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Determinants of loss to follow-up and tuberculosis patients' awareness

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Abstract

Background: The highest rate of patients with the low disease outcome is represented by the lost to follow-up and died cases. The aim of the study was to assess the major determinants of low tuberculosis treatment outcome.
Material and methods: A retrospective selective, descriptive, case-control study targeting social, demographic, economic and epidemiological peculiarities, case-management, radiological aspects and microbiological characteristics of 437 patients with pulmonary tuberculosis with different outcomes: cured and lost to follow-up was performed. Patients' awareness was established by performing a pre-designed schedule containing open-ended and close-ended questions, reflecting knowledge about disease. There were interviewed 151 patients treated after a previous lost to follow-up.
Results: It was established that the major risk factors for loss to follow-up were: the history of detention, migration, patients with MDR-TB, patient's addressing to the hospital, previous history of treatment and social vulnerability. Most of the patients were aware about the disease through the health personnel and were satisfied with the received knowledge. The proportion of those who were informed through the mass media was high. They knew that tuberculosis is curable with a complete treatment; however, every tenth considered that two-three months are sufficient.
Conclusions: Raising awareness among patients with high risks about the compliance and the duration of the treatment, emphasizing that the treatment is free of charge and will not be started after a previous drop up will improve disease outcome.

Key words: tuberculosis, risk factors, loss to follow up.

Introduction

Tuberculosis represents a major global health problem, well recognized in the Republic of Moldova (MD) [1]. According to the WHO report in 2015, 10.4 million new cases were reported worldwide, of which 5,9 million (56%) were among men, 5.5 million (34%) among women and 1.0 million (10%) among children. Among all new tuberculosis cases, 1.2 million (11%) were people living with HIV infection. Two thirds of all cases were living in 6 countries: India, Indonesia, China, Nigeria, Pakistan and South Africa [17]. In the Republic of Moldova 4.211 cases were notified in 2015, 3.608 were new cases, 85% of them were tested by rapid diagnostic methods, 95% had known HIV status, 90% had pulmonary tuberculosis and 64% were bacteriological confirmed [1].

The national implementation of the DOT (Directly Observed Treatment) strategy in the tuberculosis patient's management determined the epidemic extension of primary drug-resistant infection in the population (2005 – 13%, 2006 – 19%, 2007 – 18%, 2008 – 24%, 2009 – 22%, 2010 –25%, 2011 –26%, 2012 – 24%, 2013 – 25%, 2014 –25% from the total registered MDR-TB cases) that in consequence contributed to the reduction of treatment effectiveness (2005 – 62%, 2006 – 62%, 2007 – 62%, 2008 – 58%, 2009 – 57%, 2010 –52%, 2011 –62%, 2012 – 62%, 2013 – 62%) which was the lowest among the European region countries and lower in average by 20% compared with targeted 85% recommended by the WHO [1]. The low success rate was directly linked with the high rate of lost to follow-up patients: 2001-5.5%, 2002-15.6%, 2003-10.5%, 2004-10.4%, 2005-10.9%, 2006-11.7%, 2007-10.7%, 2008-7.4%, 2009-6.2%, 2010-7.9%, 2011-7.7%, 2012 – 5.2% [1].

The standard treatment for new drug-susceptible tuberculosis, according to WHO recommendations in MD is used since 2000 as a part of DOT strategy and lasts 6 months in new cases and 8 months in previously treated cases. The treatment of the new drug-susceptible patients consists in a two phase regimen with four first-line anti-tuberculosis drugs [isoniazid (H), rifampicine (R), ethambutol (E) and pyrazinamide (Z)] in the intensive phase and two drugs [H and R] in the continuation phase [13]. An eight month regimen consisted in H, R, E, Z and streptomycine (S) during the intensive phase and H, R and E in the continuation phase is used for the treatment of previously treated cases (relapses, failed and lost to follow-up cases). Multidrug-resistant patients are treated using the standard regimen for resistant tuberculosis that consists of second-line anti-tuberculosis drugs during 18 months or more [6]. The major contributing factor of the treatment effectiveness represents the right combination of the drugs according to the susceptibility results [7]. Without an appropriate treatment tuberculosis-related death occurs in average within 2 years. Due to high global epidemiological burden tuberculosis was located on the 5th place in the top of the causes of death [13]. Worldwide, there were estimated 580.000 new MDR-TB cases in 2015, but only 125.000 received an adequate regimen (DOTS-Plus) [18]. In the Republic of Moldova 25.5% of new cases and 70,6% of retreating cases were MDR-TB in 2015 [1]. All patients were treated with standard regimen for MDR-TB. The treatment succes rate in 2014 in the drug-susceptible HIV-negative cases constituted 79%, HIV-positive patients 47% and in multidrug-resistant tuberculosis (MDR-TB) cohort 53% [1]. For a better drug-resistance surveillance and precocious onset of the correct treatment rapid molecular test (GeneXpert MTB/Rif) is used by 15 Moldovan health care specialized institutions offering a 45% sensibility [5, 6]. However, the conventional methods: Lowenstein Jenson and BACTEC cultures remain the golden standard for *Mycobacterum tuberculosis* complex detection due to the simplicity

and low cost [6]. Low treatment adherence and high rate of lost to follow-up patients contributed to the development of a shorter conventional MDR-TB regimen lasting less than 12 months with low costs (<1.000$/patient) [18]. It showed promising results in selected MDR-TB patients and WHO updated its treatment guidelines in 2016 by including the recommendation to use the shorter MDR-TB regimen in patients with non-complicated tuberculosis (excluding extrapulmonary tuberculosis and pregnancy) [18]. Fluoroquinolones and pyrazinamide are key drugs in the new MDR-TB regimen, however, surveillance of the cross resistance in five high burden countries: Azerbaijan, Bangladesh, Belarus, Pakistan and South Africa established that resistance to rifampicine is frequently associated with resistance to pyrazinamide, so the effectiveness of the short regimen might be lower than predicted [13].

According to the WHO estimations MD remains a high risk zone showing an inadequate concern regarding tuberculosis social determinants that represent major barriers in achieving the health related Millennium Development Goals [10]. In the actual globalization process, MD is the least economically developed country of the Eastern European region. The major social determinants of tuberculosis and poor outcome are social and economic inequalities, high levels of internal/external migration, rapid urbanization and population growth in urban areas [4]. Such determinants result in the polarization of the public health interventions, poor housing, low environmental conditions, malnutrition, geographic and cultural barriers in access to the health care [11]. A profound interest is paid to the assessment of social determinants of low outcome among extremely poor populations: migrants, Gypsies, drug users, alcohol consumers, homeless people, as well as Inuit populations, North Indians, Arctic communities in North America [12, 14, 15]. There was identified a strong association of overcrowding, social isolation, poverty, unhealthy nutrition and persistence of tuberculosis in those marginalized populations.

There are several risk factors predictive of the disease outcome. First of all it is the infection with resistant and virulent mycobacteria [7]. It depends on the prevalence of sick people in the community. It is increased by the overcrowding, urban residence, poor indoor ventilation and pollution. It can be successfully managed at the administrative governmental level and by sanitation agencies. The second group includes the factors with risk for the disease relapse or recrudescence of the latent tuberculosis infection induced by such factors: phtysiogenic ages (infants less than 5 years, teenagers, elders aged 65 and more), the poverty-related conditions that contribute to malnutrition and co-morbid state, lack of BCG vaccination [16]. At this level more efficient are the activities of the epidemiologic agencies. The third group of risk factors influencing tuberculosis outcome are the determinants of the patient's immune status: HIV infection, immune suppressive drugs (>15mg/day of prednisolone for 1 month or more, immune modulators: TNF-α blockers or oral steroids, antineoplastic agents), diabetes, cancer, silicosis, chronic respiratory diseases, gastrointestinal diseases, underweight, phtysiogenic ages, harmful habits (tobacco smoking, alcohol abuse, illicit drug using) [9]. The most relevant actions for reducing the impact of those conditions must be performed by the primary health care sector and civil societies, through the active screening of high risk groups and their education [2, 3, 8]. The fourth group influencing the final outcome consists of the following risk factors: the accessibility of the sick people to the tuberculosis screening and health care, treatment compliance and patient's nursing [12]. In this group are included: lack of social protection and medical insurance, geographic and economic barriers, cultural behavior or stigma. Only the complementary relationship between primary health care, specialized sectors, social and community services can ensure the highest effectiveness of the disease control.

The aim of the study was to assess the determinants of loss to follow-up and tuberculosis patient's awareness. Objectives were: 1. Comparative assessment of tuberculosis indices in Chisinau and the Republic of Moldova during 2011-2015. 2. Assessment of the general, social, economic and epidemiological risk factors of lost to follow-up tuberculosis patients. 3. Evaluation of case-management, diagnosis, radiological aspects and microbiological characteristics of lost to follow-up patients.

Material and methods

It was performed a retrospective selective, descriptive study targeting social, demographic, economic and epidemiological peculiarities, case-management, diagnosis, radiological aspects and microbiological characteristics of 437 patients with pulmonary tuberculosis. The electronic system for monitoring and follow-up of tuberculosis cases (SIME TB) was used for the selection. Data were extracted from the statistic templates F089/1-e "Declaration about the patient's established diagnosis of new case/relapse of active tuberculosis and restart of the treatment and its outcomes". The inclusion criteria were: age > 18 years old, pulmonary tuberculosis, signed informed consent. The research schedule included demographic, social and epidemiological data: sex (male/female ratio), age, demographic characteristics (urban/rural), educational level, economical status (employed, unemployed, retired, disabled, student), health insurance status (presence/lack), history of migration and detention, high risks: close contact with an infectious source, co-morbidities (HIV-infection, diabetes, psychiatric diseases, immune suppressive treatment), health care seeking behavior, way of the patient's detection, patient's microscopic status. All selected patients were diagnosed and managed according to the National Clinical Protocol. Enrolled patients were distributed in two groups: the 1st group (1) was constituted of 165 patients successfully treated (cured - CG) in the period 01.01.2015-31.12.2015 and the 2nd group (2) was constituted of 272 patients lost to follow-up (LFUG) in the period of 01.01.2010-31.1201.2016.

Population awareness regarding various aspects of tuberculosis is important for the disease control at the na-

tional level. For the assessment of patient's knowledge was performed a pre-designed schedule containing open-ended and close-ended questions, reflecting various aspects of the tuberculosis. It included questions on how the patients heard about the disease, mode of transmission, symptoms, curability, type of drugs, duration of the regimen and the place of the treatment. Study technique was by exit interview. The sample size was constituted from 151 interviewed patients, that were 55.51% of the 2nd group. They were informed about the purpose of the study, were assured about their confidentiality and anonymity and the informed consent was taken. Statistic analysis was carried out using the quantitative and qualitative research methods. Statistical survey was performed using Microsoft Excel XP soft.

Results and discussion

According to the published data by the Moldovan National Centre for Management in Health during the period 2011-2015 it was registered an important decline of all notified cases (new case, retreated for relapse, loss to follow-up and failure) in MD by 27,8/100.000 and in Chisinau by 22,2/100.000 population (fig. 1).

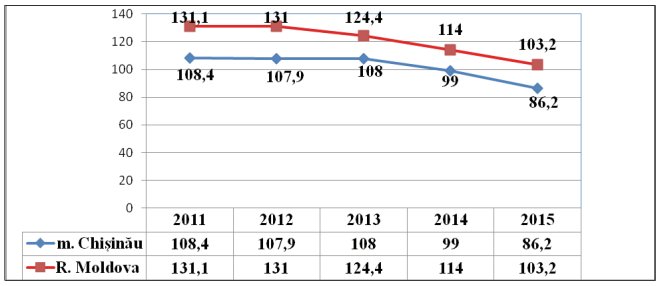

Fig. 1. Tuberculosis notification rate in MD and Chisinau/100.000 during 2011-2015.

Detection of the suspects for tuberculosis is based on the microbiological investigation. Ziehl-Neelsen method of acid fast bacilli staining and culture on the conventional media was performed in the assessment of every patient exposing clinical signs: productive cough for more than 3 weeks, weakness, decreased appetite, weight loss, fever and night sweats [6]. At least two sputum samples are collected in 8-24 hour interval, one sample being an early morning specimen [6]. However, the poor sensitivity of smear microscopy (less than 25%) and long delay in obtaining culture results (at least 120 days for providing a positive result) contribute to the late detection and increased proportion of severe and chronic forms of pulmonary tuberculosis [5]. The high rate of drug-resistant strains circulating in the population made compulsory the performing the nucleic acid amplification testing (GeneXpert MTB/Rif) to each suspected case [6]. By including the polymerase chain reaction in the standard algorithm was increased the sensibility of suspect's investigation [6]. As the consequence the rate of pulmonary clinical forms of tuberculosis is the highest among all diagnosed forms and maintains the similar value in the assessed period of time (fig. 2).

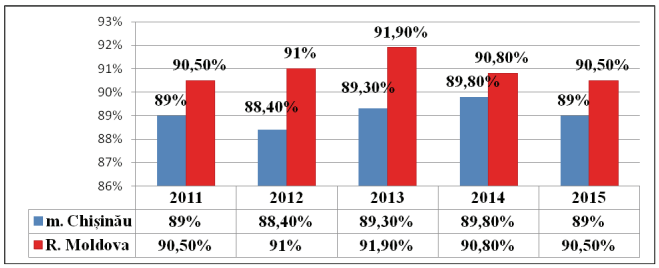

Fig. 2. Rate of pulmonary TB in MD and Chisinau during 2011-2015 (%).

Due to the improving of the treatment quality, the rate of died MDR-TB patients was continuously decreasing: 2011 – 51.7%, 2012 – 47.2%, 2013 – 46%, 2014 – 34.6%, 2015 – 23.2%. The treatment success rate increased (by 3.7%) from 2010 to 2014 in the microscopic positive patients: 2010 – 45%, 2011 – 56.7%, 2012 – 57.5% and culture positive cases 2013 – 70.3%, 2014 – 78.7% (fig. 3).

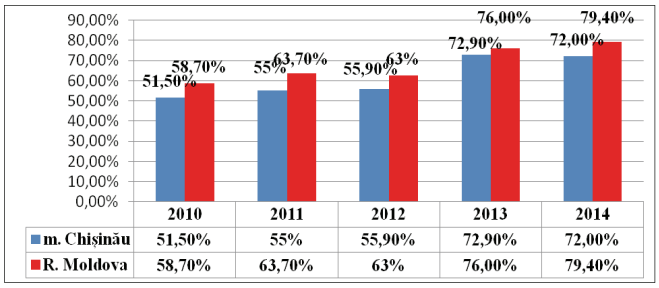

Fig. 3. Treatment success rate in MD and Chisinau during 2011-2015 (%).

The treatment failure rate showed a sharp decrease from 2010 to 2015 due to definition changes: 2010 – 26.9%, 2011 – 23.6% and 2012 – 18.2%. During this period of time all cases identified with MDR-TB and performing treatment for drug-susceptible TB were considered a therapeutic failure. Starting from 2013 patients with treatment failure were considered only patients with microbiological smear positive after 5 months of treatment. Actually the rate of treatment failure is very low: 2013 – 6% and 2014 – 2.8%. The rate of patients lost to follow-up decreased evidently: 2010 – 15.8%, 2011 – 16%, 2012 – 13.7%, 2013 – 9.3% and 2014 – 11.2%.

The proportion of patients lost to follow-up decreased during the period 2010-2015 by 16.4% in MD and by 4.7% in Chisinau due to implementation of the patient's centered health care (fig. 4).

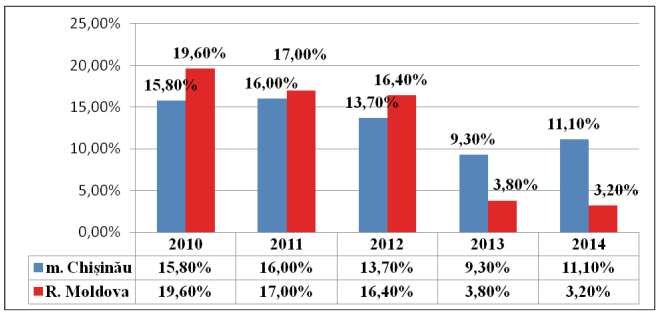

Fig. 4. Rate of lost to follow-up patients in MD and Chisinau during 2011-2015 (%).

Clinical study established a similar sex distribution in the cured (the 1st group) and lost to follow-up group (the 2nd group), with male/female ratio=4/1 in the 1st group and 3,86/1 in the 2nd group. Repartition of the patients into three age groups, identified that the largest was 35-54 year group, consisting from one half of every sample. Comparing the groups it was established that the rate of young, economically vulnerable and reproductive patients (aged 18-34) predominated in the 2nd group: 121 (44.48%) *vs.* 40 (24.24%) in the 1st group. Older patients (aged 55 and more) predominated in the 1st group. So, according to the biological characteristics of the selected patients it was established that men and women had the same probability to be cured or to default the treatment, but young cases have a higher risk for default than older patients. When distributing patients by demographic residence it was established a high predominance of rural residents in the lost to the follow-up group.

Table 1

Distribution of patients by demographic data

Indices	Sex Age Residence	CG (1) N= 165 (P %)	LFUG (2) N= 272(P %)	P value
Sex	Men	132 (80.00)	216 (79.41)	>0,05
	Women	33 (20.00)	56 (20.58)	>0,05
Age groups	18-34 years	40 (24.24)	121 (44.48)	**<0,001**
	35-54 years	91 (55.15)	137 (50.37)	>0,05
	> 55 years	34 (20.61)	14 (5.15)	**<0,001**
Residence	Urban	134 (81.21)	42 (15.44)	**<0,001**
	Rural	31 (18.78)	229 (84.51)	**<0,001**

When distributing the patients, according to the case-type it was established a higher rate of new cases in the 1st than in the 2nd group, without achieving statistical threshold. Relapse was in every fifth patient from both groups. Patients with a previous loss to follow-up statistically predominated in the 2nd group. The totality of the retreated patients predominated in the 2nd group – 116 (42.65%) comparing with 53 (32.12%) cases in the 1st group (p<0,05). Data are shown in the table 2.

Table 2

Distrbution in case-type according to the previous tuberculosis treatment history

Characteristics N= 165 (P %)		CG (1) N= 272(P %)	LFUG (2)	P value
New case (never treated)		112 (67.88)	156 (57.35)	>0,05
Retreatment	Relapse	35 (21.21)	49 (18.01)	>0,05
	After loss to follow-up	8 (4.85)	52 (19.12)	**<0,05**
	After treatment failure	10 (6.06)	15 (5.51)	>0,05

When distributing patients, according to the economic status, it was established that employed persons, contributing to the health budget by paying taxes, health insurance policy and social taxes predominated in the 1st group. The low rate of disabled patients in all groups demonstrated that most of them had no social protection and financial aid. Unemployed patients constituted the largest part of the 2nd group and one half of the 1st group. Patients in social vulnerable state, that included unemployed, disabled, retired and students predominated in 2nd group: 254 (93.38%) comparing with 124 (75.15%) cases, p<0,001. Patients without insurance were more numerous in the 2nd group (tab. 3).

Table 3

Economic status of patients with pulmonary tuberculosis

Economic indices	State	CG (1) N= 165 (P %)	LFUG (2) N= 272(P %)	P value
Stable	Employed	41 (24.85)	18 (6.62)	**<0,001**
	Disabled	9 (5.45)	16 (5.88)	>0,05
	Retired	12 (7.27)	4 (1.47)	>0,05
	Students	8 (4.85)	0	>0,05
Vulnerable	Unemployed	95 (57.57)	234 (86.03)	**<0,001**
	Lack of insurance	97 (57.57)	234 (86.03)	**<0,001**

When assessing the educational level it was established that one half of the 2nd group and one third of the 1st group graduated general school. The incomplete general studies had more frequently the patients from the 2nd group. Higher education was established in a limited number of cases. The totality of patients with low level of education which included no school attendance, primary and incomplete general school predominated in the 2nd group: 90 (33.09%) comparing with 45 (27.73%) cases in the 1st group. Exposed data are revealed in the table 4.

Table 4

Distribution of patients according to the last graduated level

Educational level	Educational status	CG (1) N= 165 (P %)	LFUG (2) N= 272 (P %)	P value
Illiteracy	No school attendance	1 (0.61)	9 (3.31)	>0,05
Primary level	Primary & general incomplete school	44 (26.67)	81 (29.79)	>0,05
Secondary level	Completed general school	57 (34.4)	147 (54.04)	**<0,001**
	Professional school	47 (28.48)	31 (11.39)	**<0,001**
Higher education	Superior studies	16 (9.69)	4 (1.47)	>0,05

When distributing patients in high risk groups, it was determined that poor living conditions and extreme poverty (homeless) predominated in the 2nd group. History of migration during the last year and history of imprisonment statistically predominated in the 2nd group. The lowest rate of the family TB clusters affiliated to each investigated patient was linked with the low quality of epidemiological cross-examination. Patients with associated diseases were every fourth from each group. Among associated diseases, HIV infection was

established in a similar proportion in both groups. Chronic alcohol abusers were 26 (9.59%), drug users – 5 (1.84%) and psychiatric disorders had 4 (1.47%) patients in the 2nd group. No such cases were established in the 1st group. Data are shown in the table 5.

Table 5

Distribution of patients in high risk groups

Risk groups	CG (1) N= 165 (P %)	LFUG (2) N= 272(P %)	P value
Poor living conditions	42 (25.45)	127 (46.69)	<0,001
Homelessness	12 (7.27)	36 (13.23)	>0,05
Migration	20 (12.12)	70 (25.73)	<0,001
History of detention	3 (1.81)	56 (20.58)	<0,001
Closed contact	4 (2.42)	19 (6.98)	>0,05
Associated diseases	42 (25.45)	72 (26.47)	>0,05
HIV infection	15 (9.09)	25 (9.19)	>0,05

Studying case-management, it was identified that the staff of the primary health care detected one half of the 1st group and every fourth patient in the 2nd group as symptomatic cases. The rate of patients detected by the high risk groups screening was low and demonstrated poor control of the vulnerable populations. Pulmonologists diagnosed as symptomatic and by high risk group screening a low rate of patients from both groups. Direct addressing to the specialized hospitals was used more frequently by the patients from the 2nd group due to the lack of health insurance and avoidance of primary health care staff. Other ways of detection were rarely used and included detection of patients hospitalized in the clinical hospital (tab. 6).

Table 6

Case-management characteristics of selected patients

Health level	Detection ways	CG (1) N= 165 (P %)	LFUG (2) N= 272 (P %)	P value
PHC	Detected by GPs as symptomatic cases	69 (41.82)	73 (26.83)	**<0,01**
	Detected by GPs through the screening of HRG	30 (18.18)	35 (12.87)	>0,05
Ambulatory specialised level	Detected by SP as symptomatic cases	22 (13.33)	31 (11.39)	>0,05
	Detected by SP through the screening of HRG	11 (6.67)	23 (8.45)	>0,05
Hospital level	Direct addressing to the specialized hospital	30 (18.18)	107 (39.34)	**<0,001**
Other	Other ways	3 (1.82)	3 (1.11)	>0,05

Note: PHC-primary health care, GPs-general practitioners, SP-specialist pneumophtysiologist, HRG-high risk groups.

When identifying the clinical radiological forms of pulmonary tuberculosis it was established that infiltrative tuberculosis was diagnosed in the most of the patients of both samples, however, it predominated in the 1st group. Severe, chronic forms, which included disseminated, generalized and fibro-cavernous tuberculosis predominated in the 2nd group – 41 (15.07%) comparing with 11 (6.67%) patients in the 1st group, p<0,01. Distributing patients, according to the number of the affected lungs, it was established that one lung was involved in two thirds of the 2nd and one half of the 1st group and both lungs were affected in two thirds of the 2nd group and one half of the 1st group. Destructive forms of pulmonary tuberculosis were identified in a similar proportion in both groups. Extrapulmonary localizations were identified only in the 2nd group (tab. 7).

Table 7

Distribution of patients according to the radiological characteristics

Parameters	Detection ways	CG (1) N= 165 (P %)	LFUG (2) N= 272 (P %)	P value
Forms of TB	PIT	154 (93.33)	223 (81.98)	>0,05
	PDT	9 (5.45)	21 (7.72)	>0,05
	Generalized TB	0	1 (0.36)	>0,05
	FCVTB	2 (1.21)	19 (6.98)	>0,05
Localization and features	1 lung	90 (54.54)	61 (22.42)	**<0,001**
	Both lungs	75 (45.54)	211 (77.57)	**<0,001**
	Lung destruction	79 (47.88)	150 (55.15)	>0,05
Extrapulmonary	Pleurisy	0	3 (1.11)	>0,05
	Other forms	0	5 (1.84)	>0,05

Note: PIT – pulmonary infiltrative tuberculosis, PDT- pulmonary disseminated tuberculosis, FCVTB – fibro-cavernous tuberculosis.

When assessing the laboratory features it was identified that one half of both samples were microscopic positive for acid-fast-bacilli. Culture positive have been more numerous patients from the 2nd group. Multidrug-resistance was established in one third of the 2nd group and every tenth patient from the 1st group. Drug sensitivity testing identified a low proportion of patients with mono- and poly-resistant tuberculosis in both groups (tab. 8).

Table 8

Distribution of patients according to the microbiological features

Characteristics N= 165 (P %)		CG (1) N= 272 (P %)	LFUG (2)	P value
Microbiological	Microscopic positive	86 (52.12)	149 (54.78)	>0,05
	Culture positive	73 (44.24)	156 (57.35)	**<0,01**
	MDR-TB	22 (13.33)	79 (29.04)	**<0,001**
	Mono-resistance	6 (3.64)	3 (1.11)	>0,05
	Poly-resistance	4 (2.42)	6 (2.26)	>0,05
GeneXpert MTB/Rif	Sensible	98 (59.39)	N/A	-
	Resistant	15 (9.09)	N/A	-
	GeneXpert MTB/Rif positive	117 (70.91)	N/A	-

An important research outcome represents the calculation of the likelihood ratio, relative risk (RR), odds ratio

(OR) and the attributable risk (AR). They were used for identifying the high risk groups targeted for the priority interventions for reducing the probability of loss to follow-up. All risk factors exposed statistical difference between groups. The hierarchy of risk groups according to the probability (likelihood ratio) to default the treatment had patients from rural areas, living in poor conditions, with the life history of detention, unemployed and those who addressed to the specialized hospitals avoiding the primary health care. Major factors assessed through relative risk and odds ratio were: life history of detention, rural residence, poverty, unemployment and direct addressing to the hospital. According to the attributable risk hierarchy of risk groups was: life history of detention, rural residence, recent history of migration, patients with MDR-TB, direct addressing to the hospital, poverty, previously treated patients and unemployment. Data are shown in the table 8.

Table 8

Risk factors of tuberculosis patients for loss to follow-up

Factors P		Statistical indices				AR
		LR	RR	OR	%	
Demographic	Rural residence	0	194,966	6,38	23,56	80.98
Treatment	Previously treated	0,02	4,85	1,33	1,57	43.96
Social economical features	Unemployment	0	43,77	2,24	5,53	33.08
	Poverty	0	171,029	5,3	18,31	45.49
	Migration	0,0006	12,358	1,88	2,51	52.89
	History of detention	0	101,51	3,29	46,07	91.20
Case-related	Direct addressing to the hospital	0	76,49	2,57	8,16	53.78
	MDR-TB	0,00016	15,141	1,93	2,66	54.09

Note: P value according to the Pearson's test, LR-likelihood ratio, RR-relative risk, OR-odds ratio; AR-attributable risk.

Population awareness regarding various aspects of tuberculosis is important for the disease control at the national level. For the assessment of patient's knowledge was performed a pre-designed schedule containing open-ended and close-ended questions, reflecting various aspects of the tuberculosis. It included questions on how the patients heard about the disease, mode of transmission, symptoms, curability, type of drugs, duration of the regimen and the place of the treatment. Study technique was by exit interview. The sample size was constituted from 151 interviewed patients. They were informed about the purpose of the study, were assured about their confidentiality and anonymity and the informed consent was taken.

When the patients were asked about how they received information related to tuberculosis it was revealed that most of all [121 (80%)] were informed by the health personnel. About 30 (19.87%) had heard from an informal contact: 17 (11%) mass media (radio, television, posters), 8 (5%) family and 5 (4%) from friends (figure 5). When they were asked if they were satisfied by the conversation with health personnel about their disease 141 (51,845) answered "yes".

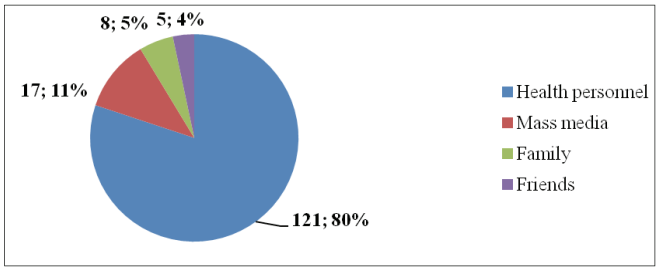

Fig. 5. Distribution of the patients according to the source of knowledge (abs., %).

When the patients were asked about the cause of tuberculosis, 142 (94.04%) answered "infection". Regarding the mode of the spread of infection most of them, 132 (87.42%) patients, answered, correctly choosing multiple choice: cough, spit, speaking and talking face-to-face with a sick person (fig. 6).

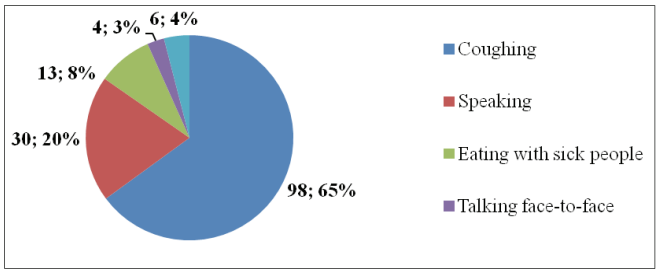

Fig. 6. Distrbution of patients according to the knowledge about the mode of the spread of infection (abs.,%).

The patients were asked about which organ can be affected by tuberculosis. Most of them [140 (92.72%)] answered "lung" and only a low proportion "lungs and other organs" (fig. 7).

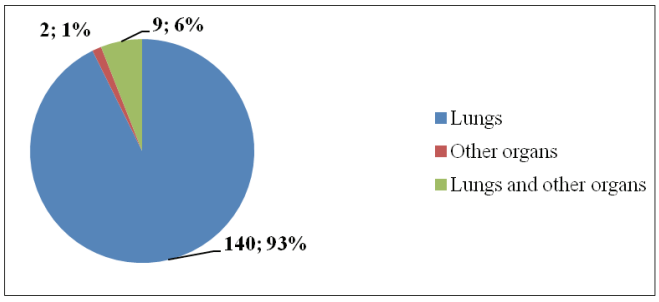

Fig. 7. Distrbution of the patients according to knowledge about the affected by tuberculosis organs (abs.,%).

When they were asked if the disease is curable, 140 (92.71%) patients answered "yes", but only 52 (34.44%) recognized that were previously treated for tuberculosis. For the establishing the patient's therapeutic compliance they were asked if there is a risk to develop resistance if the treatment

is taken irregularly or interrupted. Only 110 (72.85%) patients answered "yes". They were asked if the smear microscopy is negative, it is allowed to interrupt the treatment and 16 (10.59%) patients answered correctly "yes". At the question if they can take two dosages if the previous dosage was lost, 143 (94.71%) patients answered correctly "no". When asked how many months it is necessary to be treated to be cured, 77 (50.99%) said "more than 6 months", 55 (36.42%) – "more than one year", 8 (5.29%) – "two-three months" and 11 (7.28%) did not answer. They were asked where they want to be treated and 111 (73.51%) answered "in the hospital" and only 40 (26.49%) in outpatient settings.

Conclusions

The standard treatment of a new drug-susceptible case, according to WHO guidelines, lasts 6 months and of drug-resistant case – 18-24 months. It must achieve a treatment success rate of at least 85%. Long duration, the high rate of drug adverse reactions and low patient's awareness about treatment compliance contribute to loss to follow-up of at least every tenth patient in MD.

The tuberculosis notification rate in MD decreased evidently in the last 5 years due to the low rate of sreening performed in the high risk groups. The treatment success rate in MD increased evidently due to the excluding of the MDR-TB group from the general cohort. The rate of lost to follow-up patients remains high in Chisinau, despite an evident decrease in the entire country.

No differences were identified distributing patients, according to the sex. Younger patients were more frequent among those who drop up the treatment, but older patients were more frequently cured. Rural residence was associated with loss to follow-up, probably due to low accessibility to specialized health care settings.

Patients previously treated, constituted one half of the lost to the follow-up group. Treated after a previous loss to follow-up was every fifth patient.

Most of the patients from the lost to follow-up group were economically vulnerable. Lack of health insurance and social vulnerability constituted the major barriers for health care seeking. Low level of education had one third of both samples.

Patients from high risk groups designed by the national policy (HIV-infected, close contacts) represented only every tenth case. The highest proportion constituted TB-HIV co-infected patients. However, high risks such as poverty and comorbid status were established in every second patient from the group of lost to follow-up.

Cured patients were detected by general practitioner more frequently and patients treated after loss to follow-up came to the specialized hospitals avoiding primary health care. Severe forms, involving both lungs complicated with extrapulmonary localizations have been more frequent in the group of the lost to follow-up patients.

The proportion of bacteriological positive and drug-resistant patients was the highest in the lost to follow-up group, demonstrating the epidemiological danger that they expose on the healthy population.

The hierarchy of risk groups according to the highest proportion was established: ex-detainees, rural residents, migrants, infected with drug-resistant strains, addressed to the hospital, poor cases, unemployed and previously treated.

The awareness of the patients was good. Most of them were informed by the health personnel and were satisfied by the received knowledge. The proportion of those who were informed through the mass media was high. Most of the patients knew that the disease is contagious, is spread through the air and affects the lungs.

Despite the received information, every third patient lied that had never been treated before, all of them being patients treated after loss to follow-up. Most of the patients knew that the disease is curable with a complete treatment; however, every tenth considered that two-three months are sufficient. Considering their economic vulnerability two thirds wanted to be treated in the hospital.

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