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The Role of Microbiological and Radiological Tests in the Diagnosis of Pulmonary Tuberculosis in the Conditions of the Pandemic COVID-19

The impact of the methods for diagnosis of pulmonary tuberculosis is perceived in the fastness in setting up the actions aiming to isolate the source infection and to treat it in due time.

Objective — to establish the role of microbiological and radiological tests in diagnosis of pulmonary tuberculosis in actual epidemiological context of tuberculosis associated to the COVID-19 pandemics (2020—2022).

Materials and methods. It was conducted a case-control study which included 172 patients diagnosed with pulmonary tuberculosis, as new case, distributed in two groups, the 1st group — 116 patients diagnosed through the radiological methods and the 2nd group — 56 patients, diagnosed through microbiological methods.

Results and discussion. The main peculiarities of patients diagnosed with tuberculosis regardless of methods of investigation were male gender, low social and economic state and high prevalence of the harmful habits with impact on the health state. Patients diagnosed through the microbiological methods were residing more frequently in rural areas, with low accessibility to healthcare services, identified through a long-evolving symptomatology, late detection, expressiveness of the clinical symptomatology and a high rate of poor treatment outcome. Recommendations were established that systematic screening for tuberculosis should be performed in all social-vulnerable groups, fortified by the individualised therapeutic approach.

Conclusions. The case-control study identified that the main peculiarities of patients diagnosed with tuberculosis regardless of methods of investigation were male gender, low social and economic state and high prevalence of harmful habits such as smoking and alcohol consumption. Patients diagnosed through the microbiological methods were residing more frequently in rural areas, with low accessibility to healthcare services, concluded through a long-lasting symptomatology, late detected forms of tuberculosis, high expressiveness of the clinical symptomatology and severe evolution, followed by a high rate of poor treatment outcomes, including death. Patients diagnosed through the radiological methods were more frequently from urban sectors, from tuberculosis clusters, with comorbidities with high risk for tuberculosis sickness, such as HIV infection, diabetes and mental disorders which constituted included in active screening programs. The lack of positive microbiological assay results was the consequence of the unilateral and limited forms of pulmonary and determined a higher rate of treatment success rate.

Keywords

Tuberculosis, risk factors, X-ray examination, microbiological examination, result of treatment.

Tuberculosis (TB) is a social-determinate disease with a high prevalence in the Eastern European Region (EER), including in the Republic of Moldova (RM) [2—5]. The main barriers to achieving TB control in EER are social, economic, educational and psychological issues [3, 6]. According to World Health Organization (WHO), EER is a high-risk zone for communicable diseases, with an inadequate concern regarding social determinants of health [1, 5, 6, 14, 16]. Almost all countries listed

in the WHO list with the highest burden of multidrug resistant TB (MDR-TB) are located in the EER [1, 4, 13, 15]. The countries with the highest rates of TB are the poorest and have many unequal social inequalities including very limited access to healthcare [1, 3, 16]. The studies showed that affected by TB people usually live in absolute poverty, which provides the ideal condition for the spreading of *Mycobacteria tuberculosis* [3, 5, 6, 9, 10]. Often in those households, poverty is associated with malnutrition and HIV infection, which both conditions diminish the immune resistance of the organism making them vulnerable to TB [6, 10, 11].

In the RM TB is one of the priority public health problems, and its prevention and control are strategic objectives of the Strategy «European Moldova» which integrates the principles of the National Public Health Programme [12]. Statistical data from recent years demonstrated an improvement in the epidemiological indicators, as a result of the provision of patient-centred TB healthcare services, based on prevention, detection and treatment [2, 7, 8]. The constantly positive trend from the pre-pandemic period (until 2019) experienced an alarming decline in the context of the COVID-19 pandemic [7—9, 12, 13, 15]. The monitoring indicators assessing the response to TB, which included data from 2019, known as the pre-pandemic year established a 38.7 % reduction in the number of new, relapse cases detected in 2020 compared to 2019 and a slight increase of 2.7 % in 2022 compared with 2021. Starting with 2020, followed by 2021 and 2022 the TB epidemiological indicators were reported to the Moldovan population of 3,079,908 people (including right bank — 2,053,238, left bank — 378,329) and children — 648,341 (right bank — 561,961, left bank — 86,380). The incidence of new cases and relapses in 2022 was 68.8/100,000 population (2,121 cases) and in 2021 — 67.1/100,000 population (2,068 cases) with the rate of TB-HIV coinfection of 13 %. In 2022, 1,666 new cases of TB were register compared with 1,614 new cases in 2021 the incidence was calculated to 54.1/100,000 population and was compared to 52.4/100,000 population in 2021. The incidence of TB relapses in 2022 was 14.8/100,000 population (457 cases), compared to 2021 — 14.7/100,000 population (454 cases), constituting 22 % of the global incidence. The rate of pulmonary forms with lung destruction in new pulmonary TB cases in 2022 was 37 % (559 cases) and in 2021 — 41 % (591 cases), which is double compared with pre-pandemic period [7, 8]. The mortality was 5.7/100,000 population and death registered until one year after detection constituted 43 % [7, 8]. Exposed data demonstrated delayed diagnosis of late detected forms of pulmonary TB, but no clinical and radiological aspects were assess in correlation with the methods of diagnosis — microbiological and radiological.

Objective — to establish the role of microbiological and radiological tests in diagnosis of pulmonary tuberculosis in actual epidemiological context of tuberculosis associated to the COVID-19 pandemics.

Materials and methods

The research was conduct as retrospective, selective, and descriptive and included a cohort of 172 patients diagnosed with pulmonary TB during the period 1.1.2020—31.12.2022 in Chisinau, RM. The inclusion criteria were: age older than 18 years, TB diagnosed by the pulmonologist, detected as the new case and signed informed consent.

The patients were distributed in two groups, 1st group included 116 patients diagnosed with pulmonary TB through radiological investigations, without microbiological positive tests and were compared with the 2nd group of 56 patients with positive for TB assays (Ziehl-Neelson staining, PCR assay Gene Xpert MTB/Rif). The diagnosis of pulmonary TB was established according to the criteria provided by the national policy Nr. 123. Every patient was investigated through the sputum examination at Ziehl-Neelson staining, PCR assay Gene Xpert MTB/Rif and culture on the Lowenstein—Jensen and liquid BACTEC media. In the 1st group, the radiological methods were applied — chest X-ray examination in 2 incidences — 116 (100 %), tomosynthesis — 23 (20 %) and high-resolution computed tomography — 14 (12 %). In 35 (30 %) cases, 3D bronchial fibroscopy with the aspiration of tracheo-alveolar liquid was performed.

The study's schedule included data about:

a) biological and social peculiarities, demographic characteristics (living in urban/rural areas);
b) economic peculiarities: economic state (employed, unemployed, retired, disabled,) and health-insurance coverage (presence/lack of health insurance);
c) characteristics with high risk: homelessness, migration, history of detention, infectious contact;
d) case-management: health care seeking behaviour and addressability to healthcare settings, methods used for TB detection, the medical staff involved in the detection, comorbidities, complications and HIV status;
e) TB-related characteristics: localization (pulmonary/secondary extrapulmonary), results of microbiological assays, anti-tuberculosis treatment and the outcome.

Other investigations performed were: hemoleucogramme, urine analysis, serum biochemical tests (transaminases, urea, creatinine, lactate dehydrogenase), and tests for HIV markers.

Table 1. **Distribution according to the biological peculiarities and demographics (%)**

Indicators	1st group (n = 116)	2nd group (n = 56)	p
Men	72 (62 %)	44 (78 %)	< 0.05
Women	44 (38 %)	12 (22 %)	< 0.05
Age, y.o.			
18—24	16 (14 %)	6 (11 %)	> 0.05
25—34	20 (17 %)	12 (22 %)	> 0.05
35—44	32 (27 %)	16 (28 %)	> 0.05
45—54	28 (24 %)	14 (25 %)	> 0.05
> 55	20 (17 %)	8 (14 %)	> 0.05
Urban	88 (75 %)	38 (65 %)	> 0.05
Rural	20 (17 %)	20 (36 %)	> 0.05
Homeless	4 (3 %)	5 (9 %)	< 0.01

Note. p — significance at ANOVA test.

The statistical assays have been used for the analysis of variation (ANOVA test) and Student's t-test. Statistical significance was determined by the value of $p < 0.05$. Multiple linear regression (RML) was performed to calculate the odds ratio (OR) for the evaluation of the risks.

Results and discussion

Distributing patients by sex, was determined that in the 1st group 62 % were men and 38 % women, the male/female ratio — 1.6/1.0, while in the 2nd group 78 % were men and 22 % women, the male/female ratio — 3.7/1.0. The comparative analysis showed that men were more often diagnosed through microbiolgoical methods, which is associated with high contagiousness, with an OR = 3.1 (95 % CI: 1.25—4.19), $\chi^2 = 0.03$. By distributing the patients into age groups according to the WHO classification was estabished in the 1st the highest rate were integrated in the group 35—44 years old (y.o.) — 27 %, 45—54 y.o. — 24 %, 25—34 y.o. and > 55 y.o. — with a similar rate 17 %, 18—24 y.o. — 14 % of patients. In the 2nd group predominated patients between 35—44 y.o. — 28 %, 45—54 y.o. — 25 %, 25—34 y.o. — 22 %, > 55 y.o. — 14 %, 18—24 y.o. — 11 %. Distributing patients in two age groups, younger 35 and older 35, there were no statistical differences between them. The biological peculiarities of the patients confirmed that both young age people and older have a similar chance of developing TB and are to be detected through microbiological or radiological assays. So, for patients of any age we will apply the prevention measures to reduce the risk of developing TB and in cases with clinical suspicion to be investigated according to the national policy, performing microbiological and radiological tests.

Evaluating the place of residence of patients when TB was diagnosed, the urban location was established in majority of patients of all groups — 76 % in the 1st group and 65 % in the 2nd group. Patients from the 2nd group were living more frequently in rural localities 36 % *vs.* 24 % cases in the 1st group. So, radiological methods for diagnosis were more accessible to patients living in urban sectors compared with rural areas, without statistic evidence. The homeless were identified in a small proportion in both groups: 3 % *vs.* 9 %. The data are displayed in Table 1.

The patients were evaluate according to the last level of academic education and divided into several groups: primary, incomplete secondary, completed secondary (general school, specialised secondary) and superior studies. In the 1st group predominated the patients with secondary level 48 %, followed by incomplete secondary 27 %, then specialised level 14 % followed in a minor proportion primary 7 % and superior studies — 2 %. In the 2nd group every second had secondary graduated education 50 %, followed by incomplete secondary studies 25 %, then primary education 14 % and specialised degree in 11 % cases. Low level of academic education slightly predominated in the 2nd group — 50 (89 %) *vs.* 98 (84 %) cases in the 1st group. This finding demonstrated that the low level of academic education predisposes the development of TB, but has no impact on access to certain detection methods.

Tuberculosis affects socially vulnerable groups and while evaluating the economic status was found that in the 1st group predominated employed individuals 42 %, then unemployed 34 % and in a lower proportion students 10 % and retired 7 %. In the 2nd group the patients with a stable economic state as being employed were only 25 % and the majority were socio-economical vulnerable — 42 %, retired 14 %, disabled 11 % and students 7 %. So, this finding demonstrated the fact that the low socio-economical level predisposed to detection by microbiological methods as being symptomatic, because they have a limited access to radiological methods, with an OR = 2.9 (95 % CI: 1.19—3.96), $\chi^2 = 0.02$. The obtained data confirmed that socio-economical support and awareness should be provide to all socially vulnerable groups, giving them accessibility to radiological investigations.

The distribution of patients according to marital status classified them in groups: married, single, divorced, widowed. In the 1st group predominated married individuals — 60 %, followed by single state — 24 % and in a similar proportion divorced/widowed 16 % of cases. In the 2nd group predominated married 57 %, followed by singles 33 % and divorced/widowed 10 %. Single either married state was established in a similar proportion in

patients from both groups. Exposed data are reflected in the Table 2.

Considering the totality of the particularities with an impact on the case-detection was established that men and patients residing in rural localities, with the socially vulnerable state were more predisposed to the detection through the microbiological methods, which involves an important epidemiological risk and women. Patients residing in urban localities and economically stable were more detected through the radiological investigations without a positive microbiological state.

Analyzing the scientific review, which demonstrated that the harmful habits with high risk for TB are: smoking, alcohol consumption and the illicit drug use was identified that in the 1st group active smoking was identified in 62 %, chronic or abusive alcohol consumption in 2 % and no drug use. While in the 2nd group smoking was established in 77 %, alcohol consumption 16 % and 4 % of patients were drug users. Epidemiological contact was established at 21 % of the 1st group which involved the systematic screening and in 11 % of the 2nd group and represented a contributing and facilitating factor for radiological investigation in scope of diagnosis OR = 4.1 (95 % CI: 2.1—5.8), $\chi^2 = 0.01$. Returned from abroad during the last 12 months 7 % in the and 4 former detainees (3 %). All these characteristics related to the socio-economic peculiarities exposed an important impact on the diagnosing methods of TB in the epidemiological conditions of COVID-19 epidemics.

National policy recommends the detection of the new cases of the pulmonary TB through the microbiological examination of the symptomatic cases. Studying the case-detection characteristics of the patients, it was found that in the 1st group 27 % of the cases were people from high-risk groups and were detected through the systematic screening compared with 15 % from the 2nd group, represents an indicator of accessibility to the preventive healthcare services. By the other side an increased use of the systematic screening in the 1st group was conditioned by a higher rate o patients with high risks: HIV-infection 10 % *vs.* 4 %, comorbidities such as diabetes mellitus 4 % *vs.* 1 %, mental disorders in 6 % *vs.* 1 % in the 1st group *vs.* 2nd group, respectively, immunosuppressive conditions and chronic immunosuppressive treatment for autoimmune pathologies in 2 % in the 1st group. Passive detection of symptomatic cases predominated in the 2nd group 73 % *vs.* 48 % and constitute an indicator of the late detection of contagious forms. The direct addressing to the specialised services in physiology was used in a slightly higher proportion by the patients of the 2nd group 32 % *vs.* 25 % in the 1st group which is an indicator of reduced accessibilities either of lack of confidence in the primary healthcare services.

Table 2. **Distribution according to the social peculiarities (%)**

Indicators	1st group (n = 116)	2nd group (n = 56)	p
Education			
Primary	8 (7 %)	8 (14 %)	> 0.05
Incompleted secondary	32 (27 %)	14 (25 %)	> 0.05
Secondary general	56 (48 %)	28 (50 %)	> 0.05
Specialised training	16 (14 %)	6 (11 %)	> 0.05
Superior studies	2 (2 %)	0	> 0.05
Employed	48 (42 %)	14 (25 %)	< 0.05
Unemployed	40 (34 %)	24 (42 %)	> 0.05
People with disabilities	8 (7 %)	6 (11 %)	> 0.05
Student	12 (10 %)	4 (7 %)	> 0.05
Retired	8 (7 %)	8 (14 %)	> 0.05
Married	70 (60 %)	32 (57 %)	> 0.05
Single	28 (24 %)	18 (33 %)	> 0.05
Divorced/widowed	16 (16 %)	6 (10 %)	> 0.05

Note. p — significance at ANOVA test.

Clinical aspects when diagnosis of TB was established were characterized by subacute onset (7—30 days) in 67 % patients from the 1st group *vs.* 9 % in the 2nd group and a lost lasting evolution (> 90 days) in the 2nd group 60 % *vs.* 7 % in the 1st group. A similar proportion of the patients in both groups complained of TB with suspicious symptomatology between 30 and 90 days till diagnosis 25 % *vs.* 31 %, respectively. Obtained data demonstrated the presence of a significant number of patients detected in more than 1 month after the onset of the symptoms in the 2nd group as being characteristic for accessing the microbiological methods of investigations. Clinical signs of the intoxication syndrome — asthenia, lost of weight, night sweats, fever/feverish and the bronchopulmonary syndrome — cough, mucopurulent expectorations were identified in all patients of the 2nd group and only in 76 % of the 1st group. Data demonstrated an important number of symptomatic individuals in the group detected by microbiological assays as being characteristic for passive detection. Distributing patients into the groups according to the clinical diagnosis was established infiltrative form in all patients from the 1st group *vs.* 86 % in the 2nd group. While disseminated form and cavernous were diagnosed only in the 2nd group, with 7 % for each form. Both lungs were involved in the infectious process in every second patient from 2nd group and in every fourth in the 1st group and extensive forms to more than 3 lung segments were detected in all patients from the 2nd group vs one fourth in the 1st group (Table 3).

Table 3. **Distribution according to the radiological peculiarities (%)**

Indicator	1st group (n = 116)	2nd group (n = 56)	p
Infiltrative	116 (100 %)	48 (86 %)	> 0.05
Diseminated	0	4 (7 %)	> 0.05
Fibro-cavernous	0	4 (7 %)	> 0.05
Both lungs affected	30 (26 %)	32 (57 %)	< 0.001
One lung affected	86 (74 %)	24 (43 %)	< 0.001
Extensive TB on 3 + lung segments	31 (27 %)	56 (100 %)	< 0.001
Limited TB	85 (73 %)	0	< 0.001

Note. p — significance at ANOVA test.

Table 4. **The indicators of the treatment's effectiveness in the groups of patients (%)**

Indicator	1st group (n = 116)	2nd group (n = 56)	p
Treatment success	95 (82 %)	36 (62 %)	< 0.05
Therapeutical failure	4 (2 %)	2 (4 %)	> 0.05
Interrupted/lost to follow-up	3 (6 %)	3 (6 %)	> 0.05
Died	0	4 (8 %)	< 0.05
Fully compliant	89 (77 %)	52 (93 %)	> 0.05
Adverse drug reactions	16 (14 %)	9 (16 %)	< 0.05
Limited TB	95 (82 %)	36 (62 %)	< 0.05

Note. p — significance at ANOVA test.

So, infiltrative form of pulmonary TB ware diagnosed in the majority of patients in all investigated groups, in similar rates reported by the epidemiological indicators for the RM. While extensive forms on more than three segments was confirmed in the majority of patients from the 2nd group as being straightly and positively correlated with the presence of the bronchopulmonary symptomatology (r = 0.89) and low correlated with the general intoxication syndrome (r = 0.21). In the mean, the bilateral location of the infectious process was tightly positively correlated with the bronchopulmonary symptomatology (r = 0.82) and tightly positively correlated with the general intoxication syndrome (r = 0.11).

The most important indicators of the interruption of the infection transmission and epidemiological danger are those representing the treatment effectiveness (Table 4). So, in the 1st group the therapeutic success was registered at 82 % *vs.* 62 % in the 2nd group, which included all patients who completed the treatment. In the 2nd group the therapeutic success was established at 62 % of which all the cases were cured. Therapeutic failure was identified in a similar low proportion of cases — 2 % *vs.* 4 %, respectively, and the patients lost to follow-up were as well a few 6 % in both groups. Deaths were estbalished only in a few cases of the 2nd group 4 (8 %). Therapeutically interruptions and incompliance were more often detected in the 1st group 23 % *vs.* 7 %, argued by a higher rate of comorbid patients which interrupted due to clinical intolerance, but a few cases interrupted as the clinical state improved and they left the country. Adverse drug reactions were registered in every seventh patient in both groups.

The research evaluated the clinical-radiological peculiarities of the patients diagnosed with pulmonary TB through the radiological and microbiological methods in the actual epidemiological context associated with COVID-19 pandemics. The results of the study demonstrated that the biological peculiarities of the patients was male gender, with no differences while distributing them in age groups and the predomination of cases residing in urban sectors having detected TB through the radiological methods and in rural areas having diagnosed TB through the microbiological assays. Similar results are often reported in local and international studies [3—5, 7—11]. Social peculiarities of the patients regardless the methods of diagnosis were economical vulnerable state, primary and secondary incomplete academic level and harmful habits, such as tobacco smoking and alcohol abuse. The epidemiological risk factor which was more involved in the development of TB among patients detected through the radiological investigations was TB contact, similar to other research [8—10]. The medical factors, such as comorbidities with high risk for TB (HIV infection, diabetes mellitus, mental disorders and immune suppressive treatment/conditions) were more involved in the same group [9—11]. Both TB contact and associated diseases are eligibility criteria for active screening for TB, which are fully recognised by local studies [9—11]. Synthetically analyzing the groups, was concluded that patients diagnosed by microbiological methods showed severe, late detected and long lasting evolution compared with those diagnosed through the radiological methods [12]. The correlation was very tight between the radiological extensiveness and clinical expressiveness of the bronchopulmonary and general intoxication syndromes in patients diagnosed by microbiological methods. The indicators of the treatment effectiveness was highly superior in the groups diagnosed through the radiological methods, in which were not detected died patients. Therapeutic failure was identified in a similar proportion of cases, and the loss to follow-up were found in a limited number of cases in both groups.

Conclusions

The case-control study identified that the main peculiarities of patients diagnosed with TB regardless of methods of investigation were: male gender, low social and economic state and high prevalence of harmful habits such as smoking and alcohol consumption.

Patients diagnosed through the microbiological methods were residing more frequently in rural areas, with low accessibility to healthcare services, concluded through a long-lasting symptomatology, late detected forms of TB, high expressiveness of the clinical symptomatology and severe evolution, followed by a high rate of poor treatment outcomes, including death.

Patients diagnosed through the radiological methods were more frequently from urban sectors, from TB clusters, with comorbidities with high risk for TB sickness, such as HIV infection, diabetes and mental disorders which constituted included in active screening programs. The lack of positive microbiological assay results was the consequence of the unilateral and limited forms of pulmonary and determined a higher rate of treatment success rate.

As practical recommendations with applicative value were established:

Screening of the subpopulations with high risk should be supported through various ways including clinical, radiological and microbiological investigations for TB.

The standardized clinical-case management of TB patients should be oriented to actions aiming to address the main challenges for early detection and improve the treatment effectiveness, such as: social economical vulnerability, harmful habits and associated diseases.

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Клініко-рентгенологічні особливості перебігу легеневого туберкульозу в умовах пандемії COVID-19

Методи діагностики туберкульозу легень мають виразний вплив на швидкість проведення заходів, спрямованих на виявлення вогнища інфекції та своєчасне лікування.

Мета роботи — установити роль мікробіологічних і рентгенологічних досліджень у ранній діагностиці туберкульозу легень в умовах пандемії коронавірусної хвороби-2019 (COVID-19).

Матеріали та методи. Проведено дослідження типу випадок—контроль, в яке було залучено 172 хворих на вперше діагностований туберкульозу легень, що були розподілені на дві групи: 1-ша група — 116 пацієнтів, діагностованих рентгенологічними методами, 2-га група — 56 пацієнтів, діагностованих мікробіологічними методами.

Результати та обговорення. Основними особливостями хворих на туберкульоз, в яких діагноз верифіковано за допомогою рентгенологічних та мікробіологічних методів обстеження, в умовах пандемії COVID-19 (2020—2022) були: чоловіча стать, низький соціально-економічний стан та висока поширеність шкідливих звичок, що впливають на стан здоров'я. Пацієнти, в яких туберкульоз діагностовано за допомогою мікробіологічних методів, частіше проживали в сільській місцевості з низькою доступністю медичних послуг, неідентифіковані своєчасно через тривалу еволюцію симптоматики, пізнє виявлення, виразність клінічної симптоматики та велику частоту поганого результату лікування. Рекомендовано проводити систематичний скринінг на туберкульоз у всіх соціально-вразливих групах населення та застосовувати індивідуальний терапевтичний підхід. Пацієнти, в яких діагноз верифіковано за допомогою радіологічних методів, частіше мешкали в місті, мали супутні захворювання з високим ризиком захворювання на туберкульоз (вірус імунодефіциту людини, цукровий діабет), психічні розлади, були залучені в активну скринінгову програму. Негативний результат мікробіологічних досліджень був наслідком однобічних та обмежених форм легеневої хвороби, що зумовлювало більшу частку пацієнтів з успішним лікуванням.

Висновки. У дослідженні типу випадок—контроль установлено, що основними особливостями хворих на туберкульоз незалежно від методів обстеження є чоловіча стать, низький соціально-економічний стан і висока поширеність шкідливих звичок (куріння та вживання алкоголю). Пацієнти, в яких туберкульоз діагностовано за допомогою мікробіологічних методів, частіше проживали в сільській місцевості, мали низьку доступність до медичних послуг, що спричиняло тривалу симптоматику, пізнє виявлення форм туберкульозу, високу виразність клінічної симптоматики, тяжкий перебіг, велику частоту негативних результатів лікування, зокрема смерті. Пацієнти, в яких діагноз верифіковано за допомогою радіологічних методів, частіше проживали в місті, мали супутні захворювання та високий ризик захворювання на туберкульоз. Негативний результат мікробіологічних досліджень був наслідком односторонніх та обмежених форм легеневого туберкульозу, що сприяло збільшенню частоти успішного лікування.

Ключові слова: туберкульоз, чинники ризику, рентгенологічне дослідження, мікробіологічне дослідження, результат лікування.

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