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Method for predicting the development of tuberculosis in persons infected with HIV and held in penitentiary institutions

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Abstract

Aim. To create a new prognostic index that allows screening and predicting the development of tuberculosis in persons infected with human immunodeficiency virus (HIV), from among the suspects, accused, convicts, and assessment of how an additional diagnostic criterion can become a justification for additional preventive and anti-epidemic measures.

Methods. A mathematical model was developed by using expert opinions and applying the logical-mathematical approach of hierarchical analysis. It includes characteristics and criteria described in the modern scientific literature that does not exclude the presence of active tuberculosis or cause its unfavorable course in HIV-infected patients. The research was carried out in two stages. At the first stage, the weighting coefficients of the predictors used were calculated, and a prognostic index was created. At the second stage, the technique was applied in practice. As a result of the study in the observation group, which consisted of 157 clinical cases, the probability of tuberculosis was calculated by using the statistical grouping method.

Results. A model for calculating the prognostic index of the development of tuberculosis in patients with HIV infection has been developed. Based on the example of patients held in prisons, a graphical method is proposed for assessing the possibility of development/absence of tuberculosis in HIV-infected individuals, depending on the value of the prognostic index. In the practical application of the developed prognostic index, tuberculosis was diagnosed in 37 patients, and plans of preventive measures were developed in 120 patients.

Conclusion. The developed method of screening and predicting the development of tuberculosis in patients with HIV infection makes it possible to improve the timeliness of diagnosis of tuberculosis in the early stages and to determine the need for additional preventive or anti-epidemic measures during the work to counter the spread of this disease in the institutions of the Federal Penitentiary Service.

Keywords: tuberculosis, HIV-infection, penitentiary system, mathematical modeling.

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Background. The tuberculosis (TB) epidemic is witnessing a radical change with respect to mortality and morbidity rates. Although these parameters are showing a steady decline, the proportion of patients suffering from TB associated with human immunodeficiency virus (TB/HIV) infection is growing every year [1]. Treatment of TB in this category of patients is rather difficult, and the combination of TB/HIV infection associated with resistance to anti-tuberculous treatment by mycobacteria, as well as manifestations of underlying comorbid conditions results in a higher mortality risk. Similar trends are also typically seen in patients kept in institutions of the Federal Penitentiary Service (FPS) [2]. At the same time, there is a high incidence of acutely progressive and generalized forms of TB associated with a poor prognosis in patients with combined TB/HIV infection in prisons [1, 3, 4].

The efficacy of TB/HIV therapy largely depends on timely detection of the disease, and medical organizations providing primary health care play a critical role [5]. However, TB/HIV patients often do not have specific radiological or clinical signs, or they may have a subtle course of the disease, frequently resulting in diagnostic errors [6, 7]. In view

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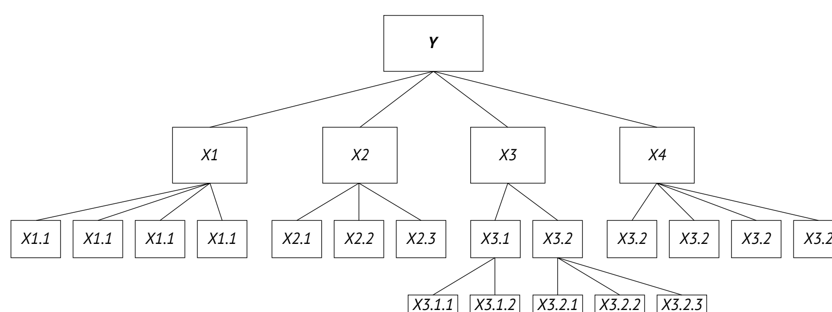

Fig. 1. The hierarchical structure of the mathematical model for assessing the risk of tuberculosis in an HIV-infected patient from among persons kept in institutions of the Federal Penitentiary Service

of the above limitations, it seems relevant to develop a mathematical model to estimate TB risk in HIV-infected patients, which could help improve diagnostic accuracy, and put in place preventive measures to counter the spread of TB.

The current work aimed to create a new prognostic index that enables screening and prediction of risk of development of TB in HIV-infected persons from among suspects, accused, and convicted persons, and to evaluate it as an additional diagnostic criterion, which would justify the adoption of additional preventive and safety measures.

Scientific novelty. Using the mathematical model, a methodology for calculating the prognostic index of risk of TB in HIV-infected patients seen in the medical units of the FPS of Russia was proposed for the first time. The introduction of this methodology would enable early diagnosis and identification of groups at high risk of developing TB, and timely implementation of preventive measures in such institutions.

Materials and methods. The mathematical model was created by expert analysts applying the logical-mathematical method of hierarchy analysis. The experts included seven persons who were leading specialists of the Medical Unit No. 18 of the FPS of Russia. During discussions with these experts, as well as analysis of sources of scientific literature [7–10], 16 predictive/prognostic factors were identified that could predispose to the development of TB in HIV-infected patients. For each factor, a weight coefficient was calculated, which determines its significance (weight) in contributing to the development of TB.

The development of the described prognostic method involves a hierarchical schematic structure, where the target of the problem under study is located at the top, and the criteria and characteristics being analyzed are at the lower levels of the hierarchy. In the next stage, matrices are constructed for pair-wise comparisons of elements at the same level with one other (x_i) on a 9-point scale, taking into account expert opinions, estimates of the geometric mean of the various factors (ω_i), and then the normalized priority vector (NPV), which determines the weight coefficient of each factor, is calculated. For matrices of paired comparisons, the consistency of expert opinions was assessed by calculating the maximum value of each matrix (l_{max}), the consistency index (CI), and the consistency ratio (CR). In the case of CR values being lower than 0.1, the opinions of experts are considered consistent. The essence of the method is presented in more detail in scientific papers [11, 12].

Results and discussion. The hierarchical model for calculating the prognostic index of developing TB in HIV-infected persons from among the suspects, accused, and convicts in prisons is represented by four levels (Fig. 1).

According to this hierarchical structure, variable *Y* is placed at the top level and represents the problem under study (determination of the risk of development of TB in an HIV-infected patient). Subsequent levels are represented by groups of factors (X_i) characterizing the probability of developing active TB in a patient (choice of experts): *X1* is a group of diagnostic characteristics obtained during the collection of patient complaints and physical examination; *X2* represents results of chest X-ray examination; *X3* represents the results of assessment of laboratory parameters of the patient's blood tests; *X4* represents a group of diagnostic characteristics obtained during the collection of the patient's history, related to the development of TB and the unfavorable course of HIV infection; *X1.1* represents the presence of cough; *X1.2* represents the presence of night sweats; *X1.3* represents fever; *X1.4* represents weight loss; *X2.1.* implies absence of visible changes on the radiograph; *X2.2* represents pneumonia-like changes on chest X-ray; *X2.3* represents focal and infiltrative changes in the upper fields of the lungs; *X3.1* represents

Table 1. Matrix of paired comparisons “Groups of characteristics that do not rule out active tuberculosis in an HIV-infected patient”

Criteria	X1	X2	X3	X4	ω_i	NPV (q)
X1	1	0.2	0.3333	0.5	0.427	0.075
X2	5	1	4	7	3.440	0.6034
X3	3	0.25	1	4	1.316	0.2308
X4	2	0.143	0.25	1	0.517	0.0906
Total	11	1.593	5.583	12.5	5.7	1.0

Note: NPV is a normalized priority vector. Assessment of consistency of expert opinions: l_{max} = 4.2209, the index of consistency is 0.0736, the ratio of consistency is 0.0818.

Table 2. Matrix of paired comparisons “Group of diagnostic characteristics obtained during the recording of complaints and physical examination”

Criteria	X1.1	X1.2	X1.3	X1.4	ω_i	NPV (q)
X1.1	1	0.5	0.125	0.25	0.354	0.0606
X1.2	2	1	0.2	0.333	0.604	0.1036
X1.3	8	5	1	4	3.557	0.6099
X1.4	4	3.000	0.25	1	1.316	0.2257
Total	15	9.500	1.575	5.584	5.830	1.0

Note: NPV is a normalized priority vector. Assessment of the consistency of expert opinions: l_{max} = 4.0921, the index of consistency is 0.0307, the ratio of consistency is 0.0341.

immunogram indices; *X3.2* represents indicators of general blood tests; *X4.1* represents absent or insufficient course of TB chemoprophylaxis; *X4.2* represents duration of HIV infection over 10 years; *X4.3* represents intravenous use of psychoactive drugs; *X.4.4* represents prior history of TB; *X3.1.1* represents CD4 count less than 200 cells/μL; *X3.1.2* means HIV ribonucleic acid is higher than 10,000 cop/μL; *X3.2.1* implies erythrocyte sedimentation rate above 30 mm/hr; *X3.2.2* represents leukocytosis; *X3.2.2* represents lymphopenia.

To determine the weight values (significance) of the various characteristics (factors) that determine the risk of development of TB in an HIV-infected patient, calculations were performed with the construction of matrices of paired comparisons and an assessment of consistency of expert opinions (Tables 1, 2).

Similarly, matrices of paired comparisons were made to evaluate the following parameters, namely, “Results of X-ray examination” (NPV of characteristics *X2.1* = 0.0754, *X2.2* = 0.229, *X2.3* = 0.6955, assessment of consistency of expert opinions: l_{max} = 3.0764, CI = 0.0382, CR = 0.0658.), “Laboratory parameters of the patient's blood test” (NPV of characteristics *X3.1* and *X3.2* were 0.5, assessment of consistency of expert opinions was l_{max} = 2, CI = 0, CR = 0), “Immunogram indices” (NPV of predictors *X3.1.1* = 0.8333, *X3.1.2* = 0.1666, assessment of consistency of expert opinions was l_{max} = 2, CI = 0, CR = 0), “General blood test indices” (NPV of predictors *X3.2.1* = 0.7142, *X3.2.2* = 0.1428, *X3.2.3* = 0.1428, assessment of consistency of expert opinions was l_{max} = 3.0, CI = 0, CR = 0), and “Groups of diagnostic characteristics obtained in the course of collecting the patient's history” (NPV of characteristics *X4.1* = 0.4811, *X4.2* = 0.09, *X4.3* = 0.0462, *X4.4* = 0.3826, assessment of consistency of expert opinions was l_{max} = 4.207, CI = 0.069, CR = 0.0766).

Further processing involved calculating the proportion of each weight coefficient from the sum of the weight coefficients of all criteria of one group, which was equal to 1.0. The obtained share values of the studied indicators are presented in Table 3.

The value of the prognostic index is calculated as the sum of the products of the weight coefficients of the various parameters/factors under study and their qualitative or quantitative characteristics, determined after comprehensive examination of an HIV-infected patient upon admission to prison.

The proposed method for predicting risk of development of TB in patients living with HIV has been applied in practice. The study group consisted of 157 HIV-infected people who were admitted to prison facilities from June 2019 to July 2020. The representativeness of the sample for HIV-infected patients held in the Russian FPS institutions during the study period was determined by the L. Sachs formula [13]. Among them, 37 patients

Table 3. Predictive factors for the development of tuberculosis in HIV-infected patients and their weight coefficients calculated by the hierarchy analysis method

n/n	Characteristic/criterion	Variable	Weight coefficient (NVP), %
1	Cough	X1.1	0.454
2	Night sweats	X1.2	0.776
3	Fever	X1.3	4.568
4	Weight loss	X1.4	1.690
5	Absence of visible changes on the chest radiograph	X2.1	4.550
6	Pneumonia-like presentation on chest X-ray	X2.2	13.818
7	Focal and infiltrative abnormalities in the upper fields of the lungs	X2.3	41.966
8	CD4 less than 200 cells/μL	X3.1.1	9.616
9	HIV ribonucleic acid above 10,000 cop/μL	X3.1.2	1.923
10	Erythrocyte sedimentation rate above 30 mm/hr	X3.2.1	8.242
11	Leukocytosis	X3.2.2	1.648
12	Lymphopenia	X3.2.3	1.648
13	Absent or insufficient course of chemoprophylaxis of tuberculosis	X4.1	4.359
14	Duration of HIV infection over 10 years	X4.2	0.815
15	Intravenous use of psychoactive drugs	X4.3	0.419
16	Dispensary registration with a TB-specialist or a history of tuberculosis	X4.4	3.466

Note: NPV is a normalized priority vector.

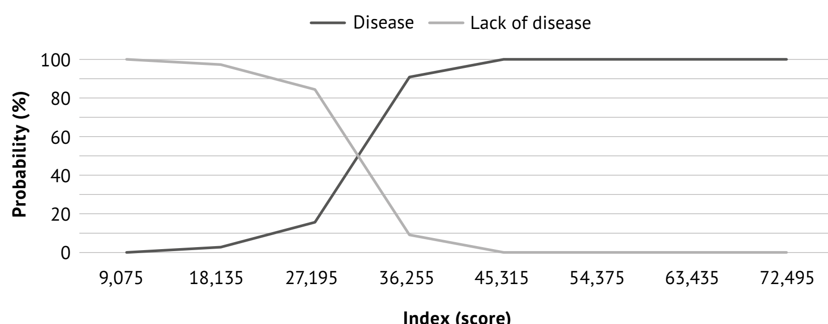

Fig. 2. The probability of the development and absence of tuberculosis among HIV-infected patients, depending on the prognostic index value

were diagnosed with TB after a comprehensive examination, and 120 patients did not have a diagnosis of TB. The probability of developing TB was calculated using the statistical clustering method.

Thus, the maximum value of the prognostic index for disease development was 77.02 points, and the minimum was 4.55 points. The optimal number of intervals of index values (according to the Sturges' formula $k = 1 + 3.322 \times \lg157$) is 8.3. Therefore, the interval values would amount to [(77.02–4.55)/8] 9.05. Furthermore, out of the total number of cases (157), cases with the development and absence of TB were distributed according to the intervals obtained (Table 4).

The resulting ratio can be presented graphically, where the "disease" curve is represented by the proportion of TB cases in each fractional interval, and the "no disease" curve has the opposite meaning and represents the share of clinical cases where the development of TB is not demonstrated.

To optimize the application of the technique, the prognostic index is calculated automatically using the MS Excel application package.

Since the prognostic assessment developed in the course of the study is essentially a formalized expert opinion, but at the same time available to the medical fraternity in FPS institutions that provide primary health care, its application assumes high practical importance.

Under conditions of detention in institutions of the penal system, timely diagnosis of TB in HIV-infected patients is undoubtedly difficult. Furthermore, branches of medical and sanitary units of the FPS in Russia are often staffed with only para-

Table 4. Correlation of cases of development and absence of tuberculosis among HIV-infected patients

Interval (in order)	Prognostic index, points	Number of cases of tuberculosis, n	Number of cases of lack of tuberculosis, n	Share of cases of tuberculosis, %	Share of cases of lack of tuberculosis, %
1	4.55–13.61	55	0	0	100
2	13.61–22.67	36	1	2.7027	97.2973
3	22.67–31.73	27	5	15.625	84.375
4	31.73–40.79	2	20	90.91	9.09
5	40.79–49.85	0	5	100	0
6	49.85–58.91	0	4	100	0
7	58.91–67.97	0	1	100	0
8	67.97–77.02	0	1	100	0

medical staff (medical assistants) or general practitioners. In light of this, the application of this methodology for predicting the development of TB and its screening, based on the assessment of measurable parameters available at the stage of primary health care, will help to improve the results of anti-TB programs in the FPS institutions on par with traditional and heuristic approaches.

Conclusion. The study was conducted with the aim of developing a methodology for screening and predicting risk of development of TB in HIV-infected patients in prisons. The methodology involves the calculation of the weight coefficients of 16 predictors (factors) proposed by experts and the calculation of the total prognostic index. The scope of this study can be applied in TB screening and diagnosis, as well as the initiation of preventive measures to counter the spread of TB in institutions of the FPS. The advantages of the method include its simplicity and availability, since there is no need for any additional expensive or invasive diagnostic methods.

CONCLUSIONS

1. Calculation of the prognostic index can become one of the methods of screening of patients with HIV infection from among those held in prisons.
2. Timely information regarding the prognostic factors contributing to development of tuberculosis under conditions of servicing a sentence, as well as diagnosing it at the early stages would enable putting in place suitable measures to prevent the spread of this disease in institutions of the FPS.

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