

Comparative assessment of pulmonary tuberculosis cases from Chişinău, Iaşi county and Chernivtsi region

Evaluarea comparativă a cazurilor de tuberculoză din oraşul Chişinău, judeţul Iaşi şi regiunea Chernivtsi

Gilda Georgeta Popescu¹,
 Marius Dumitru²,
 Todoriko Lilia³,
 Evelina Lesnic⁴,
 Adriana Sorete-Arbore⁵, Carmen
 Monica Pop⁶,
 Semianiv Igor³,
 Eremenchuk Inga³

1. "Marius Nasta" Institute of Pneumophthysiology, Bucharest, Romania

2. Romania TB Patients Association, Bucharest

3. Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine

4. "Nicolae Testemiţanu" State University of Medicine and Pharmacy, Chişinău, Republic of Moldova

5. Dispensary of Pneumophthysiology, Iaşi, Romania

6. "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

The burden of tuberculosis (TB) is measured in terms of incidence, prevalence and mortality. The incidence is defined as the number of new and relapse cases arising in one year, the prevalence is the total number of TB cases in one year and mortality is the total number of deaths caused by TB in one year. According to the published data by the Moldavian National Centre for Health Management in 2015, it was registered an important decline of all TB indices in Republic of Moldova (MDA) and a low decrease in Romania. The global incidence in MDA decreased between 2013 and 2015 by 22%, and in Chişinău by 22.4%. A similar vector was established regarding the prevalence (the total number of TB patients), which decreased between 2013 and 2015 in MDA with 23.3%, and in Chişinău with 25.5%. Multiple causes are contributing to this rapid decline of recorded values: the low rate of high risks groups investigated in the frame of active TB screening (the annual chest radiological examination), the high rate of migrant population inaccessible for screening procedures, low health care seeking behavior of the population, high rate of citizens without health insurance and a low accessibility to health care services. The mortality due to TB progression was very high, despite the decreasing trend of morbidity indices. During the 2013-2015 period, the mortality decreased from 16.1 to 8.8 per 100.000 people in MDA, as well as from 10.8 to 6.9 per 100.000 people in Chişinău.

Keywords: tuberculosis, risk factors, socioeconomic status

Rezumat

Impactul tuberculozei (TB) se măsoară prin incidenţă, prevalenţă şi mortalitate. Incidenţa se defineşte ca numărul de cazuri noi şi recidive pe an, prevalenţa reprezintă numărul total de cazuri de TB pe an, iar mortalitatea este definită ca numărul de decese cauzate de TB pe an. Conform datelor publicate de Centrul Naţional din Moldova pentru Managementul Sănătăţii din 2015, s-a înregistrat un important declin al indicilor TB şi o scădere uşoară în România. Indicenţa globală în Republica Moldova (MDA) a scăzut între 2013 şi 2015 cu 22%, iar în Chişinău cu 22,4%. De asemenea, prevalenţa a scăzut între 2013 şi 2015 cu 23,3% în MDA, iar în Chişinău cu 25,5%. La baza acestui declin au stat: rata scăzută a grupurilor de risc investigate la momentul al screeningului (radiografiile anuale de torace), rata crescută de migrare a populaţiei (inaccesibilă pentru investigaţii), educaţia medicală precară, creşterea populaţiei fără asigurare medicală, accesibilitatea scăzută la servicii medicale. Mortalitatea secundară progresiei TB rămâne ridicată, în ciuda scăderii indicelui de morbiditate. În perioada 2013-2015, mortalitatea a scăzut de la 16,1 la 8,8 la 100.000 de locuitori în MDA şi de la 10,8 la 6,9 la 100.000 de locuitori în Chişinău.

Cuvinte-cheie: tuberculoză, factori de risc, status socioeconomic

Background

The aim of the study was to calculate the cost in a comparative assessment of the pulmonary tuberculosis cases diagnosed through microbiological methods in Chişinău, Iaşi county and Chernivtsi region.

Objectives

1. A comparative assessment of epidemiological indices registered in Chişinău, Iaşi county and Chernivtsi region in 2015.

2. The evaluation of demographic, socio-economic state and epidemiological risk factors of new pulmonary tuberculosis patients from three high TB burden trans-border regions: Chişinău, Iaşi county and Chernivtsi region.

3. The study of case management, clinical aspects, radiological aspects and treatment outcome of pulmonary tuberculosis cases.

Material and methods

A retrospective, selective, randomized, and descriptive study was performed on risk factors for the development of TB, case management, clinical and radiological features and treatment outcome of new pulmonary cases diagnosed through microbiological methods (conventional culture on Lowenstein-Jensen or BACTEC MGIT medium) from three high TB burden trans-border regions: 99 new cases from the Moldavian city Chişinău and suburbs villages, 100 new cases from Iaşi county and 568 new cases from Chernivtsi region. The inclusion criteria were: age >18-years-old, new case of pulmonary TB diagnosed with microbiological methods, signed informed consent. The Moldavian group included 99 patients selected as being diagnosed and therapeutically managed in the medical specialized organization of Chişinău (the Municipal Hospital of Pneumophthysiology)

Table 1 Epidemiological indices of tuberculosis in MDA, Romania and the Chernivtsi region

Indices	2015		Indices	2015	
	abs.	/100.000		abs.	/100.000
Global incidence MDA	2870	80,7	Prevalence MDA	3073	86,4
Global incidence Chisinau	579	71,7	Prevalence Chisinau City	808	100,1
Global incidence RO	14225	71,5	Prevalence RO	27000	116,7<8,7%
Global incidence Iasi	712	90,9	Prevalence Iasi county	813	105,26
Global incidence UA	27087	63,3	Prevalence UA	36,2	84,7
Global incidence	568	48,8	Prevalence	760	83,8
Chernivtsi			Chernivtsi		
Incidence NC MDA	2299	64,6	Mortality RM	314	8,8
Incidence NC Chisinau	435	53,9	Mortality Chisinau City	56	6,9
Incidence NC RO	12001	60,1	Mortality RO	1055	5,29
Incidence NC Iasi county	617	78,7	Mortality Iasi county	37	4,10
Incidence NC UA	23896	55,9	Mortality UA	4602	10,8
Incidence NC Chernivtsi	364	40,1	Mortality Chernivtsi	69	7,6

Note: NC - new cases; N/A - not available.

between 1.01.2015 and 31.12.2015. The Iași group consisted of 100 new pulmonary TB cases randomly selected from the Iași County Register, who were treated and monitored in Iași Pneumophthysiology Dispensary between 1.01.2015 and 31.12.2015. The Chernivtsi group included 568 patients with pulmonary TB cases randomly selected in the period 1.01.2015 - 31.12.2015. For the comparative epidemiological assessment of major TB indices in all three partner countries we used official statistic data. There were used social, epidemiological collection methods, statistical analysis, graphic representation and analytical assessment using the Microsoft Excel XP software. The information gathered was tabled in simple and complex groups.

Results

The burden of TB is measured in terms of incidence, prevalence and mortality. The incidence is defined as the number of new and relapse cases arising in one year, prevalence is the total number of TB cases in one year and mortality is defined as the total number of deaths caused by TB in one year. According to the published data by the Moldavian National Centre for Health Management in 2015, it was registered an important decline of all TB indices in Republic of Moldova (MDA) and a low decreased in Romania. The global incidence in MDA decreased between 2013 and 2015 by 22%, and in Chișinău by 22.4%.

A similar vector was established regarding the prevalence (the total number of TB patients), which decreased between 2013 and 2015 in MDA by 23.3%, and in

Chișinău by 25.5%. Multiple causes are contributing to this rapid decline of recorded values: the low rate of high risks groups investigated in active TB screening (annual chest radiological examination), the high rate of migrant population (inaccessible for screening procedures), low health care seeking behavior of the population, the high rate of citizens without health insurance and the low accessibility to health care services.

The mortality due to TB progression was very high, despite the decreasing trend of morbidity indices. During the period 2013-2015, the mortality decreased from 16.1 to 8.8 per 100.000 people in MDA, as well as from 10.8 to 6.9 per 100.000 people in Chișinău. Concomitantly, in Romania the global incidence decreased insignificantly between 2013 and 2015 with 7.5% (1284 cases), although in Iași county increased with 3%. The increasing in Iași might be attributed to the regional implementation of molecular genetics assay GeneXpert MTB/Rif for the detection of *M. tuberculosis* DNA and mutations of the *rpoB* gene. The same increasing trend was identified regarding the incidence of new TB cases. In spite of a stable state of new case incidence in Romania, the index increased in Iași county with 6.2%. The sharp decreasing trend of prevalence in MDA (23.3%) and Chișinău (25.5%) during the same period of time contrasted with a slow decreasing index in Romania (3.3%) and the sharply increased trend in Iași county (15.5%). The mortality due to TB decreased two times in MDA and less evidently in Chișinău. Concomitantly, the mortality rate was stable in Romania, as well as in Iași county.

Table 2 Distribution of patients by their sex and age in subgroups

Biological segregation	Sex	Chisinau group	Iasi group	Chernivtsi group
		N=99 (M±m %)	N=100 (M±m%)	N=568 (M±m)
Sex distribution	Men	74 (74,74±4,36)	66(66±4,73)	447 (32±4.94)
	Women	25 (25,25±4,36)	34(34±4,73)	121 (23.1±2.17)
Age distribution (reproductive groups)	15-24 years	13 (13,13±3,39)	18(18±3,84)	31 (2.12±0.16)
	25-34 years	20 (20,20±4,03)	15(15±3,57)	102 (12±4.17)
	35-44 years	32 (32,32±4,71)	21(21±4,07)	174 (21±4.03)
>45 years old	45-54 years	24 (24,24±4,31)	23(23±4,21)	135 (18±3.16)
	≥55 years	11 (11,11±3,16)	19(19±3,92)	126 (15±2.13)

Table 3 The socio-economic status of patients with pulmonary tuberculosis

Economic state N=99 (M±m %)		Chisinau group	Iasi group	Chernivtsi group
		N=100(M±m%)	N=568 (M±m)	
Economically stable	Employed	24 (24,24±4,31)	26(26±4,38)	210 (210.16±5.14)
	Unemployed	57 (57,57±4,96)	46(46±4,98)	277 (271±4,16)
Economically vulnerable	Retired	5 (5,05±2,21)	13(13±3,36)	70 (69.8±4.22)
	Student	13(13,13±3,39)	12(12±3,25)	11 (11.3±1.16)
	Disease disability	0	3(3±1,71)	0

When distributing patients according to sex, it was noticed the predominance of men, with a male/female ratio=2.93/1 in Chişinău and the same distribution by gender in Iaşi, with male/female ratio=2.58/1. The repartition of patients by age groups according to WHO recommendations identified the prevalence of patients from the reproductive age subgroups (15-44 years) in both samples. So, when segregating patients according to the biological parameters it was demonstrated that men and young people must be targeted by the screening methods and risk reduction measures.

When segregating patients according to the economic status, it was established that employed persons, which are contributing to the health budget by paying taxes, health insurance policy and social taxes, were the fifth part of both Moldavian groups. One fourth received specialized health care as being retired, disabled persons or students. Two thirds of patients were unemployed, without any personal financial income for living.

Health insurance represents the major condition for accessing health care in MDA. Uninsured patients were one half of cases 57 (57.57%) in CG. Considering these reported results, *mass-media* must raise awareness in the general population, emphasizing that specialized health

care, full accessibility to all related diagnostic tools and specific treatment for tuberculosis is free of charge for all Moldavian patients regardless of their health insurance status. Assessing the educational level, it was established that one third of investigated patients from both countries graduated secondary school, high school or professional school, and one third of them graduated only primary or incomplete elementary school. Comparing the number of patients with secondary level of education (general school or professional school) with those with low level of education, it was identified the predominance of patients from the first group. So, awareness and information about the signs of the disease, as well as education for risk reduction measures of persons with low degree of education are the most important tools that must be performed by the civil society organizations and could improve the TB control at the community level. The data are presented in Table 4.

The hierarchy of risk groups according to the widest rate of patients identified that the following conditions have the most significant impact on the developing of active pulmonary TB: vulnerable economical state (unemployed, students, retired and disabled were three quarter of both groups), living in poor conditions (one

Table 4 The distribution of patients according to the last graduated school

Educational segregation	Educational status	Chisinau group	Iași group	Chernivtsi group
		N=99 (M±m %)	N=100 (M±m%)	N=568 (M±m)
Low level	Primary&general incomplete school	33 (33,33±4,74)	24(24±4,27)	66 (10±4,37)
Secondary education	General (secondary) school	37 (37,37 ± 4,86)	41(41±4,91)	344 (18±6.07)
	Profesional school	21 (4,11±4,11)	25(25±4,33)	48 (3.2±1.7)
Superior level	Superior studies	9 (9,09 ±2,89)	10(10±3,0)	100 (11±4,1)

Table 5 The rate of high risk groups

Social groups	Risk groups	Chisinau group	Iasi group	Chernivtsi group
		N=99 (M±m %)	N= 100(M±m%)	N=568 (M±m)
Social groups	Unemployed	57 (57,57±4,36)	46 (46,00±4,98)	277 (277±21.14)
	Low financial income	18 (18,18±3,87)	25 (25±4,33)	493 (493±32.16)
	Poor living conditions	40 (40,41±4,92)	37 (37±4,93)	312 (312±16,9)
	Homelessness	12(12,12±3,28)	5 (5±2,18)	9 (9±0,08)
	Migrants	13 (13,13±3,39)	3 (3±1.76)	4 (4±0,01)
	History of detention	5 (5,05±2,21)	0	0
	Epidemiological group	Closed contacts	6(6,06±2,39)	15(15±3.57)
Epidemiological group	Associated diseases, incl.	28 (28,28±5,46)	29 (29±4,53)	324 (324±21,8)
	HIV positive status	12 (42.86±9,32)	1(3,45±3,38)	55 (55±4,3)
	Chronic alcoholism	7 (25,0±8,18)	20 (68,97±8,59)	66 (66±8,6)
	Psychiatric diseases	2 (7,14±4,86)	4 (13,79±6,41)	3 (3±0,001)
	Injection drug use	3 (10,71±5,84)	0	7 (7±0,02)
	Diabetes mellitus	4 (14,28±6,61)	4 (13,79±6,41)	25 (25±0,11)

half of CG and one third of IG), associated diseases (one third of both groups), extreme poverty (homelessness), migration and alcohol abuse (the fifth part). The stratification of pulmonary TB patients established that the primary target groups of which awareness, education, and improvement of health behavior must be performed are: social and economical vulnerable groups, comorbid, migrants and alcohol abusers. Inside those groups, the screening methods for TB are the most efficient. In this context it is important to note a very low rate of family TB clusters affiliated to each investigated patient, probably due to a low-quality epidemiological cross-examination, rather than to the lack of closed (family) contacts. In a lower proportion were identified groups of patients with history of detention, chronic alcohol-

ism, illicit drug use and psychiatric diseases. It is important to emphasize that of the total number of 28 patients with comorbidities, 12 (42.86%) were HIV infected cases, and 4 (14.28%) had diabetes mellitus.

Studying case management, it was identified that medical staff was involved in the patients' detection. According to the actual recommendations, the major method for new case detection is based on the microscopic examination of the symptomatic patients. So, one half of them were detected by family doctor due to specific symptomatology (passive way), in 32 patients (32.32%), while 17 patients (17.17%) were detected through screening and by performing chest X-ray examination of high risk groups. One third of patients were diagnosed after addressing directly the pneumophthisi-

Table 6 Case-management segregation and disease-related characteristics

Management characteristics		Chisinau group	Iasi group	Chernivtsi group
		N=99 (M±m %)	N=100 (M±m%)	N=568 (M±m)
Management	Detected by family doctor as symptomatic patients	32 (32.32±4,71)	11(11±3,13)	295 (295±16,4)
	Detected by family doctor through screening of risk groups	17 (17,17±3,79)	0	96 (96±7,3)
	Detected by pneumophthysiologist as symptomatic patients	22 (22,22±4,17)	79(79±4,07)	164 (164±11,6)
	Detected by pneumophthysiologist through screening of risk groups	3 (3,03±1,72)	0	0
	Other	26 (26,26±4,42)	10(10±3,00)	13 (13±3,7)
Clinical-radiological features	Parenchymal destructive forms in 1 lung	49 (49,49±5,02)	N/A	244 (244±15,1)
	Parenchymal destructive forms in both lungs	16 (16,17±3,71)	N/A	295 (295±16,9)
	Infiltrative opacities without destructions	35 (35,35±4,81)	N/A	29 (29±5,2)
	Infiltrative pulmonary TB	89 (89,89±3,23)	52 (52±4,99)	226 (226±14,3)
	Fibro-cavity pulmonary TB	1 (1,01±1,05)	47 (47±4,98)	11 (11±1,08)
	Disseminated pulmonary TB	9 (9,09±2,89)	1(1±0,99)	331 (331±17,5)

Note: N/A - not available.

ologist, having specific signs recognized by them as being relevant for pulmonary tuberculosis. In “other” conditions were included patients detected by radiological investigations performed in the frame of other than the aforementioned conditions and institutions.

The evaluation of microbiological data was based on the microscopic positivity for acid-fast bacilli (AFB) in one half of patients (53; 53.53%) of CG and 64 (64%) of IG. Evaluating microbiological data, it was established that microscopic positive for acid-fast bacilli (AFB) were one half of patients 53 (53.53±5.01%) of CG and X of IG.

Two-thirds of all selected patients had positive cultures at conventional Lowenstein-Jensen medium. The degree of positivity of cultures on Lowenstein-Jensen medium was established according to the number of colonies identified on the medium.

It is important to note that in the total sample of 99 new pulmonary tuberculosis cases of Moldovan patients, 73 were positive on Lowenstein-Jensen medium and the rest of them, 26, were negative on Lowenstein-Jensen medium, but positive at MGIT BACTEC medium. In this context, 87 (87.87±3.28%) of them were positive at the molecular genetic test GeneXpert MTB/RIF. Drug sensitivity test revealed that in 27 cases (27.27±4.48%) were found drug-resistant strains of *Mycobacterium tuberculosis*. Two-thirds of all selected patients had positive cultures for conventional Lowenstein-Jensen medium. The degree of positivity of the cultures on Lowenstein-Jensen medium was established according to the number of colonies identified on the medium. For the IG, out of the total of 100 positive cultures, 14 had less than 10 colonies on three

replicate tubes. It is important to note that of the 99 new pulmonary tuberculosis cases of Moldavian patients, 73 were positive on Lowenstein-Jensen medium and the rest of them, 26, were negative on Lowenstein-Jensen medium but positive at MGIT BACTEC medium. In this context, 87 (87.87±3.28%) of them were positive at the molecular genetic test GeneXpert MTB/RIF. Drug sensitivity testing confirmed that 27 cases (27.27±4.48%) were drug-resistant strains of *M. tuberculosis*.

Conclusions

The Republic of Moldova shows a continuously decreasing population, especially in the economic and reproductive active groups. Moldavian health care system is based on the health insurance mechanisms. Due to the fact that one third of the population is uninsured, the low national health budget doesn't allow an extensive screening. The assessment of the social, economic and epidemiological features of the patients with pulmonary tuberculosis and positive bacteriological test for *M. tuberculosis* identified several high risk groups for developing active tuberculosis: social risk groups – unemployed and persons with low financial income, people living in poor conditions –, and groups with medical conditions that suppress the immune response. The evaluation of microbiological data has established that among the patients diagnosed by general practitioner doctors, one half of them were microscopic positive for acid-fast bacilli. The pulmonary infiltrative tuberculosis complicated with lung destructions included the largest part of patients. Disseminated pulmonary

Table 7 Microscopical features of new cases of pulmonary tuberculosis

Microscopical features	Chisinau group	Iasi group	Chernivtsi group
	N=53 (M±m %)	N=68 (M±m%)	N=546 (M±m)
1-9 AFB/100 visual camp	22 (41,61±6,78)	3,125	279 (279±18,4)
1+	18 (33,96±6,51)	50,00	205 (205±14,5)
2+	9 (16,98±5,16)	28,12	28 (28±3,3)
3+	4 (7,54±3,62)	18,75	34 (34±3,5)

Note: AFB - acid-fast-bacilli;

Table 8 The microbiological features of new cases of pulmonary tuberculosis

Microbiological features	Chisinau group	Iasi group	Chernivtsi group
LJ culture	N=73 (M±m %)	N=92 (M±m%)	N=568 (M±m)
1+	46 (63,01±5,61)	36 (41,86±5,32)	337 (336,8±4,18)
2+	18 (24,65±5,04)	14 (16,28±3,98)	125 (125±5,21)
3+	9 (12,32±3,84)	36 (41,86±5,32)	106 (106±11,01)

Note: LJ - Lowenstein-Jensen medium;

tuberculosis was diagnosed in every tenth patient, being associated to HIV infection. Target groups, including social risk groups, epidemiological endangered and specific groups of tuberculosis morbidity, must receive community support in awareness, screening and adherence measures. In Ukraine, the incidence of TB in 2015 was 63.3 per 100,000 people against a background of prevalence 84.7 per 100 thousand population; mortality - 10.8. In Chernivtsi region, TB has the following burden: morbidity - 48.8; prevalence - 83.8; mortality rate - 7.6 per 100,000 people. Among all people with TB from Chernivtsi region, 77% were of working age (18-54 years), the age group 25-44 years old being dominant

(47.9%), as well as males (78.6%). According to the socio-economic characteristics of TB patients, in the Chernivtsi region most of them were unemployed people (48.7%), persons with complete general education (60.5%) and low income (86.5%), and living in poor conditions (54.9%). 57% of patients had comorbidities. The majority of cases (52%) identified in reference to a family doctor and in 29% of cases - to TB. In the study sample dominated by disseminated clinical form of TB common process in both lungs (52%). Almost all cases were patients with MBT + in microscopy; microscopy positive results in all cases confirmed by the results of microbiological studies. ■

References

1. Aveyard H. Literature review in health and social care: a practical guide, McGraw-Hill, 2010.
2. Bivol S, Turcanu G, Mosneaga A, et al. Barriers and facilitating factors in access to health services in the R. Moldova. Chişinău, 2012: 139.
3. Centrul National de Management în Sănătate [National Centre for Health Management] Chişinău, 2015.
4. Hargreaves J, Boccia D, Evans C et al. The social determinants of tuberculosis from evidence to action. *Am J Public Health*. 2011 April; 101(4): 654-662.
5. Jenkins H, Ciobanu A, Plesca V, et al. Risk factors and timing of default from treatment for non-MDR TB in Moldova. *Inter J Tuberculosis and Lung Diseases*, 2013;17(3): 373-380.
6. Lonnroth K, Jaramillo E, Williams BG, Dye C, Ravigione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *SocSci Med*. 2009; 68(12):2240-2246.
7. Rasanathan K, Sivasankara K, Jaramillo E, et al. The social determinants of health: key to global tuberculosis control. *Inter Journal Tuberculosis Lung Diseases*, 2011, 30-6.
8. Todoriko L, Semianiv I. Analysis of the GSTM1 gene polymorphism in patients with tuberculosis with regard to the version of MBT resistance, Science and Education, a New Dimension. Natural and Technical Sciences. 2016. Issue: 83, no IV (9), p 61-63.
9. United Nations. Report on Millenium Development Goals. Republic of Moldova. Chişinău, 2013.
10. World Health Organization. Human Rights, Health and Poverty Reduction Strategies. Geneva, Switzerland; 2008.
11. World Health Organization. Equity, social determinants and public health programmes, Geneva, 2010, 219 – 241.
12. World Health Organization. The global plan to stop TB 2011-2015: transforming the fight towards elimination of tuberculosis. Geneva, 2011. <http://statbank.statistica.md>
13. <http://www.statista.com/statistics/513335/gross-domestic-product-gdp-per-capita-inmoldova>