in the National Electronic TB data base (SIME TB) during 2012-2016. Only patients with positive culture and proven isoniazid monoresistance or pan-susceptibility to the first line drugs were included.

Results. During 2012-2016, 191 monoresistant and 1889 pan-susceptible pulmonary TB cases were registered in SIME TB. No differences in age, gender, previous history of TB and comorbidities between monoresistant and pan-susceptible patients have been identified. All study subjects were treated with first line TB drugs regimens recommended by National Treatment Guidelines. Contrary to the expectations no differences were identified between pan-susceptible and isoniazid monoresistant subjects regarding the rates of cure (84.2% vs 84.8%, $p > 0.05$), treatment failure (3.54 vs 5.24%, $p > 0.05$) and death (6.65% vs 5.76%, $p > 0.05$). At the same time monoresistant subjects had a shorter treatment duration than those with pan-susceptibility (141 vs 224 days, $p < 0.0001$)

Conclusion. Our findings suggest that compared with pan-susceptible TB, patients in with isoniazid monoresistant TB treated under programmatic condition in Republic of Moldova have similar final TB treatment outcomes including all-cause mortality.

Key words: susceptible TB, treatment outcomes, treatment regimens

DEPARTMENT OF PNEUMOPHTYSIOLOGY

102. RISK STRATIFICATION BY A SIMPLE CLINICAL SCORE (CRD-45) IN PATIENTS WITH TUBERCULOSIS

Author: **Peter Lange**

Scientific adviser: Lange C., MD, PhD, FISA, FERS, Professor, Division of Clinical Infectious Diseases, Research Center Borstel, Germany

International Health/Infectious Diseases, University of Lübeck, Germany

Introduction. Tuberculosis is a leading cause of morbidity and mortality worldwide. According to the World Health Organization, 10.4 million people developed tuberculosis in 2016 and 1.7 million people died from this disease.

Materials and methods. We evaluated risk factors from in-hospital death in patients admitted with tuberculosis between January 2012 and March 2017 at a tuberculosis referral hospital in Borstel, Germany.

Aim of the study. Risk factors assessment in patients with tuberculosis as mortality predictors.

Results. Among 354 patients admitted to the Medical Clinic of the Research Center Borstel, Germany, 12 patients died in hospital. Median duration from admission to in-hospital death was 70 days (Interquartile range (IQR) 23 - 129). Four variables 1) >50 pack years of cigarette smoking, 2) renal insufficiency, 3) diabetes mellitus and 4) >45 years of age were predictors of mortality in patients with tuberculosis. When none of these variables were present the risk of in-hospital mortality was 1.0%. With 2, 3 and 4 of the variables present the risk of in-house mortality increased to 3.7%, 6.5%, 33% and 50%.

Conclusions. A simple score (CRD-45 TB-score) based on 4 clinical variables was highly predictive for the in-house mortality in patients with tuberculosis from this cohort. Generability of this score to predict in-house morbidity of patients with tuberculosis should be prospectively evaluated in a larger multicenter cohort.

Key words: tuberculosis, in-hospital death, risk evaluation, CRD-45 TB-score

103. COMPARISON OF MOLECULAR DRUG RESISTANCE TESTING AND PHENOTYPIC DRUGRESISTANCE TESTING IN MULTI- AND EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS

Author: **Hape Grobbel**

Scientific advisers: Heyckendorf J, Lange C, Division of Clinical Infectious Diseases, Research Center Borstel, Germany

International Health/Infectious Diseases, University of Lübeck, Germany

Introduction. For the treatment of MDR and XDR tuberculosis, it is important to select the most suitable drug regimen. The resistance testing procedure should be as fast and accurate as possible. Within the framework of personalized medicine, the most suitable therapy approach for the individual patient should be found. With the faster available information from a new form of susceptibility testing, the best regimen could be created in a shorter period of time and the appropriate therapy for the patient could be initiated.

Aim of the study. With our study we want to compare the genotypic drug resistance testing with phenotypic drug resistance testing. It will demonstrate to what extent the measured resistance results overlap and where there may be differences.

Materials and methods. We compared the utility of genotypic DST assays with phenotypic DST (pDST) using Bactec 960 MGIT or Löwenstein-Jensen to construct M/XDR-TB treatment regimens for a cohort of 25 consecutive M/XDR-TB patients and 15 possible anti-TB drugs. Genotypic DST results from Cepheid GeneXpert MTB/RIF (Xpert) and line probe assays (LPAs; Hain GenoType MTBDRplus 2.0 and MTBDRsl 2.0) and whole-genome sequencing (WGS) were translated into individual algorithm-derived treatment regimens for each patient. We further analyzed if discrepancies between the various methods were due to flaws in the genotypic or phenotypic test using MIC results.

Results. Compared with pDST, the average agreement in the number of drugs prescribed in genotypic regimens ranged from just 49% (95% confidence interval [CI], 39 to 59%) for Xpert and 63% (95% CI, 56 to 70%) for LPAs to 93% (95% CI, 88 to 98%) for WGS. Only the WGS regimens did not contain any drugs to which pDST showed resistance. Importantly, MIC testing revealed that pDST likely underestimated the true rate of resistance for key drugs (rifampin, levofloxacin, moxifloxacin, and kanamycin) because critical concentrations (CCs) were too high.

Conclusions. With the analysis of the genome, even in M/XDR strains with complex resistance patterns it is possible to characterize these resistances. The procedure is fast and the results are very similar to those of phenotypic testing. Only for some drugs, the susceptibility test has to be carried out phenotypically in order to compile the final regimes.

Key words: Mycobacterium tuberculosis; drug resistance testing; molecular genetics

104. ADDITIONAL SECOND LINE TB DRUG RESISTANCE IN HIGH BURDEN MDR TB SETTING

Authors: **Angela Osmatescu, Elena Chesov**

Scientific adviser: Valeriu Crudu, MD, Lecturer, Department of Pneumophthysiology

Nicolae Testemitanu State University of Medicine and Pharmacy of the Republic of Moldova