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The risk factors for developing primarily detected pulmonary tuberculosis requiring hospitalization

*Veronica Feller, Aurelia Ustian

Department of Pneumophthisiology, *Nicolae Testemitanu* Sate University of Medicine and Pharmacy
Chisinau, the Republic of Moldova

Authors' ORCID iDs, academic degrees and contributions are available at the end of the article

*Corresponding author: veronica.feller@gmx.de
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Abstract

Background: The risk factors assessment and updating will enable to establish an efficient and targeted policy in the fight against tuberculosis, thus providing a much more efficient management of the limited resources available in the Republic of Moldova. The purpose of the research is to study the impact of risk factors in patients with pulmonary tuberculosis treated within inpatient and outpatient units, as well as the effectiveness of treatment.
Material and methods: A case-control analytical, cross-sectional, retrospective study was conducted on 243 patients with pulmonary tuberculosis, with negative and positive microbiological results, which were sensitive to treatment. The patients were divided into two groups: the study group (190), the inpatients and the control group (53) that were treated in the outpatient setting.
Results: The risk factors for developing TB that require hospital admission include the following: demographic factors: men (Odds Ratio) (OR) = 3.29, confidence interval (CI) 95% 1.75-6.17), and passive detection method (OR = 3.25, CI95% 1.72-6.11) epidemiological – contact (OR = 3.66, CI95% 1.63-8.21); socio-economic: unfavorable living conditions (OR = 7.4, CI95% 3.63-15.09), unemployment (OR = 4.77, CI95% 2.27-10.06), primary education (OR = 4, 59, CI95% 1.05-19.91), secondary education (OR = 5.02, CI95% 1.49-16.89), smoking (OR = 13.86, CI95% 1.86-103.4), alcohol and smoking abuse (OR = 3.47, CI95% 1.18-10.18); medical and biological data: two chronic pathologies (OR = 13.86, CI95% 1.86-103.41), liver pathologies (OR = 3.06, CI95% 1.04-9.01).
Conclusions: Inpatients exhibit more risk factors than outpatients, which leads to a more serious development of TB pathogenesis. The efficient sorting of patients according to hospitalization criteria has contributed to a highly successful treatment rate.
Key words: pulmonary tuberculosis, risk factors.

Introduction

Tuberculosis is an infectious disease, which according to mortality rate is overcome only by HIV. According to WHO data, 1/3 of the global population is infected with *Mycobacterium tuberculosis*. The risk of developing tuberculosis during life have 10% of the population; however, immunocompromised people show a higher risk of disease. The prevalence of tuberculosis infection and the disease itself, as well as mortality from this disease remains a major global health problem [1].

According to the results stated in the WHO report on the fight against TB for 2018, 10 million people have contracted tuberculosis in the world (confidence interval) (CI) = 9.0-11.1 million); this indicator has remained relatively stable lately. In the Republic of Moldova there were 3500 cases of tuberculosis (the incidence of tuberculosis represents 84 cases per 100 000 population), 1400 of them being multidrug-resistant tuberculosis (MDR) (34 per 100 000). Therefore, the Republic of Moldova is one of the 30 coun-

tries in the world with a high burden of multidrug-resistant tuberculosis [1].

Assessment of risk factor for contraction of TB and of its unfavorable evolution, might justify the opportunity to change the groups structure that are at high risk for developing this disease, thus, a prompt identification of tuberculosis patients will reduce the number and need for their specific inpatient treatment.

Material and methods

In order to achieve the purpose and objectives of the study a documentary research was performed, which included a retrospective cross-sectional analytical study of case-control type to assess the risk factors involved in the development of primary pulmonary tuberculosis detected. The information was collected by extracting and analyzing the data from the observation sheets of patients admitted to the Municipal Clinical Hospital of Phthisiopneomology and from patient's medical records who received outpa-

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tient treatment in the Medical-Territorial Associations of Chisinau.

243 new cases of pulmonary tuberculosis showing negative and positive sensitivity to treatment bacteriological results were included in the study during 01/01/2017-31/12/2017. All the study parameters were compared between two groups: the study group (190, 78.2%) included patients, treated in inpatient settings during the intensive stage, and the control group (53, 21.8%) included patients, treated at both stages within outpatient conditions.

Based on the study results, the database was established. The primary data collected were verified and computer-processed by using Excel of the 2007 Microsoft Office site and the Epi Info 7.2 program. The data were found as absolute, relative (rates, proportions and ratios) and mean values. The statistical data significance was determined by calculating the confidence interval for the significance of the results of 95% (CI95%). The significance of the relative values was assessed by determining the "p" value using the "t" – Student test for assessing the quantitative parameters and the "Chi-square" non-parametric test (criterion χ2) or the Fisher exact test for the qualitative ones. The probability ratio – Odds Ratio (OR) was calculated to assess the strength of the epidemiological association of risk factors and assigned risk (AR) via the Epi Info 7.2 program. The Excel program helped to calculate the means, ratios, standard deviation (SD), followed by graphical representation.

Results

In 2017, 310 of new cases were registered in Chisinau. Of these – 112 (36.1%) showed negative bacteriological results, – 130 (41.9%) were positive, sensitive to anti-tuberculosis treatment and 68 (22.00%) were positively resistant to treatment.
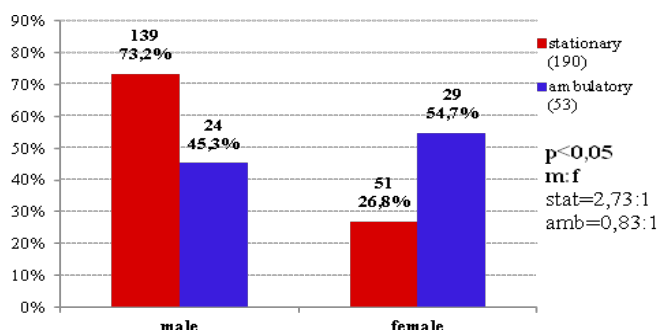

Fig. 1. Gender distribution

Almost 3/4 of the hospitalized patients were men (fig. 1), the men: women ratio being of 2.73: 1, while more than half were women from outpatient department (p <0.05).

In both groups, more than half of the patients were aged between 25-44 years (fig. 2) (p> 0.05). The average age (SD) of inpatients was 42.4 years (14.3), and of outpatients was 41.7 years (15.8).

The inpatients were mostly detected by a passive method (by referral), accounting for 2/3 of the patients, whereas only 1/3 of cases were identified by the active method (by prophylactics) (fig. 3). Both methods show an equal occurrence within outpatient settings, viz. half of the cases per each (p<0.05).
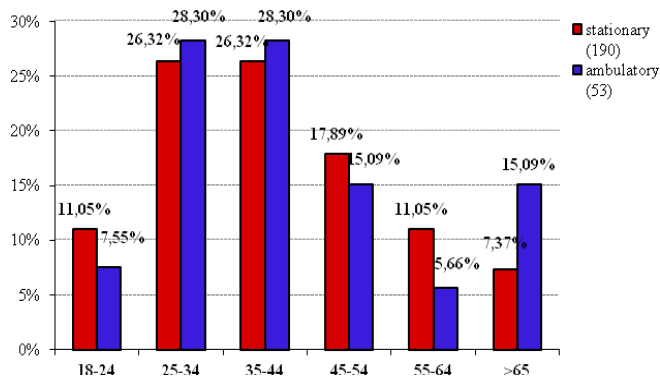
Fig. 2. Age distribution
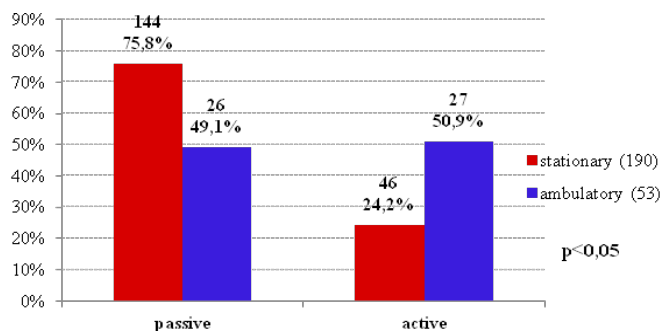
Fig. 3. Detection method

From an epidemiological point of view, the study assessed the possible contact of patients on being migrants from countries with a high-burden of tuberculosis. The present study also analyzed data of homeless people, given the fact that they have a much higher probability to contact tuberculosis, as well as they are more prone to a multitude of risk factors: epidemiological, socio-economic and medico-biological.

Table 1

Epidemiological factors

Epidemiological factors	Inpatients (190)		Outpatients (53)		p
	N	%	N	%	</>0,05
Contact	75	39,47	8	15,09	<0,05
Migrants	49	25,79	7	13,21	>0,05
Homeless	19	10,00	0	0	<0,05
Penitentiary	20	11	2	4	>0,05
No factor	92	48,42	38	71,70	<0,05

Based on the table data, 39.47% of the inpatients and only 15.09% of outpatients had contact with a tuberculosis patient (p <0.05). There were 19 homeless patients who

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received treatment at both stages of inpatient treatment (p<0.05). 1/4 of the patients from the hospital had a migrant status, whereas 7 (13.21%) patients underwent outpatient treatment (p>0.05). 20 patients who received inpatient treatment returned from the penitentiary, which represents 10.5%, and only 2 (3.7%) patients were treated in outpatient conditions (p>0.05). A large number of patients showed no epidemiological risk factors. Thus, almost 1/2 of the inpatients and almost 3/4 of the outpatient did not register any epidemiological factor (p<0.05).

The socio-economic aspects of the patients were examined in terms of living conditions, marital status, occupation and level of education.
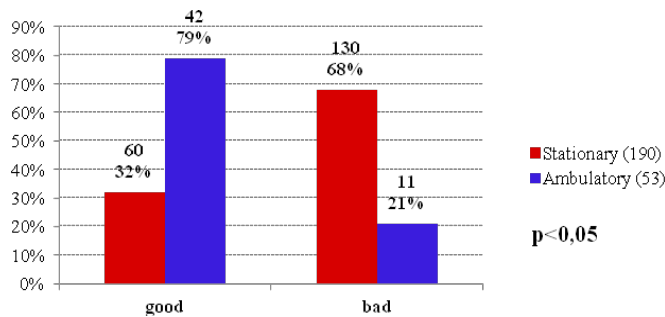

Fig. 4. Living conditions

2/3 of inpatients and only 1/5 of cases from outpatient department had unsatisfactory living conditions (fig. 4), (p <0.05).

Table 2

Occupation and level of education

Occupation / education	Inpatients (190)		Outpatients (53)		p
	N	%	N	%	</>0,05
Employed	58	30,53	34	64,15	<0,05
Unemployed	100	52,63	10	18,87	<0,05
Limited work capacity	9	4,74	0		>0,05
Retired	16	8,42	6	11,32	>0,05
Student	5	2,63	2	3,77	>0,05
Maternity leave	2	1,05	1	1,89	>0,05
Primary education	29	15,26	2	3,77	<0,05
Gymnasium studies	44	23,16	3	5,66	<0,05
Secondary education	86	45,26	33	62,26	<0,05
Higher education	21	11,05	14	26,42	<0,05
Incomplete higher education	10	5,26	1	1,89	>0,05

Only 30% of inpatients were employed and more than a half were unemployed. However, almost 2/3 of patients from outpatient department were employed and less than 1/5 unemployed (p<0.05). There were registered 9 people with limited work capacity, who received treatment under inpatient conditions (tab. 2).

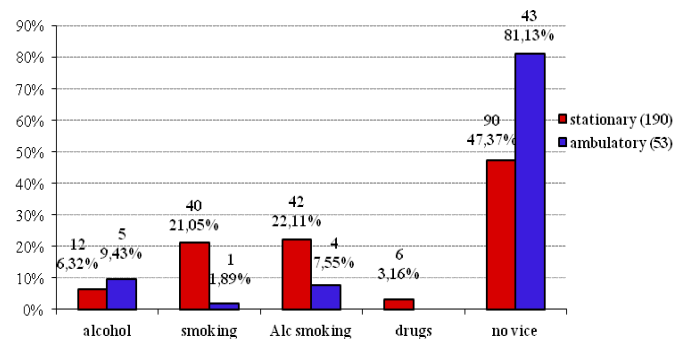Almost 40% of the inpatients had a low level of education, thus accounting for about 10%, compared to most of patients who had a profession or higher education (p<0.05) (tab. 2).

Fig. 5. Vice-aassociated risk factors

More than half of the inpatients had at least one associated bad habit, whereas only every fifth of individuals was from the outpatient department (p<0.05). Among the inpatients, 6.32% recorded an alcohol abuse, 22.11% – tobacco smoking and 21.05% of cases combined these two bad habits. The ratio of patients from outpatient department showed a more significantly reduced number of alcohol users and smokers compared to the inpatients. Drug users were registered among those admitted to hospital as compared to the outpatients. The distribution difference between these two groups shows statistically significant values (p<0.05) in cases of smoking-associated and both smoking and alcohol-associated risk factors (fig. 5).

The associations of chronic pathologies, such as HIV, diabetes mellitus, lung diseases, liver pathologies, gastrointestinal tract diseases, cardiovascular diseases, psychiatric disorders, etc. were studied from both medical and biological point of view. In addition, the study analyzed whether there is a difference when patients have one, two or three associated pathologies.
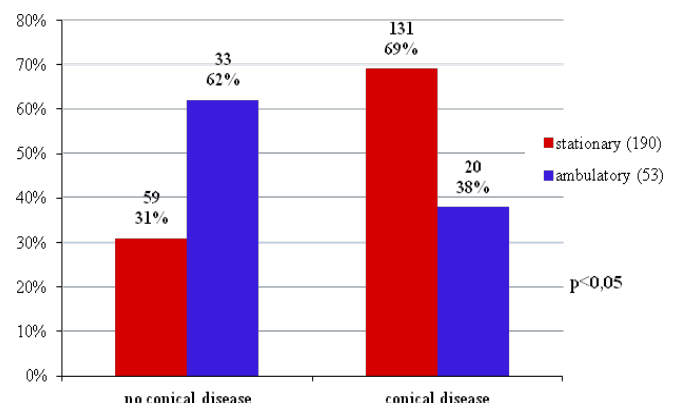

Fig. 6. Associated chronic pathologies

Almost 70% of inpatients had at least one associated chronic pathology, while less than 40% were from the outpatient settings (p<0.05) (fig. 6).

More than 1/3 of the inpatients and outpatients presented with an associated chronic pathology, but in the inpatients each fifth patient had associated 2 chronic pathologies
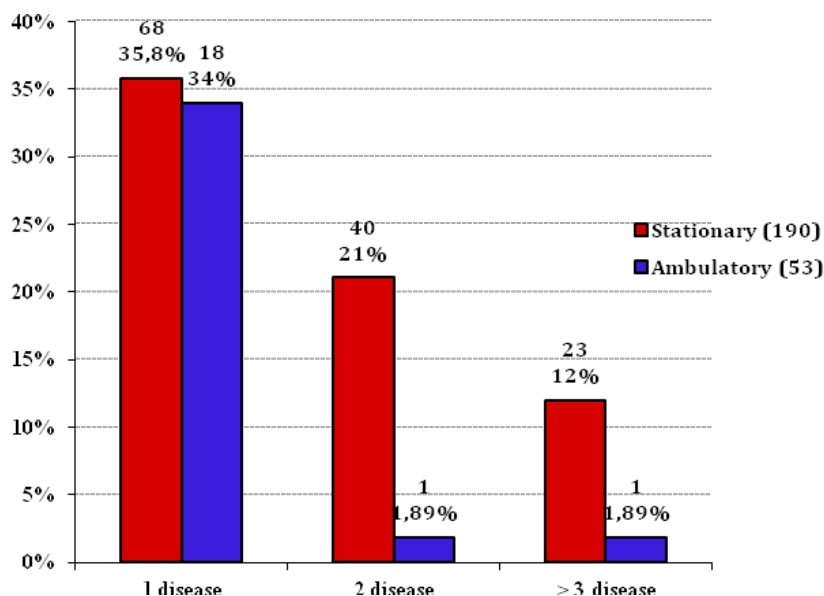
Fig. 7. Number of associated chronic pathologies

Table 3

Associated chronic pathologies

Associated chronic pathologies	Inpatiens (190)		Outpatients (53)		p
	N	%	N	%	</>0,05
Liver diseases	38	20	4	7,55	<0,05
Lung diseases	29	15,26	3	5,66	>0,05
Cardiovascular diseases	25	13,16	2	3,77	>0,05
HIV	23	12,11	0	0	<0,05
Diseases of the gastrointestinal tract	20	10,53	2	3,77	>0,05
Neurological diseases	21	11,05	1	1,89	>0,05
Diabetes mellitus	15	7,89	1	1,89	>0,05
Immunosuppressive therapy	9	4,74	4	7,55	>0,05
Anemia	10	5,2	0	0	>0,05
Lues	7	3,68	0	0	>0,05
Psychiatric diseases	6	3,16	0	0	>0,05
Vascular diseases	3	1,58	1	1,89	>0,05
Other diseases	31	16,32	2	3,77	<0,05

Table 4

Ranking of risk factors

Parameter	OR, CI95	AR (%)	Ranking
Smoking	13,86 (1,85-103,41)	92,78	I
2 chronic diseases	13,86 (1,85-103,41)	92,78	I
Bad living conditions	7,4 (3,63-15,09)	86,50	II
Gymnasium studies	5,02 (1,49-16,89)	80	III
Unemployed	4,77 (2,27-10,06)	79,03	IV
Primary education	4,59 (1,05-19,91)	78,21	V
Contact	3,66 (1,63-8,21)	72,67	VI
Alcohol and smoking	3,47 (1,18-10,18)	71,18	VII
Men	3,29 (1,75-6,17)	69,60	VIII
Passive detection	3,25 (1,72-6,11)	69,23	IX
Liver diseases	3,06 (1,04-9,01)	67,3	X

(p <0.05), and each ninth three or more (fig. 7).

The most common pathologies associated among hospitalized patients were liver (p <0.05), pulmonary and cardiovascular disorders. There were registered 23 patients with HIV, all of them received inpatient treatment (tab. 3).

The present study is a comparative assessment of the epidemiological associations of determinants in tuberculosis, performed in patients diagnosed with primary pulmonary tuberculosis detected in 2017, who received inpatient treatment, as well as in patients who received outpatient treatment. For this purpose, 46 risk factors were determined and analyzed, of which 11 showed a statistically significant

difference between samples (p <0.05). Thus, it was possible to calculate the ratio of the probability – Odds Ratio (OR) and the assigned risk (AR). The present study assessed and analyzed the epidemiological relationship of the determinant factors for tuberculosis, requiring inpatient treatment, among patients who are mostly exposed to their action, followed by their ranking.

The highest risk is attributed to social, medical and biological factors (tab. 4). Thus, smokers and people with two associated chronic pathologies had a 13.86 (OR = 13.86; CI95 1.85-103.41) or higher probability to develop tuberculosis, requiring hospital admission. These are followed by patients who exhibited unfavorable living conditions (OR = 7.4; CI95 3.63-15.09), low level of education (OR = 5.02; CI95 1.49-16.89), were unemployed (OR = 4.77; CI95 2.27-10.06), contacted other persons (OR = 3.66; CI95 1.63-

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8.21), as well as alcohol and tobacco consumers (OR = 3.47; CI95 1.18-10.18), men (OR = 3.29; CI95 1.75-6.17), subjects detected by passive method (OR = 3.25; CI95 1, 72-6.11), people suffering from chronic liver diseases (OR = 3.06; CI95 1.04-9.01).

Table 5

The treatment outcomes

The result of the treatment		Inpatients (190)		Outpatients(53)		p
		N	%	N	%	</>0,05
Successful treatment		157	82,63	50	94,34	<0,05
	Treated	90	47,37	12	22,64	<0,05
	Completed	67	35,26	38	71,7	<0,05
Lost surveillance		14	7,37	2	3,77	>0,05
Died		19	10	1	1,89	>0,05
	TB	11	5,79	0		>0,05
	Other causes	8	4,21	1	1,89	>0,05

The successful treatment rate (tab. 5) was high in both hospitalized patients (82.63%) and outpatients (94.34%). Every tenth inpatient died, while only one death was registered in the outpatient department (1.89%).

Discussion

The study analyzed the impact of risk factors on the development of tuberculosis in hospital and outpatient departments in 2017. It recorded a predominant incidence of males compared to females. The data obtained are similar to the results provided by the WHO [2]. Most patients were of working age, between 25-54 years.

Most patients were passively detected; this factor determined the progression of the disease in a more advanced evolution. Specialists at international and national level recommend the active detection of tuberculosis cases, in order to intervene promptly in its treatment and avoid the spread of infection [2, 3].

The socioeconomic, biomedical and epidemiological risk factors were assessed within this study. Thus, from a socio-economic point of view, the marital status, the patients' occupation, the level of schooling and the associated vices were studied as risk factors in the development of tuberculosis. Statistically significant results were obtained for unemployed patients, those with primary and secondary education, in smokers, but also in patients who excessively consume alcohol and tobacco. Studies conducted by researchers say that tuberculosis is a social pathology and largely affects the socially vulnerable population. The excessive smoking and alcohol consumption of 40 g per day are also reported as risk factors in contacting tuberculosis [4-9].

From a biomedical point of view, the associated pathologies of the patients were analyzed. The study tried to find a causal link between the area affected by a chronic disease and the development of tuberculosis. Patients living with chronic pathologies have a higher risk of developing tuberculosis that requires hospitalization, however contrary to expectations most patients suffer from liver, lung and cardiovascular pathologies. The pathologies, such as diabetes, renal failure, and immunosuppressive treatment showed statistically insignificant results. Although the study group (inpatients) had a statistically significant distribution (p <0.05) for HIV/AIDS it was impossible to determine the strength of the epidemiological association and the risk assigned due to the absence of patients living with HIV/AIDS in the control group (outpatients) [4, 7, 9, 10-13].

From an epidemiological point of view, the patients who were in contact with a tuberculosis patient, the phenomenon of migration to / from countries with a high tuberculosis load, homeless patients and those released from detention were studied. Epidemiological factors were more common in inpatients; however, statistically significant results were obtained for patients who had contacts with TB-infected persons [4, 7, 9, 12, 14].

Conclusions

1. Most inpatient cases included men of working age, detected by the passive method, 1/3 of which having a contact with a TB-infected person, 1/4 being migrants, and every tenth was homeless or released from the jail. The outpatient clinic revealed a predominant number of women and people detected by the active method.

2. The social factors were more highlighted in the patients treated in the inpatient departments, such as unfavorable living conditions, lack of employment, low level of education, and vicious habits.

3. Hospitalized patients had 2-3 comorbidities, often at a decompensation stage that required permanent and thorough medical monitoring, whereas most patients in outpatient conditions did not present or have only one associated disease.

4. According to the ranking of risk factors it was established that patients who are exposed to socio-economic factors (smoking, unsatisfactory living conditions, unemployment, low level of education) and medico-biological (association of two chronic pathologies), are more likely to develop tuberculosis that requires hospitalization.

5. A multitude of risk factors present in inpatients, compared to outpatients, leads to the development of TB processes with more serious evolution, and efficient sorting of patients according to hospitalization criteria has contributed to achieving a high success rate of treatment.

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Authors' ORCID iDs and academic degrees
Veronica Feller, MD Resident – https://orcid.org/0000-0003-0929-2292.
Aurelia Ustian, MD, PhD, Professor – https://orcid.org/0000-0002-2679-5767.

Authors' contribution
VF acquired and interpreted the data and drafted the first manuscript, AU interpreted the data, revised the manuscript critically. All the authors revised and approved the final version of the manuscript.

Ethics approval and consent to participate
The research was approved by the Research Ethic Board of *Nicolae Testemitanu* State University of Medicine and Pharmacy (protocol No 55 of June 18, 2015).

Conflict of Interests
The authors have no conflict of interests to declare.