

## The Role of Molecular-Genetic Assays in Diagnosis of Pulmonary Tuberculosis in the Republic of Moldova

**Evelina Lesnic, Malic Alina** 

https://doi.org/10.1007/978-3-031-42782-4\_47

## **Abstract**

The culture with the drug susceptibility testing are the gold standard in diagnosis of tuberculosis (TB). However the use of the new molecular genetic test for identification of Mycobacterial tuberculosis DNA based on polymerase chain reaction contributed to earlier diagnosis of TB, prompt start of the treatment according to the drug resistance profile and improvement of the clinical case-management. The aim of the study was to assess the role of molecular genetic tests in diagnosis of pulmonary TB in the Republic of Moldova. A selective, prospective and case-control study on 673 new cases diagnosed with pulmonary TB in 2022 was conducted. The patients were distributed in the main study group, which included 431 patients with positive molecular genetic test GeneXpert MTB/Rif (Xpert) assay, from which 304 were sensible and 127 resistant to Rifampicin, which were compared with the control group composed of 242 patients with negative Xpert assay. Based on the collected data the predictors for positive molecular genetic assays were extensive and severe forms of pulmonary TB, high expressiveness of the clinical complains and associated disease. The risk factors for acquiring the drug-resistance were TB contact, the history on incarceration and the comorbid state. Due to precocious diagnosis of the drug-resistance and adaption of the TB treatment to the drug-resistance results, the unfavorable treatment outcomes were in a significant lower proportion in patients diagnosed through the Xpert compared with those diagnosed through the conventional



culture methods. In conclusion, the molecular genetic assays improved the TB casemanagement due to precocious diagnosis and adequate therapeutic approach. *Keywords: pulmonary tuberculosis, molecular-genetic assays* 

## References

- 1. The End TB Strategy. Global Strategy and Targets for Tuberculosis Prevention, Care, and Control After 2015. World Health Organization, Geneva (2014) (electronic version). https://www.who.int/publications/i/item/WHO-HTM-TB-2015.19
- 2. Global Tuberculosis Report 2022. World Health Organization, Geneva (2020). ISBN 978-92-4-006172-9 (electronic version). <a href="https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022">https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022</a>
- 3. Nahid, P., Dorman, S.E., Alipanah, N., et al.: Official American thoracic society/centers for disease control and prevention/infectious diseases society of America clinical practice guidelines: treatment of drug-susceptible tuberculosis. Clin. Infect. Dis. **63**(7), e147–e195 (2016). <a href="https://doi.org/10.1093/cid/ciw376">https://doi.org/10.1093/cid/ciw376</a>
- 4. European Centre for Disease Prevention and Control. WHO Regional Office for Europe. Tuberculosis Surveillance and Monitoring in Europe 2022–2020 Data.WHORegional Office for Europe and Stockholm: European Centre for Disease Prevention and Control, Copenhagen (2022). Licence: CC BY 3.0 IGO
- 5. Afsar, I., Gunes, M., Er, H., Gamze, S.A.: Comparison of culture, microscopic smear and molecular methods in diagnosis of tuberculosis. Rev. Esp. Quimioter. **31**(5), 435–438 (2018)
- 6. Rakotosamimanana, N., Lapierre, S.G., Raharimanga, V.: Performance and impact of GeneXpert MTB/RIF® and LoopampMTBCDetectionKit® assays on tuberculosis case detection in Madagascar. BMC Infect Dis. **19**(1), 542 (2019). <a href="https://doi.org/10.1186/s12879-019-4198-6">https://doi.org/10.1186/s12879-019-4198-6</a>
- 7. Penn-Nicholson, A., Georghiou, S.B., Ciobanu, N., et al.: Detection of isoniazid, fluoroquinolone, ethionamide, amikacin, kanamycin, and capreomycin resistance by the Xpert MTB/XDR assay: a cross-sectional multicentre diagnostic accuracy study. Lancet Infect Dis. **22**(2), 242–249 (2022). https://doi.org/10.1016/S1473-3099(21)00452-7
- 8. Lesnic, E., et al.: The impact of the risk factor on the incidence of tuberculosis in Chisinau. Arta Med. **81**(4), 11–17 (2021). https://doi.org/10.5281/zenodo.5856850



- 9. Lesnic, E., Malic, A.: The predictors of pulmonary tuberculosis in Xpert MBT/Rif positive and resistant assay patients with diabetes mellitus. Moldovan Med. J. **61**(2), 23–29
- 10. (2018). <a href="http://moldmedjournal.md/wp-content/uploads/2018/10/moldmedjournal-2018-612-lesnic-full-article.pdf">http://moldmedjournal.md/wp-content/uploads/2018/10/moldmedjournal-2018-612-lesnic-full-article.pdf</a>
- 11. Protocolul Clinic Nat,ional "Tuberculoza la Adult". Chis,in au (2020). [National Clinical Protocol. "Tuberculosis in adults". Chisinau; 2020]. (Romanian)
- 12. Protocolul Clinic Nat,ional "Tuberculoza la Copil". Chis,in au (2020). [National Clinical Protocol. "Tuberculosis in children". Chisinau; 2020]. (Romanian)
- 13. Teo, A.K.J., Singh, S.R., Prem, K., et al.: Delayed diagnosis and treatment of pulmonary tuberculosis in high-burden countries: a systematic review protocol. BMJ Open **9**, e029807 (2019). https://doi.org/10.1136/bmjopen-2019-029807
- 14. Saktiawati, A.M.I., Subronto, Y.W., Stienstra, Y., Sumardi, S.F., van der Werf, T.S.: Sensitivity and specificity of routine diagnostic work-up for tuberculosis in lung clinics in Yogyakarta, Indonesia: a cohort study. BMC Public Health **19**(1), 363 (2019). <a href="https://doi.org/10.1186/s12889-019-6658-8">https://doi.org/10.1186/s12889-019-6658-8</a>
- 15. Pourakbari, B., Mamish, S., Mohammadzadeh, M., Mahmoudi, S.: First-line anti-tubercular drug resistance of Mycobacterium tuberculosis in IRAN: a systematic review. Front. Microbiol. **7**, 1139 (2016). https://doi.org/10.3389/fmicb.2016.01139
- 16. Nguyen, T.N.A., Anton-Le Berre, V., Bañuls, A.L., Nguyen, T.V.A.: Molecular diagnosis of drugresistant tuberculosis; a literature review. Front. Microbiol. **10**, 794 (2019). https://doi.org/10.3389/fmicb.2019.00794
- 17. Yang, C., Sobkowiak, B., Naidu, V.: Phylogeography and transmission of M. tuberculosis in Moldova: a prospective genomic analysis. PLoS Med. **19**(2), e1003933 (2022). https://doi.org/10.1371/journal.pmed.1003933
- 18. Stosic, M., Vukovic, D., Babic, D., et al.: Risk factors for multidrug-resistant tuberculosis among tuberculosis patients in Serbia: a case-control study. BMC Public Health **18**(1), 1114 (2018). https://doi.org/10.1186/s12889-018-6021-5
- 19. Chakaya, J., Khan, M., Ntoumi, F., et al.: Global tuberculosis report 2020 reflections on the Global TB burden, treatment and prevention efforts. Int. J. Infect. Dis. **113**(Suppl 1), S7–S12 (2021). <a href="https://doi.org/10.1016/j.ijid.2021.02.107">https://doi.org/10.1016/j.ijid.2021.02.107</a>



20. Baya, B., Achenbach, C.J., Kone, B.: Clinical risk factors associated with multidrug-resistant tuberculosis (MDR-TB) in Mali. Int. J. Infect. Dis. **81**, 149–155 (2019). https://doi.org/10.1016/j.ijid.2019.02.004

**21.** WHO. Latent tuberculosis infection. Updated and consolidated guidelines for programmatic management (2018)