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Tuberculosis characteristics and risk factors in urban compared with rural patients

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Abstract

Material and methods: A retrospective selective, descriptive study of socioeconomic, epidemiological peculiarities, case-management, diagnosis and microbiological characteristics of 694 patients with tuberculosis registered in Chisinau in 2016 was performed. Among them 581, had an urban residency and 112 rural residency.

Results: Residents from rural population and young persons in urban areas were most affected. Socioeconomic vulnerability predominated in both subpopulations; however, the gravity was more represented in the urban group. Lower level of education and tuberculosis contacts were more dominating in the rural group. Comorbidities, HIV infection were more frequently identified in the urban group, but destructive forms – in the rural patients. Low treatment outcomes were more frequently established in the rural group.

Conclusions: Risk factors for tuberculosis in urban subpopulation were: unemployment, lack of health insurance, homelessness, comorbidities, HIV infection. In rural population prevailed the following risk factors: low school education and tuberculosis contact.

Key words: tuberculosis, risk factors, outcome.

Introduction

Tuberculosis is one of the 10 causes of death worldwide and is a leading cause of death in HIV infected people worldwide [1, 2, 3]. The disease represents a serious public health problem in the Republic of Moldova (RM), affecting the most active economic age group of the population. According to the published data by the Moldovan National Centre for Management in Health during the period 2013-2015 it was registered an important decline of the incidence (with 22.4/100.000) in Chisinau: 2013 – 94.1/100.000, 2014 – 81.7/100.000 and 2015 – 71.7/100.000 population, prevalence (with 25.4/100.000) 2013 – 125.6/100.000, 2014 – 108.8/100.000 and 2015 – 100.1/100.000 population also the mortality 2013 – 10.6/100.000 and in 2014 – 6.9/100.000 population. During the same period of time in the RM the total incidence decreased: in 2013 – 125.6/100.000, 2014 – 108.8/100.000 and 2015 – 100.1/100.000 population, the prevalence (with 23.3/100.000) in 2013 – 109.7/100.000, 2014 – 97/100.000 and 2015 – 86.4/100.000 population, also the mortality 2013 – 10.5/100.000 and in 2014 – 8.8/100.000 population. An important difference between epidemiological indices registered in urban and rural localities was established. In the rural localities of the RM the total incidence was by 25% more elevated than in urban localities: 103.6 /100.000 in 2014 and 90.6/100.000 in 2015 compared with 78.4/100.000 in 2014 and 67.2/100.000 in 2015. A similar trend was identified regarding the incidence of the new cases, which were more elevated (by 18%) in rural localities compared with urban areas. The incidence of the new cases diminished by 18% from 91.5/100.000 in 2013, 85.4 /100.000 in 2014 and 73.5/100.000 in 2015 in the rural localities and by 19.7% in an urban population: from 72.3/100.000 in 2013, 62.1/100.000 in 2014 and 52.6/100.000 in 2015. More evidently diminished the prevalence in the urban localities (by 21%) 115/100.000 in 2013, 99/100.000 in 2014 and 90.4/100.000 population in 2015 compared with 6% in the rural areas: 207.3/100.000 in 2013, 199/100.000 in 2014 and 201.7/100.000 population [4].

In this epidemiological context, it must be exposed that the territory of the RM extends about 350 km from North to South and 150 km from West to East and is distributed in 56.7% of agricultural land, 13.6% of forests, 1.4% of urban localities and 7.6% of rural localities. From an administrative point of view, the territory of the RM is organized in 1.682 localities, classified in 5 municipalities, 61 cities, 916 villages and 659 communes (several villages), integrated in 32 districts and the autonomous territorial unit Gagauzia. The population of the RM was 3.550.900 people, including 1.476.100 urban residents and 2.074.800 rural persons in 2016. The urban population constituted 41.3% and the rural – 58.7% of the entire population of the RM. The urban settlements account for 1.4% of the RM territory, with an average density of 128 inhabitants/km^2. The rural settlements account for 7.6% of the RM territory, with a total number 1.614 of rural localities. Some of them have formed a population less than 10.000 inhabitants, with an

average density of the rural population being 7 inhabitants/km^2 [5].

The regional system of the RM was founded on the basis of legislative acts: the law of the regional development no. 438-XVI of 28.12.2006, the National Strategy for Regional Development (decision no 158 of 04.03.2010) and the regulatory framework that establishes the institutions which are responsible for the regional development (decision no 127 of 08.02.2008) [6, 7]. The regional development of the RM is realized according to the regional policy that aims to perform the territorial cohesion, which means to reduce the gaps between urban and rural localities, between the center and the periphery of the RM [7]. Assessing the health care disparities it was established that the rural households spent for health more than the urban family groups: 5.9% vs. 5.4% in 2014, 6.6% vs. 6.5% in 2015 from the total family income [8]. It is one of the major indices that showed a reduced accessibility for public health services of the rural population [9]. The poverty rate in rural areas is 5 times higher than in urban areas [8]. It was found that 86% of the poorest people from the RM live in villages [10]. Several social categories are among the poorest persons: families which are dependent only on agricultural activities, families with a lot of children, the elderly, persons with low levels of education attainment and lack of professional skills [11].

Distributing the population, according to the area of their habitation (house) it was established that in urban localities one person possesses 19.4 meters^2 and in rural areas – 23 meters^2/person [12]. Even if the area of the rural household is larger per capita, the quality and endowment are below the basic needs, which include electricity, natural gas, heating system, safe water and sewerage, as well the telecommunication (phone line) [12]. The urban areas have a better developed infrastructure, but the rural areas have an inhomogeneous distribution of the basic needs. All exposed data demonstrated the cause of the discrepancy of the public health indicators between urban and rural localities. While analyzing the statistical reports were established multiple healthcare problems and socially determined morbidities in rural localities: malnutrition, hipovitaminosis, severe anemia, tuberculosis, scabies, pediculosis. [14]. Residents of rural communities are more exposed to polluted water and to the consumption of dangerous food, due to the infestation of the land with wastewater and pesticides [13]. Current researches demonstrated a high level of the rural residents poisoning by poor management of the pesticides, fungicides, herbicides and insecticides. Due to the unequal distribution of the natural gas system, the residents of rural areas of the RM use fossil fuels (wood, coal and oil derivatives), which increase the risk of indoor air pollution with toxic gases such as carbon monoxide and other combustion gases involving the risk of involuntary poisoning and death [14].

Current political and economic trends are based on the reduction of the accessibility to the public healthcare services and increasing of the private sector offers [15]. A significant proportion of people from rural localities have no compulsory insurance policy, lack of education and high risk habits associated with the alcohol and tobacco consumption and unhealthy diet [16, 17]. The poor management of the healthcare, human resources, a big distance between the villages and primary health care institutions multiplied the barriers for the accessibility of the rural population to low price healthcare services [9, 14, 18, 19, 20]. Enumerated conditions aggravated by the social, economical vulnerability contributed to the extension of the tuberculosis in the rural population.

So, **the aim** of the study was to assess the tuberculosis features and risk factors of patients, residents of the urban sectors and rural localities of Chisinau city.

Objectives were: 1. Assessment of the socioeconomic and epidemiological risk factors of patients with tuberculosis and comparing them according to the urban and rural residence. 2. Evaluation of the case-management, diagnosis type, radiological aspects and microbiological characteristics of tuberculosis patients and comparing them according to the urban and rural residence. 3. Identification of the risk factors for tuberculosis, according to the urban and rural residence.

Results and discussion

According to the data obtained from the monitoring and follow-up of the case system during the period of 2016 were registered 694 tuberculosis cases among all residents of Chisinau, which included 581 patients from the urban sectors and 112 from rural communes: Bacioi, Bic, Braila (Bacioi), Bubuieci, Budesti, Tohatin, Cruzesti, Ciorescu, Codru, Colonita, Singera, Ghidighici, Stauceni, Gratiesti, Truseni, Vadul lui Voda and Vatra [12].

While distributing selected patients, according to the sex it was established the statistical predominance of men, with the highest rate in the rural group. So, men were 82 (73.2%) in the rural group and 392 (67.5%) in the urban group with a male/female ratio 2.1/1 in the urban group and 2.3/1 in the rural group. Repartition of the patients into age groups, according to the WHO recommendation identified that the largest subgroup in the urban group was between 25 and 34 years old – 136 (23.4%) patients, followed by those who were between 35 and 44 years old – 125 (21.5%) patients, between 45 and 54 years old – 115 (19.7%) patients and between 55 and 64 years old – 100 (17.2%) patients. In a minor proportion were represented patients younger than 24 years old – 41 (7.1%) cases.

In the rural group predominated patients who were between 35 and 44 years – 33 (29.4%) patients, followed by those who were between 45 and 54 years – 23 (20.5%), also between 55 and 64 years – 22 (19.6%) patients. In a minor proportion of patients were included young groups, who were between 25 and 34 years old – 19 (16.9%) and younger than 24 years – 10 (8.9%) cases. While comparing the groups was identified the predominance of the young subgroup of 25-34 years old in the urban group compared with the rural group: 136 (23.4%) vs. 19 (16.9%) patients, and older adults in the rural compared with the urban group: between 35 and 44 years old – 33 (29.4%) vs. 125 (21.5%) patients,

between 45 and 54 years – 23 (20.5%) vs. 115 (19,7%) patients and between 55 and 64 years old 22 – (19.6%) vs. 100 (17.2%) patients. Distribution of patients in three age groups established that young adults who were less than 34 years old predominated in the urban group – 177 (30.4%) vs. 29 (25.9%) patients from the rural group, also older adults, more than 55 years accounted for 164 (28.3%) patients in the urban vs. 27 (24.1%) patients in the rural group. The patients who were included in the subgroup between 35 and 54 years old were in a similar proportion of 56 (50%) vs. 240 (41.3%) patients. No statistical threshold was achieved comparing patients between the age subgroups (tab. 1).

Table 1

Distribution of patients by sex, age and demographic data

Indices	Sex Age groups	Urban group N=581 (P%)	Rural group N=112 (P%)	P value
Sex	Men	392 (67.5)	82 (73.2)	>0.05
	Women	189 (32.5)	36 (26.8)	>0.05
Age groups	18-24 years	41 (7.1)	10 (8.9)	>0.05
	25-34 years	136 (23.4)	19 (16.9)	>0.05
	35-44 years	125 (21.5)	33 (29.4)	>0.05
	45-54 years	115 (19.7)	23 (20.5)	>0.05
	55-64 years	100 (17.2)	22 (19.6)	>0.05
	+65 years	64 (11.1)	5 (4.5)	**<0.01**

Note: Applied statistical test: paired simple T-test, P – probability.

When distributing patients, according to the economic status, it was established that employed persons, which were contributing to the health budget by paying taxes predominated in the urban group – 137 (23.6%) vs. 21 (18.7%) patients and patients with health insurance policy predominated in the rural group – 68 (60.8%) vs. 289 (49.7%) patients in the urban group. Unemployed patients made up the majority of both groups and predominated in the rural group – 72 (64.2%) vs. 305 (52.4%), however, the patients without health insurance predominated in the urban group – 292 (50.2%) vs. 44 (39.2%) cases. It is explained by the fact that Moldovan citizens from rural localities, owners of the agricultural land have health insurance offered by the state [23]. Disease disabled patients, retired and students predominated in the urban compared with the rural group. The highest proportion among them were retired patients – 74 (12.7%) vs. 9 (8%), followed by disease disabled – 53 (9.1%) vs. 8 (7.1%) and students –12 (2.0%) vs. 2 (1.7%) cases in urban compared with the rural group (tab. 2).

Assessment of the educational level, demonstrated that most of the patients from both groups had secondary education, however, in the rural group there were 59 (52.7%) vs. 229 (39.4%) patients with secondary education in the urban group. Technical vocational education and bachelor studies predominated in the urban group – 162 (27.8%) vs. 19 (16.9%) in the rural group and respectively 47 (8.1%) cases in the urban group vs. 2 (1.8%) in the rural group. Primary and incomplete secondary education had each fourth patient in both groups – 143 (24.6%) in the urban group vs. 29 (25.9%) in the rural group. So, lower level of education statistically predominated in the rural group – 88 (78.5%) vs. 372 (64.1%) patients in the urban group. Exposed data are revealed in the table 3.

Table 2

Distribution according to the socioeconomic data

Indices	Economic state	Urban group N=581 (P%)	Rural group N=112 (P%)	P value P value
Economically stable	Employed	137 (23.6)	21 (18.7)	>0.05
	Insured	289 (49.7)	68 (60.8)	<0.05
Economically vulnerable	Disease disabled	53 (9.1)	8 (7.1)	>0.05
	Retired	74 (12.7)	9 (8)	>0.05
	Students	12 (2.0)	2 (1.7)	>0.05
	Unemployed	305 (52.4)	72 (64.2)	<0.05
	Lack of health insurance	292 (50.2)	44 (39.2)	<0.05

Note: Applied statistical test: paired simple T-test, P – probability.

Table 3

Distribution according to the last graduate level

Education	Urban group N=581 (P%)	Rural group N=112 (P%)	P value
Primary & incomplete secondary education	143 (24.6)	29 (25.9)	>0.05
Secondary education	229 (39.4)	59 (52.7)	**<0.01**
Secondary technical vocational education	162 (27.8)	19 (16.9)	**<0.01**
Bachelor studies	47 (8.1)	2 (1.8)	**<0.001**

Note: Applied statistical test: paired simple T-test, P – probability.

The major social characteristics of patients from the three groups were caused by the vulnerable economic state and living in poor conditions. Living under the poverty threshold predominated in patients from the rural localities – 36 (32.1%) vs. 165 (28.4%) cases from the urban group. The extreme poverty, caused by homelessness statistically predominated in the urban group – 130 (22.4%) vs. 17 (15.2%) cases in the rural group. History of migration during the last year was identified in a similar proportion of 59 (10%) patients from the urban vs. 11 (9.8%) cases. History of imprisonment was established in a similar proportion of 33 (5.8%) in the urban group vs. 5 (4.5%) in the rural group.

Close infectious contact with a member of a family who was previously diagnosed statistically predominated in the rural group – 16 (14.3%) compared with the urban group – 38 (6.5%). It could be explained by the fact that most of the sources of infection in the urban population are not identified, however, in the rural localities the infectious contact is efficiently managed due to a fewer number of population. Comorbid patients statistically predominated in the urban group – 258 (44.4%) vs. 24 (21.4%), more evident due to the high prevalence of the HIV infection – 59 (10.1%) in the urban group vs. 3 (2.6%) cases in the rural group. Harmful habits with health consequences such

as chronic alcoholism predominated in the urban group – 54 (9.2%) vs. 6 (5.4%), as well as the drug use – 10 (1.7%) vs. 1 (0.9%) patients in the rural group, as well as mental disorders – 11 (1.8%) vs. 1 (0.9%) case. Chronic respiratory and gastrointestinal diseases (including hepatitis) diseases predominated in the urban group – 37 (6.4%) vs. 6 (5.4%) and respectively 51 (8.7%) vs. 5 (4.4%) cases. No other statistical differences were detected among groups regarding the associated diseases (Table 4).

While distributing patients, according to the registered type of case it was identified that new cases predominated in the rural group – 70 (82) vs. 355 (61.1%) patients in the urban group. Each fourth patient in every group had a relapse – 137 (23.6%) patients in the urban group and 28 (25%) patients in the rural group. At a similar rate were patients included in the treatment after a previous "lost to follow-up" – 12 (10.7%) patients in the urban vs. 57 (9.8%) patients in the rural group and after a "treatment failure" – 29 (4.9%) patients in the urban vs. 2 (1.8%) patients in the rural group. Diagnosed and transferred from abroad to the RM were 3 (0.5%) patients. Data were demonstrated in the table 4.

Table 4

Distribution according to the risk groups

Category	Risks factors	Urban group N=581 (P%)	Rural group N=112 (P%)	P value
Socioeconomic	Poverty	165 (28.4)	36 (32.1)	>0.05
	Homelessness	130 (22.4)	17 (15.2)	**<0.05**
	Migration	59 (10)	11 (9.8)	>0.05
	History of detention	33 (5.8)	5 (4.5)	>0.05
Biological	Close contact	38 (6.5)	16 (14.3)	<0.05
	Associated diseases	258 (44.4)	24 (21.4)	<0.001
	HIV-infection	59 (10.1)	3 (2.6)	<0.001
	Diabetes	10 (1.7)	1 (0.9)	>0.05
	Chronic alcoholism	54 (9.2)	6 (5.4)	>0.05
	CRD	37 (6.4)	6 (5.4)	>0.05
	GID	51 (8.7)	5 (4.4)	>0.05
	Mental disorders (excluding IVDU)	11 (1.8)	1 (0,9)	>0.05
	Neoplasm	7 (1.2)	0	>0.05
	Renal diseases	5 (0.8)	1 (0.9)	>0.05
	Immune suppressive treatment	3 (0.5)	0	>0.05
	Drug users	10 (1.7)	1 (0.9)	>0.05
	Others	12 (2.0)	0	>0.05

Note: Applied statistical test: paired simple T-test, P – probability; NA-non available, CRD-chronic respiratory diseases, GID-gastrointestinal diseases.

Studying case-management, it was identified that the general medical staff was involved in the detection of most of the patients from the both groups and more perceptibly in the rural group – 45 (40.1%) vs 181 (31.1%) patients from the urban group. Screening of the people with high risk performed by the general practitioners detected more frequently patients from the urban group – 63 (10.8%) vs. 10 (8.9%) cases. Pulmonologists detected more frequently symptomatic patients from the urban group – 146 (25.1%) vs. 21 (18.7%). It is the consequence of the lack of the specialized medical staff, which manages the patients from the rural localities. High risk groups screening performed by pulmonologists detected more frequently patients from the rural group – 10 (8.9%) vs. 33 (5.6%) cases. Directly for hospitalization into a specialized institution came more frequently urban residents – 158 (27.1%) vs. 26 (23.2%) patients from the rural localities. So, it can be deducted that specialized hospital is more accessible for urban residents than for rural people. Death cases were more frequently detected in tuberculosis people from the rural localities – 5 (4%) than from urban districts of Chisinau – 12 (2%). Information is exposed in the table 5.

Table 5

Case-management characteristics of tuberculosis patients

Health level	Detection ways	Urban group N=581 (P%)	Rural group N=112 (P%)	P value
PHC	Detected by GPs symptomatics	181 (31.1)	45 (40.1)	>0.05
	Detected by GPs screening of HRG	63 (10.8)	10 (8.9)	>0.05
Ambulatory specialized level	Detected by SP symptomatics	146 (25.1)	21 (18.7)	>0.05
	Detected by SP screening of HRG	33 (5.6)	10 (8.9)	>0.05
Hospital level	Direct addressing	158 (27.1)	26 (23.2)	>0.05
Others	*Postmortem*	12 (2)	5 (4)	>0.05

Note: Applied statistical test: paired simple T-test, P – probability; GP-general practitioner, SP-specialist, HRG-high risk group.

Identifying the clinical, radiological forms of pulmonary tuberculosis it was established that pulmonary tuberculosis was diagnosed in a similar proportion in both groups – 546 (93.9%) vs 106 (94.6%) patients, as to extrapulmonary forms of tuberculosis – 31 (5.4%) vs. 6 (5.4%) patients. Generalized tuberculosis was established only in the urban group – 4 (0.6%) patients. Pulmonary infiltrative tuberculosis was identified in a similar proportion in both groups – 495 (85.2%) in the urban group vs. 97 (91.6%) patients in the rural group. Disseminated pulmonary tuberculosis was established more frequently in the rural group – 5 (4.7%) vs 18 (3.3%) patients from the urban group. Destructive forms of pulmonary tuberculosis were identified in a higher proportion in both groups, however, the destructive process in both lungs was statistically more frequently identified in the rural group – 36 (32.1%) vs. 97 (16.9%) patients (tab. 6).

When assessing the laboratory features of the enrolled pulmonary tuberculosis patients, it was identified that one third of the entire sample was microscopic positive for acid-fast-bacilli, 162 (27.8%) patients in the urban vs. 38 (33.9%) patients in the rural group. A similar proportion of patients was identified to have positive bacteriological results

Table 6

Microbiological features of tuberculosis patients

Index	Radiological features	Urban group	Rural group	P value
		N=581 (P%)	N=112 (P%)	
Clinical forms of TB	Pulmonary TB	546 (93.9)	106 (94.6)	>0.05
	Extrapulmonary	31 (5.4)	6 (5.4)	>0.05
	Generalized	4 (0.6)	0	>0.05
Clinical forms of pulmonary TB	PIT	495 (85.2)	97 (91.6)	>0.05
	PDT	18 (3.3)	5 (4.7)	>0.05
	FCVT	33 (6.1)	4 (3.7)	>0.05
Localization of destruction	One lung	171 (29.4)	38 (33.9)	>0.05
	Both lungs	97 (16.9)	36 (32.1)	<0.001
Microbiological features	AFB positive	162 (27.8)	38 (33.9)	>0.05
	MBT culture positive	155 (26.7)	35 (31.2)	>0.05
	GeneXpert MTB positive	227 (39.1)	51 (45.4)	>0.05
	GeneXpert MTB/Rif sensible	142 (24.4)	17 (15.2)	**<0.05**
	GeneXpert MTB/Rif resistent	85 (14.6)	34 (30.4)	**<0.01**
	MBT culture positive AFB positive	97 (16.6)	26 (23.2)	>0.05
	MBT culture positive AFB positive GeneXpert positive	81 (13.9)	23 (20.5)	>0.05
	MDR-TB	51 (8.8)	13 (11.6)	>0.05

Note: Applied statistical test: paired simple T-test, P – probability; PIT-pulmonary infiltrative tuberculosis, PDT-pulmonary disseminated tuberculosis, FCVT-fibro-cavernous tuberculosis. Applied statistical test: paired simple T-test, P – probability.

at cultivation on solid Lowenstein-Jensen or liquid MGIT BACTEC media: 155 (26.7%) patients in the urban vs. 35 (31.2%) patients in the rural group. The molecular genetic assay was performed in all cases, but positive results were obtained more frequently in the rural group – 51 (45.4%) vs. 227 (39.1%) patients in the urban due to a high proportion of cases with destructive forms of tuberculosis. Sensitive to rifampicin were more frequently identified patients from the rural group – 142 (24.4%) vs. 17 (15.2%), however, resistant to rifampicin have been more frequent cases in the rural group – 34 (30.4%) vs. 85 (14.6%) cases in the urban group. Microscopically positive for AFB and cultivation on the conventional media proved to be *Mycobacterium tuberculosis* (MTB) more frequently in the rural group – 26 (23.2%) vs. 97 (16.6%) in the urban group, as well microscopic positive for AFB, culture positive for MTB and GeneXpert MTB Rif positive assay were 23 (20.5%) patients from rural group vs. 81 (13.9%) patients from the urban group.

The standard treatment for new drug-susceptible tuberculosis in the RM has been used since 2000, lasts 6 months and consists of two phases with four first-line drugs: isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z) in the intensive phase and two first-line drugs: isoniazid and rifampicin in the continuation phase. For previously treated cases was used a regimen which lasts 8 months: 3 months with H, R, E, Z and streptomycin and 5 months with H, R and E. Patients with rifampicin-resistance or MDR-TB were treated with second-line drugs for 18 months or more divided in two phases. The regimen composition during the intensive phase lasts 6 months and includes kanamycin (Km) or capreomycin (Cm), levofloxacin (Lfx), para-amino salicylic acid (PAS), ethionamide (Eto), cycloserine (Cs) and pyrazinamide (Z) and for continuation phases during 12-18 months – Lfx, PAS, Etho, Cs and Z.

The standard treatment for drug susceptible tuberculosis was used for the treatment of a similar proportion of patients from both groups: 530 (91.2%) patients from the urban group and respectively 99 (88.4%) patients from the rural group. Every third patient from the urban group and every fifth patient from the rural group was treated as previously treated cases – 226 (38.9%) patients from the urban group and 60 (37.5%) patients from the rural group. Even the rate of MDR-TB was in average similar in both groups, only a minor proportion of patients from both groups was treated as drug-resistant patients: 51 (8.8%) patients from the urban group and 13 (11.6%) patients from the rural group. It is important to emphasize that the standard treatment for MDR-TB could be started only if the therapeutic compliance of the patient is established and the clinical tolerance is acceptable (tab. 7).

Table 7

Types of the cases according to the history of the anti-tuberculosis treatment

Case type	Outcome	Urban group	Rural group	P value
		N=581 (P%)	N=112 (P%)	
Never treated before	New case	355 (61.1)	70 (62.5)	>0.05
Previously treated	Relapse	137 (23.6)	28 (25)	>0.05
	Recovered after default	57 (9.8)	12 (10.7)	>0.05
	Recovered after failure	29 (4.9)	2 (1.8)	<0.05
Types of the drugs	First-line anti-TB drugs	530 (91.2)	99 (88.4)	>0.05
	Second-line anti-TB drugs	51 (8.8)	13 (11.6)	>0.05

All the patients were managed and treated with the standard treatment for tuberculosis. First-line anti-tuberculosis drugs were used in 531 (91.4%) patients from urban group vs. 13 (11.7%) patients from the rural group. Successfully treated were more frequently patients in the rural group – 80 (71.4%) vs. 373 (64.2%) patients in the urban group. The low therapeutic outcome was more frequently established in the urban group, such as "lost to follow-up" – 45 (7.7%) vs. 5 (4.5%) cases in the rural group, died – 69 (11.9%) vs. 10 (8.9%) patients in the rural group. Still continuing the treatment was almost each tenth patient in both groups (tab. 8).

Table 8

Treatment outcome of tuberculosis patients

Outcome	Urban group N=581 (P%)	Rural group N=112 (P%)	P value
Treatment success	373 (64.2)	80 (71.4)	>0.05
Treatment failure	9 (1.5)	0	>0.05
Lost to follow-up	45 (7.7)	5 (4.5)	>0.05
Death	69 (11.9)	10 (8.9)	>0.05
Still continuing	63 (10.8)	10 (8.9)	>0.05
Diagnosed excluded	22 (3.8)	6 (5.4)	>0.05

Note: Applied statistical test: paired simple T-test, P – probability.

An important research outcome represents the odds ratio (OR) and the attributable risk (AR), which are indices for identifying the priority interventions in the frame of high risk groups from every type of the subpopulation [22]. The values were calculated represented only for risk factors which predominated and exposed a statistical difference between the groups. It was established that the risk factors for tuberculosis in urban patients were linked with the sociovulnerability: unemployment, associated lack of health insurance, homelessness or lack of the residence visa, comorbidities and the immune suppressive condition – HIV infection. Attributable risk revealed the hierarchy of risks in urban population: HIV infection, comorbidities, homelessness, lack of health insurance and unemployment. In rural population the risk factors for tuberculosis were low level of the school education and tuberculosis contact. Related to this was identified lung destruction in both lungs, as a hallmark of the late detection of tuberculosis process. When leveling the risk factors it was established that more relevant was the tuberculosis contact followed by the low level of education (tab. 9).

Table 9

Risk factors for tuberculosis

Risk factors		OR	AR (%)
Social economical features	Unemployment	1.63 (1,07-2,48)	**18**
	Lack of insurance	1.56 (1,03-2,35)	**18**
	Homelessness	1.61(0,928-2,794)	**31**
	Low secondary education	2.06 (1,27-3,35)	**17**
Epidemiological and comorbidties	Close contact	2.32 (1,27-4,44)	**57**
	Associated diseases	2.9 (1,81-4,73)	**52**
	HIV-infection	4.1 (1,26-13,4)	**80**
Disease related	Both lungs involvement	2.36 (1,5-3,71)	**52**

Note: OR – odds ratio; AR – attributable risk.

The relation between tuberculosis indices and demographic particularities was widely studied [24, 25, 26, 27, 11, 28]. Globally, the epidemics of tuberculosis is much higher in urban areas than in rural localitites, because almost one half of the world's population lives in cities [29, 25, 26]. Our research identified high indices of tuberculosis in the rural subpopulation than in urban areas. It can be explained by the complexity of risk factors, which reflects the barriers for accessing the healthcare services of the rural population [30, 31, 32]. Several studies identified a poor quality of healthcare in private system which manages patients with tuberculosis [33, 26, 34]. In the RM the specialized institutions offer a standard approach, which corresponds to the international recommendations and national regulations [35, 21, 36]. The uncontrolled urbanisation is associated with extension of drug resistance and poor treatment outcome [37, 38, 39]. Our research established more increased rate of the drug resistance in the rural population. It can be explained by a deeper investigation of tuberculosis contacts in the rural areas. The uncontrolled urbanization is associated with lack of healthcare service at low price and expansion of the private sector [26, 27]. Our research established that the major proportion of patients was detected by public general practitioners and every fifth patient came directly to the hospital. No similar studies were conducted in the RM. Urbanization is associated with overcrowding, low level of sanitation and low socioeconomic state [40, 32, 41]. Our research identified also an important proportion of patients from both subpopulations, which were unemployed, homeless and without health insurance, however, their amount was more prevalent in the urban group which constituted risk factors.

Conclusions

Residents from the rural localities were more affected by tuberculosis compared with the urban population.

The age for acquiring tuberculosis was younger in urban population than in that from rural areas.

Socioeconomic vulnerability was extended in all patients with tuberculosis; however, the gravity was more evident in patients from the urban districts of Chisinau.

Low level of education predominated in the patients from rural localities.

Close contact with a sick patient predominated in the patients with tuberculosis from rural localities, which contributed to a higher rate of MDR-TB.

Associated diseases predominated in the urban group, more expressed was HIV infection.

Risk factors for tuberculosis in urban population were: unemployment and associated lack of health insurance, patient's homeless state, comorbidities and the immune suppressive condition – HIV infection. Risk factors for the rural population were tuberculosis contact and low level of the education.

References

1. World Health Organization. Global tuberculosis control 2011. Epidemiology, strategy, finances. Geneva: WHO; 2011. 258 p.
2. World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015. 192 p.
3. World Health Organization. Global tuberculosis report 2017. Geneva: WHO; 2017. 249 p.
4. Centrul Național de Management în Sănătate al Republicii Moldova [National Center for Health Management of the Republic of Moldova]. Indicatori preliminari în format prescurtat privind sănătatea populației și activitatea instituțiilor medico-sanitare pe anii 2014-2015 [Preliminary indicators on population health and on healthcare institutions activity for 2014-2015]. Chisinau: The Center; 2016. 216 p. Romanian.
5. Biroul Național de Statistică al Republicii Moldova [National Bureau of Statistics of the Republic of Moldova]. Raport demografic 2017 [Demographic report 2017].
6. Guvernul Republicii Moldova [Government of the Republic of Moldova]. Hotărârea nr. 685 din 4.09.2013 privind Strategia Națională de Dezvoltare Regională pentru anii 2013-2015 [Decision no. 685 of 2013 September 4, on the National Strategy for Regional Development for the years 2013-2015]. Monitorul Oficial al Republicii Moldova. 2013 Sep 13;(198-204):art. no. 792. Romanian.
7. Guvernul Republicii Moldova [Government of the Republic of Moldova]. Legea nr. 438 din 28.12.2006 cu privire la dezvoltarea regională în Republica Moldova [Law no. 438 of 28 December 2006 on regional development in the Republic of Moldova]. Monitorul Oficial al Republicii Moldova. 2007 Feb 16;(21-24):art. no. 68. Romanian.
8. Pintea D, Gumene I. Analiza cheltuielilor destinate ocrotirii sănătății în Republica Moldova [Analysis of expenditures for health care in the Republic of Moldova]. Chisinau; 2016. 26 p. Romanian.
9. Berdaga V, Stefanet S, Bivol O. Access of the population of the Republic of Moldova to health services. Chisinau: Gunivas; 2010.
10. Government of the Republic of Moldova, UN Agencies in Moldova. The third Report on Millenium Development Goals. Republic of Moldova. Chisinau, 2013. 90 p.
11. World Health Organization. Commission on Social Determinants of Health. Action on the social determinants of health. Geneva: WHO; 2005. 50 p.
12. Biroul Național de Statistică al Republicii Moldova [National Bureau of Statistics of the Republic of Moldova]. Anuarul statistic al Republicii Moldova, 2017 = Statistical Yearbook of the Republic of Moldova, 2017. Chisinau: The Bureau; 2017. 486 p.
13. Centrul Național de Management în Sănătate [National Center for Health Management of the Republic of Moldova]. Sănătatea publică în Moldova, 2016: Raport [Public health in Moldova, 2016: Report]. Chisinau: The Center; 2016. Romanian.
14. National Bureau of Statistics of the Republic of Moldova. Results of the study of population health status and access to health services in the Republic of Moldova. Chisinau; 2016.
15. Ministerul Sănătății al Republicii Moldova [Ministry of Health of the Republic of Moldova]. Accelerarea reformelor: abordarea necesitatilor din domeniul sanatatii prin politici investitionale: Raport [Accelerating reforms: addressing the needs of the health area through investment policies: Report]. Chisinau; 2016. Romanian.
16. Bivol S, Vladicescu N; [Ministry of Health of the Republic of Moldova]. Vulnerabilitatea femeilor din Republica Moldova la HIV si SIDA: 2010 = Women's vulnerability to HIV and AIDS in the Republic of Moldova: 2010. Chisinau: Elan Poligraf; 2010. 138 p.
17. Lesnic E, Ustian A, Niguleanu A, Malic A, Paladi C. Social features of patients with pulmonary tueberculosis. [Tuberculosis, Lung Diseases, HIV Infection] (Kiev). 2016;25(2):36-40.
18. Centrul Național de Management în Sănătate al Republicii Moldova [National Center for Health Management of the Republic of Moldova]. Potențialul uman din sistemul sănătății implicat în acordarea asistenței medicale în ftiziopneumologie [The human potential of the healthcare system involved in the medical assistance in phthisiopulmonology]. Chisinau: The Center; 2011. Romanian.
19. Ciocanu M. Expertiza calitatii serviciilor spitalicești prestate persoanelor asigurate [Quality assessment of hospital services provided to insured persons]. Curierul Medical (Chisinau). 2007;(5):56-60.
20. Galan A. Expertiza Strategiei "Dezvoltarea resurselor umane pentru sănătate" și a Planului de Acțiuni în Republica Moldova: Raport final [Assessment of the strategy paper "Development of Human Resources for Health" and of the Action Plan in the Republic of Moldova: Final report]. Chisinau; 2011. 34 p. Romanian.
21. Domente L, Alexandru S, Iavorschi C, et al.; [Ministry of Health of the Republic of Moldova]. Tuberculoza la adult: Protocol clinic național [Tuberculosis in adults : National clinical protocol]. Chisinau: The Ministry; 2015, 140 p. (PCN-123). Romanian.
22. Spinei L, Lozan O, Badan V. Biostatistica [Biostatistics]. Chișinău; 2009. 186 p. Romanian.
23. Guvernul Republicii Moldova [Government of the Republic of Moldova]. Legea nr. 1585 din 27.02.1998 cu privire la asigurarea obligatorie de asistență medicală 30.04.1998 [Law no. 1585 of 27 February 1998 on compulsory health insurance]. Monitorul Oficial al Republicii Moldova. 1998 Apr 30;(38-39): art. no. 280. Romanian.
24. Kulzhabaeva A, Nabirova D, et al. Linkage between diagnosis and treatment of smear-positive pulmonary tuberculosis in urban and rural areas in Kyrgyzstan. Public Health Panorama. 2016;2(1):104-109.
25. Prasad A, Ross A, et al. A world of cities and the end of TB. Trans R Soc Trop Med Hyg. 2016;110:151-152. doi:10.1093/trstmh/trw004.
26. Rangan S, Gupte H, et al. Tackling tuberculosis in urban areas: experiences from Mumbai city. Health Administrator. 2006;15(1):72-79.
27. Sumaiya Rahman, Shohel Ahmed. To assess the tuberculosis situation in urban and rural areas of Bangladesh with special emphasis on the facility of treatment scenarios. Pub Health Res. 2017;7(3):73-77.
28. Shen X, Xia Z, et al. Tuberculosis in an urban area in China: differences between urban migrants and local residents. PLoS ONE. 2012;7(11):e51133. doi:10.1371/journal.pone.0051133.
29. Paquette K, Cheng MP, Kadatz MJ, et al. Chest radiography for active tuberculosis case finding in the homeless : a systematic review and meta-analysis. Int J Tuberc Lung Dis. 2014;18(10):1231-6.
30. Lesnic E. The assessment of different tuberculosis-related features in Moldova regions. Moldovan Medical Journal. 2017;60(3):3-10.
31. Lesnic E, Todorico L, Niguleanu A, et al. The socio-economic risk factors of tuberculosis in condition of a high migration in trans-border region. [Bukovinian Medical Herald] (Chernivtsy). 2016;20(4):109-111.
32. Tafuni O, Lesnic E. Condițiile de trai ale bolnavilor de tuberculoză din municipiul Chișinău în perioada rece a anului [The living conditions of patients with tuberculosis in the city of Chișinău in the cold period of the year]. Sănătate publică, Economie și Management în Medicină (Chisinau). 2016;(3(67)):138-141.
33. Ibiene Tobin-West Ch, Isodje Anastasia. Quality and rural-urban comparison of tuberculosis care in Rivers State, Nigeria. Pan Afr Med J. 2016;24:60. doi:10.11604/pamj.2016.24.60.8497.
34. Dye C, Lönnroth K, Jaramillo E, Williams BG, Raviglione M. Trends in tuberculosis incidence and their determinants in 134 countries. Bull World Health Organ. 2009 Sep;87(9):683-91.
35. Guvernul Republicii Moldova [Government of the Republic of Moldova]. Hotărârea nr.1171 din 21.12.2010 privind aprobarea Programului național de control a tuberculozei pentru anii 2011-2015 [Decision no. 1171 of 2010 December 21, on approving the National Tuberculosis Control Program for the years 2011-2015]. Monitorul Oficial al Republicii Moldova. 2010 Dec 31;(259-263):art. no. 1316. Romanian.
36. World Health Organization. Treatment of tuberculosis: guidelines. Geneva: WHO; 2014. 420 p.
37. Abubakar I, Crofts J, et al. Investigating urban-rural disparities in tuberculosis treatment outcome in England and Wales. Epidemiol Infect. 2008;136(1):122-127.
38. Almeida D, Rodrigues C, Udwadia Z, et al. Incidence of multidrug-resistant tuberculosis in urban and rural India and implications for prevention. Clin Infect Dis. 2003;36(12):e152-e154. doi: 10.1086/374931.
39. Centrul Național de Management în Sănătate al Republicii Moldova [National Center for Health Management of the Republic of Moldova]. Evaluarea costului catastrofal asociat tuberculozei drogrezistente în gospodăriile din Republica Moldova [Assessment of catastrophic cost associated with multidrug resistant tuberculosis in the Republic of Moldova]. Chișinău; 2017. Romanian.
40. Lobo MA, Paiva Neto HC, Bello LA. Spatial distribution of pulmonary tuberculosis in urban areas: a case from Belém, Brazil. Acta Biomedica Brasiliensia. 2016;7(2):1-14.
41. World Health Organization. The global plan to stop TB 2011-2015: transforming the fight towards elimination of tuberculosis. Geneva: WHO; 2010. 96 p.