# The predictive factors for positive molecular-genetic assay in patients with pulmonary tuberculosis from Chisinau city

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**Abstract**

**Background**: One of the most important tuberculosis control action is the early detection, especially of multidrug-resistant tuberculosis. Cultural methods remain the golden standard for pulmonary tuberculosis diagnosis. The microscopic identification of acid-fast-bacilli in sputum is still a worldwide used method for TB detection. The low sensibility of conventional microscopic methods endangers the actual epidemiological situation. Starting with 2012, the genetic-molecular technology – Xpert MTB/RIF Assay - was implemented in the Republic of Moldova. The assessment of initial experience of Xpert MTB/RIF Assay is compulsory for improving the early case detection. The aim of the study is the assessment of extrinsic factors predictable in positive Xpert MTB/RIF patients.

**Material and methods**: A retrospective, selective, descriptive and case-control study was performed. There were enrolled 361 new pulmonary tuberculosis patients, diagnosed and hospitalized in the Muncipal Clinical Hospital of Phthysiopneumology of Chisinau in the period of 01.01.2014 - 01.01.2015. The patients were disributed into 2 groups: I - 174 patients with positive Xpert MTB/RIF Assay result; II - 187 patients with negative Xpert MTB/RIF Assay result. Investigations were performed according to the National Clinical Protocol – 123 Tuberculosis in adults.

**Results**: The male gender was predominating above the female gender in both groups: 67,8% vs 32,2% in the 1st group and 55,6% vs 44,4% in the 2nd group. According to the economical status, disadvantaged patients were predominating in the 1st group (71,3%), as compared with the 2nd group (50.8%), with the degree of concludence, p<0,001. The hystory of household TB contact was predominating in the 1st group – 17,2% vs 9,1% in the 2nd group, (p<0.05).

**Conclusions**: The implementation of Xpert MTB/RIF Assay improves the early TB detection and the prompt initiation of an adequate treatment regimen, according to the susceptibility testing results.

**Key words**: tuberculosis, Xpert MBT/RIF Assay, risk factors.

## Introduction

Tuberculosis (TB) is one of the most important challenges for the health care system of any state. World Health Organization (WHO) declared tuberculosis a global emergency in 1993 [6]. In 2014, 9 million new cases were registered globally, the Republic of Moldova ranking among 30 countries with the biggest burden of multidrug-resistant tuberculosis (MDR-TB). One of the most relevant tuberculosis control action represents the early case detection, especially of MDR-TB cases [21]. So, precocious treatment of early detected new case is considered the most efficient tool for interrupting the epidemiological chain of infectious transmission [9]. The cultural methods still remain the golden standard for pulmonary tuberculosis diagnosis. Conventional microscopy for identification of acid-fast-bacilli is the first step in the TB detection algorithm and the largely extended investigation method for the TB diagnosis [18]. The low sensibility of conventional microscopy methods endangers the actual epidemiological situation. There is not enough sensibility in some individual cases, and the long duration in obtaining of culture results make difficult to achieve Millennium Goals [13, 17]. In addition, WHO established conditional recommendations to use Xpert MTB/RIF assay in adults, children and persons with HIV presumed to have TB (not especially MDR-TB), or for testing the non-respiratory specimens targeting the diagnosis of extrapulmonary TB [14, 20].

Xpert MTB/RIF assay represents an in-vitro diagnostic medical device, owned by Cepheid Company. Xpert MTB/RIF assay used with Cepheid Xpert MTB/RIF system is a semi-nested, quantitative, real-time polymerase chain reaction test used for the DNA detection of all Mycobacterium tuberculosis complex species and rifampicine resistance mutations of the rpoB gene [7]. Xpert MTB/RIF system integrates Xpert device, a computer and a barcode reader. The system automates sample processing, nucleic amplification and detection of the target sequences of rpoB gene. Primers used by the system amplify the portion of the rpoB gene, containing 81 base bars. So, the technique is able to differentiate the wild-type sequence and mutation in the core region of the rpoB gene. The system requires the use of a single-use disposable Xpert cartridge that contains all the reagents necessary for developing of polymerase chain reaction process. The cartridge also contains the sample processing control that ensures the adequate processing, and the Probe Check Control (PCC) that verifies reagent rehydration, tube filling in the cartridge, probe integrity and dye stability.

Any biological specimen (sputum, bronchoalveolar washout, cerebrospinal fluid, etc.) can be processed considering that it requires the minimum of 2 ml of sample volume. For the highest sensibility, the collection procedure, the storing and transportation should be performed at maximum 35°C, less than in 3 days, and from 2 to 8°C, for 4 – 10 days after the specimen harvesting [5, 8 ]. The Xpert System generates results measured according to fluorescent signals. Several standard results must be known for the appropriate interpretation of Xpert MTB/RIF system: 1. MTB detected & RIF resistant means that MTB target is present and mutation of rpoB gene is detected; 2. MTB detected & RIF susceptible means that MTB target is present and no mutation of rpoB gene has been detected; 3. MTB not detected – MTB target is not detected within the sample. Despite of clearly defined interpretations,

the test results must be always correlated with the laboratory and clinical data of the investigated patient [11].

The approved data established that three sputum samples per patient examined through Xpert MTB/RIF assay show the sensitivity among culture positive specimens on average of 97.3%, and among smear positive patients – on average of 99.5%. The specificity compared with non-tuberculosis patients was 97.9%. In the same three specimens the sensitivity for RIF resistance (rpoB gene mutation) detection among phenotypic (culture) RIF resistant patients was identified in amount of 96.1%, and specificity in phenotyping RIF sensitive patients was 98%. Error rates vary from 3% to 4%. The sensitivity is slightly decreased in a single sputum sample. Assessing the threshold of analytical sensitivity, it was argued that the biological sample must contain at least 131 colony forming units (CFU) per ml of sample with the confidence interval ranging from 106.2 CFU to 176.4 CFU. Experimentally, 9 strains of non-tuberculosis mycobacteria were mixed in sputum samples at a concentration of 106 CFU/ml, in all cases being obtained negative results at Xpert MTB/RIF Assay [2]. However, the negative result does not exclude active tuberculosis that leads to the necessary application of other important diagnostics approaches in the suspected TB patients [15]. This test couldn't be used for the treatment outcomes evaluation (success or failure), because the MTB DNA persists for a long time after the antimicrobial therapy [7].

In actual epidemiological conditions the Republic of Moldova encounters a sharp increase of MDR-TB incidence [9]. In 2011, the rates of drug-resistance were 26% among new cases and 64% among previously treated cases [12]. Starting from April 2012, the Xpert MTB/RIF technology was implemented in 15 districts and municipality laboratories, as well as in penal institutions. In total there were procured 25 Xpert MTB/RIF systems. A large number of laboratory staff was trained to use the new system. The initial experience of Xpert MTB/RIF Assay is important to be assessed for the confirmation of its role in shortening the time for TB diagnosis (including resistant forms) [11], especially in a high burden region as Chisinau municipality, the Republic of Moldova.

**The aim of the study** is the comparative research of the predictors in patients with Xpert MTB/RIF positive and Xpert MTB/RIF negative results.

**Objectives**: 1) Comparative assessment of the risk factors of pulmonary tuberculosis, according to the results of Xpert MTB/RIF assay. 2) Assessment of the predictive factors in the study groups.

## Material and methods

It was performed a retrospective, selective, descriptive and case-control study, targeting the features of pulmonary tuberculosis in patients, diagnosed and hospitalized in the Municipal Clinical Hospital of Phthysiopneumology of Chisinau in the period of 01.01.2014-01.01.2015. Including criteria of the 1st Group: age > 18 years old; patient with pulmonary tuberculosis established as a new case; positive Xpert MTB/RIF Assay; including criteria of the 2nd Group: age > 18 years old; patient with pulmonary tuberculosis established as a new case; negative Xpert MTB/RIF Assay. The total number of 361 cases was distributed into 2 groups: the 1st group (1st Group) included 174 patients and the second group (2nd Group) included 187 patients. The collection of primary material involved the extraction of data from medical record forms. The individual schedule included information about: anamnesis, clinical examination, results of radiological investigations (chest radiography, plane tomography, and computer tomography), results of microbiological investigations (smear microscopy by Ziehl-Neelson coloration and culture on classic solid medium Lowenstein-Jensen or liquid medium). Investigations were performed according to the National Clinical Protocol – 123 Tuberculosis in adults [12]. Statistical analysis methods used in the study were: comparative, synthesis, discriminate analysis. The mathematical and statistical assessment was carried out by checking the quantitative and qualitative features. The accumulated material was tabled in simple and complex groups. Statistical study was performed using Microsoft Excel XP soft. The predictability value of each involved factor was calculated using the two by two tables. Relative risk and confidence interval were calculated according to the established formula [14]. The interval of 1.2 to 1.6 was assessed as a low predictive factor, 1.6 to 2.4 – as a mild predictive factor, and more than 2.5 – as a high predictive factor [14].

## Results and discussion

Among 174 patients with positive Xpert MTB/RIF Assay from the 1st Group, 103 (59.2±3.73%) microscopic positive Ziehl-Neelson staining cases were determined by conventional sputum smear microscopy, also were identified 142 (81.6 ± 2.94) culture positive cases at solid and liquid media. Rifampicine resistance was established in 63 (36.2±3.64%) cases of the 1st Group.

In the 2d Group were included 187 Xpert MTB/RIF negative patients, 9 (4.8±1.56%) of them were positive acid-fast smears and 28 (14.9 ± 2.60%) were culture positive at solid (Lowenstein-Jensen) and liquid media (BACTEC MGIT). So, Xpert MTB/RIF Assay can't replace conventional microbiological methods.

Considering the analysis based on multivariate logistic regression, the burden of microscopic acid fast bacilli positive patients is high, being appreciated by Relative Risk (RR), RR=3.22 (95% CI: 2.63 - 3.96).

### General characteristics, social, economical, and health insurance-related determinants of patients with pulmonary tuberculosis

The sex distribution of patients established the predominance of male sex versus female sex in both groups: 118 (67.8 ± 3.54%) males in comparison with 56 (32.2 ± 3.54%) females in the 1st Group, with the degree of significance $p<0.001$, as well as in the 2nd Group - 104 (55.6 ± 3.63%) men in comparison with 83 (44.4 ± 3.63%) women, without achieving the concludence. Male-to-female sex ratio was 2.11/1 in the 1st Group and 1,25/1 in the 2nd Group. By comparing the groups, it was

identified a significant difference between gender distribution among the investigated groups. The male sex showed a low predictability in the patients with positive Xpert MTB/RIF Assay, assessed by RR=1.32 (95% CI: 1.04 - 1.67). The data are presented in the table 1.

The distribution of patients into age groups identified a similar proporion of patients in both groups. The largest representative group was the age group of 31-40 years old: 51 (29.3±3.45%) patients from the1st Group versus 48 (25.7 ± 3.19%) patients from the 2nd Group, followed by the 21-30 age group: 44 (25.3 ± 3.29%) patients of the 1st Group and 47 (25.1 ± 3.172%) cases of the 2nd Group. The distribution in other age groups was similar (table 1). Regrouping the above exposed data in two subgroups (18 - 40 years and more than 41 years) did not identify any difference between the prevalence of patients of less than 40 years comparing with older patients in the same group, as well as when comparing both groups (table 2). Considering that male sex and young age represented the significant features for both groups, it was identified that male gender was the most significant factor versus the young age in both groups. So, the young age was a neutral predictor in patients with positive Xpert MTB/RIF test assessed by RR=1.08 (95% CI: 0.8 - 1.34).

### Economic characteristics of patients with pulmonary tuberculosis

The distribution of patients according to the economic status showed that the number of patients with an economically-steady state (employed) was identified in less than 1/3 part of the 1st Group and in 1/2 part of the 2nd Group. So, the employees were more frequently identified in the 2nd Group versus the 1st Group: 92 (49.2 ± 3.65%) and 50 (28.7 ± 3.43%), respectively (p<0.001).

**Table 1**

**Distribution of patients according to sex and age groups**

| Sex | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | N | M± m(%) | N | M ± m (%) | |
| Men | 118 | 67.8 ± 3.54 | 104 | 55.6 ± 3.63 | <0.01 |
| Women | 56 | 32.2 ± 3.54 | 83 | 44.4 ± 3.63 | <0.01 |
| <20 years | 9 | 5.1 ± 1.67 | 10 | 5.3 ± 1.64 | >0,05 |
| 21 - 30 years | 44 | 25.3 ± 3.29 | 47 | 25.1 ± 3.172 | >0,05 |
| 31 - 40 years | 51 | 29.3 ± 3.45 | 48 | 25.7 ± 3.19 | >0,05 |
| 41 - 50 years | 35 | 20.1 ± 3.03 | 27 | 14.4 ± 2.57 | >0,05 |
| 51 - 60 years | 25 | 14.4 ± 2.65 | 25 | 13.4 ± 2.48 | >0,05 |
| > 60 years | 10 | 5.7 ± 1.76 | 28 | 14.9 ± 2.60 | >0,05 |

**Table 2**

**Distribution of patients according to the age determinants**

| Age | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | N | M± m (%) | N | M ± m (%) | |
| Less 40 years | 104 | 59.8 ± 3.71 | 105 | 56.2 ± 3.62 | >0.05 |
| More 41 years | 70 | 40.2 ± 3.71 | 82 | 43.9 ± 3.62 | >0.05 |

**Table 3**

**Distribution of patients according economic status**

| Economical Status | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | n | M ± m (%) | N | M ± m (%) | |
| Employed | 50 | 28.7 ± 3.43 | 92 | 49.2 ± 3.65 | <0.001 |
| Unemployed | 83 | 47.7 ± 3.78 | 61 | 32.6 ± 3.42 | <0.01 |
| Retired | 6 | 3.4 ± 1.38 | 12 | 6.4 ± 1.79 | >0.05 |
| Students | 10 | 5.7 ± 1.76 | 4 | 2.1 ± 1.05 | >0.05 |
| Disease disability | 9 | 5.2±1.67 | 10 | 5.3 ± 1.64 | >0.05 |
| Labor migrant | 15 | 8.6 ± 2.12 | 8 | 4.3 ± 1.48 | >0.05 |
| Special situation | 1 | 0.6 ± 0.57 | 0 | 0 | >0.05 |

**Table 4**

**Distribution of patients according to economical status**

| Economical Status | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | n | M± m (%) | n | M ± m (%) | |
| Steady-state | 50 | 28.7 ± 3.43 | 92 | 49.2 ± 3.65 | <0.001 |
| Disadvantaged | 124 | 71.3 ± 3.43 | 95 | 50.8 ± 3.65 | <0.001 |

**Table 5**

**Distribution of patients according to the insurance status**

| Insurance Status | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | n | M ± m (%) | n | M ± m (%) | |
| Insured | 76 | 43.7 ± 3.76 | 127 | 67.9 ± 3.41 | <0.001 |
| Uninsured | 98 | 56.3 ± 3.76 | 60 | 32.1 ± 3.41 | <0.001 |

**Table 6**

**Distribution of patients according to the civic status**

| Civic Status | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | n | M ± m (%) | n | M ± m (%) | |
| Married | 60 | 34.5 ± 3.60 | 86 | 45.9 ± 3.64 | <0.05 |
| State marriage | 8 | 4.6 ± 1.58 | 1 | 0.5 ± 0.53 | >0.05 |
| Unmarried | 59 | 33.9 ± 3.58 | 79 | 42.2 ± 3.61 | >0.05 |
| Divorced | 32 | 18.4 ± 2.93 | 17 | 9.1 ± 2.10 | <0.01 |
| Widow | 15 | 8.6 ± 2.12 | 4 | 2.1 ± 1.05 | >0.05 |

**Table 7**

**Distribution of patients according to the civic state**

| Civic Status | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | n | M ± m (%) | n | M ± m (%) | |
| In couple | 68 | 39.1 ± 3.69 | 87 | 46.5 ± 3.64 | >0.05 |
| Single-civil | 106 | 60.9 ± 3.69 | 100 | 53.5 ± 3.64 | >0.05 |

Unemployed represented the most expressed group, and were more often identified in the 1st Group versus the 2nd Group: 83 (47.7 ± 3.78%) and 61 (32.6 ± 3.42%), respectively (p<0.01). Retired patients, disease disabled and students were revealed at the same level in both groups. Labor migrants were an important part of patients from both groups (table 3).

So, economically disabled patients that included all non-economically productive patients, such as unemployed, retired and students were most prevalent in the 1st Group - 124 (71.3 ± 3.43%) patients comparing with 95 (50.8 ± 3.65%) cases in the 2nd Group. Economical vulnerability was identified as middle predictive factor in patients with positive Xpert MTB/RIF test assessed by RR=1.66 (95% CI: 1.29 - 1.2.14) (table 4).

### Health insurance related issues

Health insurance represents the major condition for accessing the health care in the Republic of Moldova. General statistics demonstrated that the uninsured part of Moldovan citizens ranges from 10% to 25% of total population, depending on the demographical state (more frequent in the rural area), ethnic origin (ethnic minorities are more frequently uninsured), and other socially disadvantaged conditions. In 2014, 971.331 uninsured persons were identified in the Republic of Moldova [24]. In spite of the free of charge tuberculosis care, the lack of medical insurance determines a delayed detection and the lack of social assistance, the deficiency of active screening, the difficulty in the follow-up evaluation, all of these leading to lower treatment outcomes. In the Republic of Moldova, there are several categories of population that benefit of free insurance coverage: children till 18 years old, students of higher educational institutions, pregnant women, disabled persons with high and medium degree of disablement, retired persons, unemployed registered at the local territorial agencies, persons who take care of severely ill

Table 8

**Distribution of patients according the harmful habits**

| Harmful habits | 1st Group (n=174) | | 2nd Group (n=187) | | P |
|---|---|---|---|---|---|
| | n | M± m (%) | N | M ± m (%) | |
| Tobacco smoking | 138 | 79.3 ± 3.07 | 152 | 81.28 ± 2.82 | >0.05 |
| Drug use | 3 | 1.7 ± 0.99 | 2 | 1.1 ± 0.75 | >0.05 |
| Alcohol abuse | 64 | 36.8 ± 3.66 | 27 | 14.4 ± 2.57 | <0.05 |

persons, mothers with 4 and more children, socially disadvantaged families benefiting of social assistance [25]. So, including all above mentioned individuals, the uninsured patients were more frequently identified in the 1st Group comparing to the 2nd Group: 98 (56.3 ± 3.76%) versus 60 (32.1 ± 3.41%) patients, respectively, p<0.001 (table 5). Uninsured state was identified as middle predictive factor in patients with positive Xpert MTB/RIF Assay and was assessed by RR=1.68 (95% CI: 1.33 - 2.14).

When studying the civil status, it was identified a higher rate of married patients in the 1st Group and a similar rate of married and unmarried patients in the 2nd Group. By comparing the groups, it was identified the prevalence of married patients in the 2nd Group versus the 1st Group: 86 (45.9 ± 3.64%) versus 60 (34.5 ± 3.60%), respectively, with a low degree of significance (p<0.05). On the other hand, the divorced patients predominated in the 1st Group comparing with the 2nd Group: 32 (18.4 ± 2.93%) versus 17 (9.1 ± 2.10%) cases, respectively, with high degree of significance (p<0.01) (table 6).

By redistributing patients into 2 groups, according to the civil status, the prevalence of married, recognized as in couple individuals was identified in the 2nd Group [87 (46.5 ± 3.64%)], comparing with cases in the 1st Group [68 (39.1 ± 3.69%) cases] and the single-civil state patients in the 2nd Group [100 (53.5 ± 3.64%) cases] compared with the 1st Group [106 (60.9 ± 3.69%) cases] without achieving the degree of significance (table 7). So, single civil state was identified as neutral predictive factor in the patients with positive Xpert MTB/RIF test being assessed by RR=1.17 (95% CI: 0.93 - 1.46).

Considering all above exposed data, a rank diagram with the most relevant general, economical and social characteristics of the pulmonary tuberculosis patients, according to the Xpert MTB/RIF test result was made. According to the schematic representation, the most relevant social features of patients with pulmonary tuberculosis are: disadvantaged economical state of the patients, followed by the male sex, single civil status, young age of the patients, lack of obligatory/ compulsory health insurance policy (fig. 1).

### Associated harmful habits at patients with pulmonary tuberculosis

During the study were identified such harmful habits with the biggest impact on all stages of the pathogenesis of tuberculosis as: tobacco smoking, alcohol abuse, and illicit drug use. The most prevalent addiction in both groups was tobacco smoking that affected 1/3 of all investigated patients: 138 (79.3 ± 3.07%) cases in the 1st Group versus 152 (81.28 ± 2.82%) cases in the 2nd Group. The subgroup of alcohol abusers was less prevalent: 64 (36.8±3.656%) cases in the 1st Group versus 27 (14.4 ± 2.570%) cases in the 2nd Group, p<0.05. A few drug users were detected in both groups (table 8).

### Public health related issues with impact on tuberculosis epidemiology

Migration has the major impact on the spread of different strains of tuberculosis. In Western Europe, the most of MDR-TB cases are diagnosed in immigrants from Eastern Europe. Short-term travelers and short-term residents are the most prevalent part of the immigrational population and the most vulnerable group. Most of them have an illegal state in the hosting country, that determins the lack of health and social insurance. Consequently, they couldn't access the screening methods and perform an effective anti-TB treatment. So,

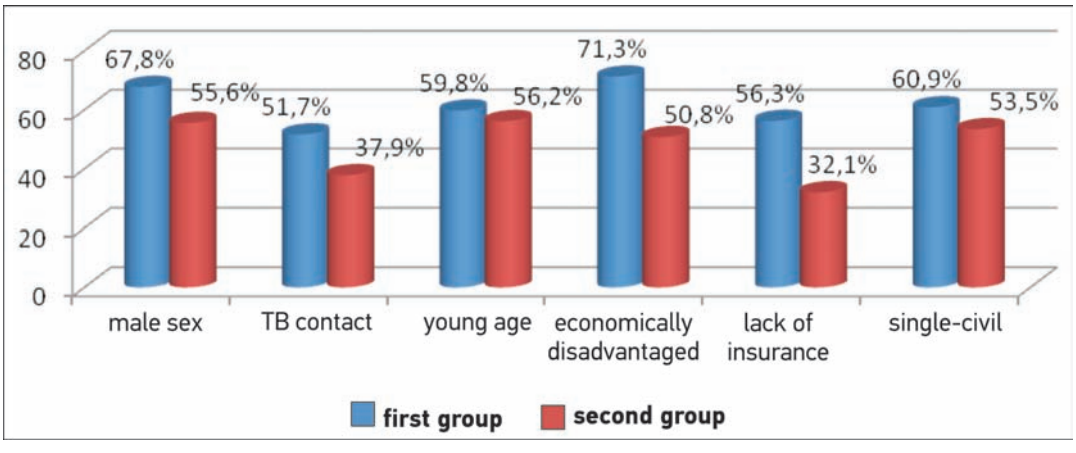


**Fig. 1. Hierarchy of biologically-related and social determinants of pulmonary tuberculosis.**

**Table 9**

**Distribution of patients according to the characteristics of epidemiological cluster**

| Index | 1st Group (n=174) | | 2nd Group n=187 | | P |
|---|---|---|---|---|---|
| | n | M ± m(%) | N | M ± m (%) | |
| Household/ Family contact | 30 | 17,2 ± 2.86 | 17 | 9.1 ± 2.1 | <0.05 |
| Close contact | 25 | 14.37 ± 2.65 | 34 | 18.18 ± 2.82 | >0.05 |
| Institutional/ Penitentiary contact | 10 | 5.7 ± 1.76 | 13 | 6.9 ± 1.86 | >0.05 |
| Total | 65 | 37,4 ± 3,66 | 64 | 34.2 ± 3.47 | >0.05 |

**Table 10**

**Relative risk from multivariate logistic regression model assessing factors associated to Xpert MTB/RIF Assay (n=361)**

| Factors | Relative Risk | 95% CI | P |
|---|---|---|---|
| Male sex | 1.32 | 1.04-1.67 | <0.01 |
| Young age (Less than 40) | 1.08 | 0.8-1.34 | >0.05 |
| Economically disadvantaged state | 1.66 | 1.29-2.14 | <0.001 |
| Uninsured state | 1.68 | 1.33-2.14 | <0.001 |
| Single-civil state | 1.17 | 0.93-1.46 | >0.05 |
| Epidemiological danger by being microscopic positive case-index | 3.22 | 2.63-3.96 | <0.001 |
| Household TB Contact | 1.467 | 1,145-1.88 | <0.05 |

external labor migrants were 15 (8.6±2.12%) cases in the 1st Group and 8 (24.24 ± 7.46%) individuals - in the 2nd Group.

Detention, as a public health issue, exposes a high threat for multidrug resistant mycobacterial infection and active tuberculosis development. Patients, who started the treatment during the detention period and then are released from the detention/prison, have an increased risk to be lost from follow up, due to the lack of interventions to ensure the continuity of tuberculosis treatment. There were limited cases of ex-detainees in both groups: 10 (5.75 ± 1.76%) cases in the 1st Group and 13 (6.95 ± 1.86%) cases - in the 2nd Group.

### Epidemiological risk factors of patients with pulmonary tuberculosis

For the TB control and interruption of epidemiological chain, it is very important to early identify the index-case. The most epidemiological danger represents MDR-TB household contact and the contact with a deceased. So, in our study were identified 3 groups of patients according to index case. The first group of TB clusters included the household or family contact, a part of this group was represented by the MDR-TB contact and the contact with a deceased. In the next group were included the patients with close contact, followed by the patients from penitentiary institutions.

Household contact prevailed in the 1st Group, 30 (17,2 ± 2,86% ) patients compared to 17 (9,1 ± 2,1%) patients from the 2nd Group, with the degree of significance, p <0.05, and close contact (labor, neighborhood) was identified in 25 (14.97 ± 2.97%) cases in the 1st Group compared to 34 (18.18 ± 2.82% ) cases in the 2nd Group, without achieving the degree of significance. Less prevalent was identified the epidemiological impact received by the institutionalization. Ex-prisoners were 10 (5.7 ± 1.76%) patients in the 1st Group and 13 (6.9 ± 1.86%) cases in the 2nd Group, without the degree of significance (table 9).

MDR-TB index-cases contact was identified in 4 (2.3 ± 1.13%) cases in the 1st Group and in 2 (1.1 ± 0.75% ) cases in the 2nd Group, without the degree of significance; 3) dead patient contact was identified in 13 (7.5 ± 1.99%) cases in the 1st Group and in 5 (2.7 ± 1.18%) cases in the 2nd Group, without the degree of significance.

So, household TB contact was identified as a low predictive factor in the patients with positive Xpert MTB/RIF test, being assessed by RR=1.467 (95% CI: 1.145 - 1.88).

### Impact of extrinsic determinants in patients with the positive Xpert MTB/RIF Assay results

By assessing all above exposed data that express the general, social, economic, and insurance-related features of patients with pulmonary tuberculosis, positive/negative Xpert MTB/RIF test through multivariate logistic regression statistical model, it was identified the prevalence only of several extrinsic factors: male sex, economically disadvantaged state, TB contact, lack of insurance (table 10).

Actual study revealed that epidemiological danger of patients with positive Xpert MTB/RIF was reduced by shortening the duration of tuberculosis diagnosis.

## Conclusions

This study was first realized in Municipal Clinical Hospital of Phthysiopneumology of Chisinau.

Despite of multiple extrinsic factors assessed in the study, the multivariate logistic regression model determined that male individuals, young age, single state and household TB contact had low risk to be positive at Xpert MTB/RIF Assay, assessed by Relative Risk; economically disadvantaged patients and patients with lack of insurance had middle risk and microscopic positive patients had high risk to be positive at Xpert MTB/RIF assay.

The use of Xpert MTB/RIF could improve TB control program and epidemiological situation by earliest TB detection for achieving the epidemiological indicators, recommended by WHO.

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