DOI: 10.5281/zenodo.1051120
UDC: 616.24-002.5-06-036.88-091(478-21)

Mortality through associated illnesses in tuberculosis patients and post-mortem pulmonary tuberculosis diagnosis in Chisinau

PopaVasile

Municipal Clinical Hospital of Phthisiopneumology, Chisinau, the Republic of Moldova
Corresponding author: popa.vasile@mail.ru. Received May 02, 2017; accepted September 15, 2017

Abstract

Background: The main cause of death of tuberculosis patients is the progression of tuberculosis, but the presence of associated diseases decreases the outcome of treatment of both the underlying and the associated disease, and the latter is the cause of death. Thus, reducing the mortality of tuberculosis patients can be solved by increasing the therapeutic success rate of tuberculosis as well as associated diseases.
Material and methods: A selective, descriptive and retrospective study was carried out in 3 time periods: period I (2001-2003) – implementation of the DOTS strategy in Chisinau municipality; period II (2007-2009) characterized by the tense epidemiological situation, the high TB mortality indicator and the implementation of the STOP TB strategy; period III (2013-2015) characterized by a shift to "End TB" strategy and a marked decrease in tuberculosis mortality.
Results: Analyzing the reference periods, we found that in the 1st period 1/4 of the total deaths were caused by tuberculosis, associated diseases and other causes, in the 2nd period there was a decrease in the number of deaths, and in the 3rd period there was about 2 times increase in the number of deaths.
Conclusions: The most common concomitant diseases were: oncological, cardiovascular, hepatic cirrhosis and other causes. The number of deaths with the post-mortem tuberculosis diagnosis was decreasing; half of them occurred at home, ½ of the deceased were without a stable place of living.
Key words: Associated pathologies, mortality, post-mortem.

Introduction

Tuberculosis (TB) remains one of the ten leading causes of mortality and is the second most common cause of infectious diseases worldwide after HIV/AIDS. The problem of TB mortality decrease is of a planetary nature [3]. According to World Health Organization (WHO) the TB mortality rate decreased worldwide by 47% between 1990 and 2015. It is estimated that 49 million lives were saved by diagnosing and treating tuberculosis between 2000 and 2014 [8, 22].

The twentieth century has been marked by a revolution in the field of fetal care with the emergence of the BCG vaccine and the first and second-line anti-tuberculosis drugs. These implementations in practice have allowed the spectacular decrease in disease frequency in developed countries over a long period of time, creating the impression that the disease will be defeated [8, 23, 24]. However, since the 1990s, the worsening of the socio-economic situation, together with the imbalance in the health care system, has contributed to the worsening epidemiological indexes [25, 27, 28, 29].

The indicator of tuberculosis mortality is one of the most important demographic indicators. It characterizes not only the demographic well-being of the population but social and medical, as well [14, 16, 18]. Between 1990 and 2015 there was an essential decline in the 47% mortality rate worldwide [3, 10, 13, 24]. The index of tuberculosis morbidity after 1990 in the Republic of Moldova has increased by 3-4 times, but in recent years it has stabilized and even decreased to 10 per 100.000 population in 2015 and in 2016 constituted 11 per 100.000 population [5, 13, 15]. In Chisinau, the mortality index registered a proportion of 6,8 per 100.000 thousand population with a decrease by approximately 50% between 1990 and 2015 [9, 10, 11]. WHO for the years 2016-2035 recommends a reduction in mortality by 90% compared to 2015. The National Program for TB Control in the Republic of Moldova for the years 2016-2020 predicts a mortality decrease by 35% [3].

The main cause of death of tuberculosis patients is the progression of tuberculosis, but the presence of associated diseases decreases the outcome of treatment of both the underlying and the associated disease, and the latter is the cause of death [1, 6]. Thus, reducing the mortality of tuberculosis patients can be solved by increasing the therapeutic success rate of tuberculosis as well as associated diseases [19, 20, 26, 28]. Post-mortem diagnosis of tuberculosis varies between 2.0 and 6.0% of new cases of TB in different countries [7, 12, 17, 21]. The veracity of the mortality rate in tuberculosis, despite the high level of informality, largely depends on the expertise quality of the cause of death [2]. Of particular importance in this context is the incorrect interpretation by the morphopathologist or forensic expert of the pathomorphological picture of tuberculosis, especially in post-mortem established diagnosis [23]. The level of post-mortem diagnosis has a decreasing trend lately. Errors in the diagnosis of tuberculosis are possible among the cases of post-mortem TB deaths in patients with acute forms of acute and epidemiological tuberculosis, predominantly in people living with HIV [26]. Cases of death with post-mortem diagnosis of TB reflect the level of detection organization, the quality of diagnosis of tuberculosis and occur more frequently in people without a stable place of living, diagnosis being determined by legal medicine or somatic stations [21].

Literature data on the causes of mortality of tuberculosis patients through concomitant diseases are contradictory. Associated diseases are recorded in one third of tuberculosis patients [28]. According to some data presented in the year 2014 tuberculosis patients on the record died due to other diseases and causes in 53.6% cases [28]. The rate of tuberculosis patients who died of HIV infection reached 23.4%

in the year 2010 [26]. The post-mortem diagnosis of TB increases the mortality index in different territories.

Thus, in the mortality structure the causes of death are the result of multifactorial action on the human body, and among the main ones both the worsening of social-economic conditions and the level of organization of the service of pneumophtiziology are emphasized.

The purpose of the study was the comparative analysis of the cases of TB patients with other diseases and causes and the evaluation of post-mortem TB diagnosis among the new cases in Chisinau in three periods of time.

Material and methods

A selective and discursive retrospective study was carried out in 3 periods of time: period I (2001-2003) - Implementation of the DOTS strategy in Chisinau; period II (2007-2009) characterized by the tense epidemiological situation, the high TB mortality indicator and the implementation of the "STOP TB" strategy; period III (2013-2015) characterized by a shift to "End TB" strategy and a marked decrease in tuberculosis mortality.

For the purpose of the research, the cases of TB deceased patients in Chisinau with post-mortem diagnosis were studied in three periods of time: during the first period in Chisinau, 494 patients died of tuberculosis and the diagnosis of post-mortem TB was established in 99 (20± 1.8%) patients; in period II of the total 456 deaths of tuberculosis, 63 (13.8± 1.6%) cases were detected post-mortem; in the third period of the total 225 deaths from tuberculosis, 29 (12.9±2.2%) cases were detected post-mortem. Also, from the total number of deaths from tuberculosis in Chisinau in the reference periods were selected the cases of patients with pulmonary tuberculosis deceased of associated diseases and other causes: 157 (25.3%) cases were selected in period I, in the period II – 110 (19.5%) cases and in period III – 112 (33.5%) cases.

Results and discussion

Analyzing the reference periods, we found that tuberculosis, associated diseases and other causes in the first period led to 1/4 of the total deaths, in the second period there was a decrease in the number of deaths, and in the third period there was an approximately twice increase in the number of deaths.

Table 1

Distribution by gender

Sex	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
Men	121	77.1±3.4	79	71.8±4.3	89	79.5±3.8
Women	36	22.9±3.4	31	28.2±4.3	23	20.5±3.8

Note: no statistically significant difference between the periods has been established, p>0.05.

Analyzing the distribution of patients by gender, we established the significant predominance of male individuals versus female subjects in all periods studied (p<0.05). The male/female ratio was 3.4/1 in the first period, 2.5/1 in the second period and 3.8/1 – in the third period. Differences between the studied periods were not significant. The breakdown of cases by gender is shown in table 1.

The distribution of deaths by age showed that in the 0-4 age group, deaths were recorded only in period I (1.3±0.8%) and in period II (0.9±0.9%). In the age group 15-24 years, the number of deaths was low: 3.2±1.4% of cases in the 1st period, 0.9±0.9% of cases in the 2nd period and 0.9±0.8% in the 3rd period, and in the age group 25-34 years: 10.8±2.4%, 13.6±3.2% and 10.7±2.9% of cases, respectively. Deaths predominated in working-age patients (35-64 years) and the distribution was similar in the studied periods: 70.9% and 69.6% respectively. In the 35-44 age group the number of deaths predominated significantly in period I versus period II, for other age groups the differences between the reference periods were not significant. In the group of patients aged 65 years and over, the number of deaths increased insignificantly: 14.7±2.8%; 13.7±3.2%; 18.8±18.7% of cases, respectively. Data are reflected in table 2.

Table 2

Distribution of cases by age

Age	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
0-4	2	1.3±0.8	1	0.9±0.9	0	0
15-24	5	3.2±1.4	1	0.9±0.9	1	0.9±0.8
25-34	17	10.8±2.4	15	13.6±3.2	12	10.7±2.9
35-44	41	26.1±3.5*	17	15.5±3.4	23	20.5±3.8
45-54	36	22.9±3.3	36	32.7±4.4	31	27.7±4.2
55-64	33	21.0±3.2	25	22.7±3.9	24	21.4±3.8
65+	23	14.7±2.8	15	13.7±3.2	21	18.8±18.7

Note: * – statistically significant difference between period I and II, p<0.05.

Studying the background of the deceased, we found the prevalence of urban people in all three studied periods (p<0.05): 86.6±2.7%, 75.5±4.1% and 54.4±4.4% of cases, respectively. During the analyzed periods, a significant increase in the number of deaths among persons in the suburbs was recorded in period II (24.5±4.1%) and III (33.0±4.4%) compared to period I (13. 4±2.7% of cases), p<0.05. The number of people living in the urban area predominated significantly in period III (12.5±3.1% of cases) compared to period II (4.5±1.9% of cases), p<0.05.

Analyzing the cases studied according to the methods of detecting the deceased, we established that the majority of patients in period I (98.7±0.8%) were detected by the passive method, by direct addressing. The dynamics shows a decrease in the direct addressing of patients to medical care: period II – 22.7±3.9% of cases and period III – 32.1±4.4% of cases, the differences compared to period I were of statistical

significance (p<0.05). The activity of the family physician is manifested in periods II and III, by the detection of symptoms, which accounted for 1/3 of the cases during periods II and III. The detection of patients by the prophylactic control (active method) was not insignificant and decreasing: in the second period – 14.5±3.3% of cases and in the third period – 8.9±2.6% of cases. The passive detection by addressing with the symptoms to other specialists was 1/5 of the deceased and the active detection was low: it is missing in period I; in period II – 8.1±2.6% of cases and in period III – 6.4±2.2% of cases. The data obtained are shown in table 3.

Table 3

Distribution of cases according to the detection method

Method	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
Direct addressing	155	98.7±0.8	25	22.7±3.9*	36	32.1±4.4●
Symptomatic by family doctor	0	0	37	33.7±4.5*	36	32.1±4.4●
Prophylactic by family doctor	0	0	16	14.5±3.3*	10	8.9±2.6●
Symptomatic by another specialist	2	1.3±0.8	23	21.0±3.8*	23	20.5±3.8●
Prophylactic by another specialist	0	0	9	8.1±2.6*	7	6.4±2.2●

Note: * – statistically significant difference between period I and II, p<0.05;

The distribution of deaths by the type of case was the following: the new case was confirmed in the majority (82.2±3.0%) of the deceased patients in period I, in period II it decreased to 51.8±4.7% of cases and in period III – to 44.6±4.6% of cases. Relapses were recorded more frequently in periods II and III compared to period I: 28.2±4.2%, 31.3±4.3%, 12.1±2.6%, respectively. The other types of cases (lost to follow up, therapeutic failure, chronic case) varied between 1.3-6.3% of cases. The distribution according to the recorded case is shown in table 4.

Table 4

Distribution by the type of case

Type of case	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
New case	129	82.2±3.0	57	51.8±4.7*	50	44.6±4.6●
Relapse	19	12.1±2.6	31	28.2±4.2*	35	31.3±4.3●
Lost to follow up	0	0	8	7.3±2.4*	16	14.3±3.3●
Therapeutic failure	0	0	11	10±2.8*	8	7.1±2.4●
Chronic case	0	0	2	1.8±1.2	3	2.7±1.5
Transferred	9	5.7±1.8	1	0.9±0.9*	0	0●

Note: * – statistically significant difference between period I and II, p<0.05;
● – *statistically* significant difference between period I and III, p<0.05.

Of the clinical-radiological forms, infiltrative pulmonary tuberculosis predominated significantly in all three periods (p<0.05): 73.2±3.5% in period I, 70.9±4.3% in period II and 88.4±3.0% of cases in period III, followed by disseminated form: 8.3±2.1%, 9.1±2.7%, 3.6±1.8%, respectively, and then fibrocystic tuberculosis: 5.1±1.7% of cases in period I and 10±2.8% of cases in period II and was not recorded in period III. Intravascular extracellular tuberculosis as well as different organs varied between 0.3-0.8% of cases. Distribution according to the clinical forms of tuberculosis is presented in table 5. Intrathoracic and various organs vary between 0.3-0.8% of cases.

Table 5

Distribution according to the clinical forms of tuberculosis

Form	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
Primary TB Complex	0	0	1	0.9±0.9	0	0
ITLN TB	2	1.±0.8	1	0.9±0.9	0	0
Peripheral TB adenopathy	1	0.6±0.6	0	0	0	0
Infiltrative TB	115	73.3±3.5●	78	70.9±4.3◊	99	88.4±3.0
Nodular TB	2	1.3±0.8●	0	0◊	7	6.3±2.3
Fibro-cavitary TB	8	5.1±1.7●	11	10±2.8◊	0	0
Disseminated TB	13	8.3±2.1	10	9.1±2.7	4	3.6±1.8
TB pleurisy	10	6.4±1.9●	6	5.5±2.1◊	0	0
TB of the bronchi	1	0.6±0.6	0	0	0	0
TB of the spine	2	1.3±0.8	0	0	2	1.7±1.3
TB of other bone locations	1	0.6±0.6	1	0.9±0.9	0	0
Renal TB (160)	1	0.6±0.6	0	0	0	0
TB of other organs	1	0.6±0.6	0	0	0	0
TB of CNS	0	0	2	1.8±1.2	0	0

Note: ITLN – intrathoracic lymph node, CNS – central nervous system,
● – statistically significant difference between period I and III, p<0.05;
◊ – statistically significant difference between IInd period and IIIrd period, p<0.05.

Respectively, the study of the results of the microscopic sputum examination at BAAR revealed a large number of deceased persons with the negative result in all periods: 59.2%; 47.3%; 55.4% of cases. Respectively, the results of MBT's cultural exams show even lower scores, increasing over the past periods: 17.2±3.0%, 30.0±4.3%, 43.7±4.6%. Absent dates on the bacteriological examination were evidenced in the Ist period at 53.4±3.9% of cases with a significant decrease in the 2nd period (12.8±3.1%) and in period III (14.3±3.3% of cases). The results of MBT sensitivity tests on anti-tuberculosis drugs reported that the sensitivity of MBT to anti-tuberculosis drugs decreased markedly in dynamics in the three periods: 55.5%, 39.4%, 22.4% respectively, and the MBT resistance to anti-tuberculosis drugs increased respec-

tively in: 44.4%; 60.6% and 77.6% of cases. The results of the microbiological examination are presented in table 6.

Table 6

The results of the microbiological exam

MBT	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
Positive	27	17.2±3.0*	33	30±4.3◊	49	43.7±4.6●
Negative	24	15.3±2.8*	35	31.8±4.4	42	37.5±4.5●
Missing data	91	57.9±3.9*	29	26.4±4.2	19	16.9±3.5●
It was not done	15	9.6±2.3	13	11.8±3.0◊	2	1.8±1.3●

Note: * – statistically significant difference between the Ist period and the 2nd period, p<0.05; ● – statistically significant difference between the Ist period and the 2nd period, p<0.05

Among cases with drug-resistant tuberculosis, multidrug resistance predominated in all periods studied with a higher frequency in the 3rd period. A similar number of patients was recorded with monoresistance, while the polyresistance was decreasing. The distribution of cases according to the spectrum of resistance is shown in table 7.

Table 7

The distribution of cases according to the spectrum of resistance

DST Results	Period I (2001-2003) n=12		Period II (2007-2009) n=20		Period III (2013-2015) n=38	
	No	M±m%	No	M±m%	No	M±m%
Mono	2	16.6±10.7	3	15±7.9	6	15.8±5.9
Poli	4	33.4±13.6●	3	15±7.9	2	5.3±3.6
MDR	6	50±14.4	14	70±10.2	30	78.9±6.6

Note: DST – drug susceptibility testing, ● – statistically significant difference between the 1st and the 3rd period, p<0.05.

Causes of death of tuberculosis patients by associated illness and other factors were broadly diverse and are reported in Table 8.The most common cause of death in all periods studied was oncological pathology (lung, head and neck, liver, prostate), followed by cardiovascular pathology (ischemic cardiopathy) and decompensated liver cirrhosis that were more frequently confirmed in period I, then more frequent community pneumonia in period II and chronic alcoholism predominantly in period III. Vascular attack followed the most frequent occurrence in period I, followed by HIV/AIDS and myocardial infarction more frequently in period II and diabetes.

Among other causes of death were: thromboembolism which was certified only in the 2nd and the 3rd period (1.8% and 2.7%, respectively) and renal insufficiency. Gastric ulcer was the cause of death only in period II (27%). Septicemia caused by other diseases was in 1.2%, 0.9%, 3.6% of cases, respectively. Other factors that caused death: road accidents (9.6%, 2.7%, 3.6%); suicide (0.6%, 1.8%, 0.9% of cases respectively); thermal combustion (0.6%) and frostbite (4.5%) were recorded only in the 1st period, and CO2 poisoning – only in the 2nd period (0.9%).

Table 8

Causes of death of tuberculosis patients by other diseases

The cause of death	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
Oncological pathology	28	17.8±3.0	21	19.1±3.7	24	21.4±3.8
Pathology of the cardio-vascular system	32	20.4±3.2*	5	4.5±1.9◊	15	13.4±3,2
Decompensated liver cirrhosis	27	17.2±3.0	15	9.6±3.2	10	8.9±2.6●
Community pneumonia	7	4.5±1.6	5	4.5±1.9◊	15	13.4±3.2●
Chronic alcoholism	7	4.5±1.6	10	9.1±2.7	10	8.9±2.6
Cerebral ischemic attack	13	8.3±2.1	7	6.4±2.3	6	5.4±2.1
HIV AIDS	6	3.8±1.5*	15	13.6±3.2◊	3	2.7±1.5
Myocardial infarction	3	1.9±1.0*	9	8.2±2.6	5	4.5±1.9
Diabetes	7	4.5±1.6	5	4.5±1.9	3	2.7±1.5
Other causes	27	17.2±3.0	18	16.4±3.5	21	18.8±3.6

Note: * – statistically significant difference between period I and II, p<0.05. ◊ – statistically significant difference between IInd period and IIIrd period, p<0.05. The distribution of cases according to the place of death is reported in table 9.

Table 9

The place of death

The place of death	Period I (2001-2003) n=157		Period II (2007-2009) n=110		Period III (2013-2015) n=112	
	No	M±m%	No	M±m%	No	M±m%
At home	92	58.6±3.9*	45	40.9±4.6	39	34.8±4.5●
Somatic Hospital	34	21.7±3.2	20	18.2±3.6	29	25.9±4.1
Specialized hospital	21	13.3±2.7*	35	31.8±4.4	26	23.2±3.9●
Other places	10	6.4±1.9	10	9.1±2.7	18	16.1±3.4●

Note: * – statistically significant difference between I period and II, p<0.05; ● – statistically significant difference between I period and III, p<0.05.

Analyzing the place of death, we found that tuberculosis patients died significantly more frequently due to associated diseases at home in the Ist period (p<0.05), the rate being decreased in the 2nd and 3rd periods. In the specialized tuberculosis hospitals, the index varied from 13.3±2.7% to 31.8±4.4%, and in the somatic one died every 5th patient from the 1st and 2nd periods and each fourth – in the third

period. Approximately 10% of patients died in other places.

In the reference years of the total post-mortem TB patients, 191 (16.3±1.1%) cases were diagnosed. Analyzing the number of deceased, diagnosed post-mortem in the studied periods, we established that in the dynamics the number of TB cases diagnosed post-mortem was decreasing. Data on the number of deaths with post-mortem tuberculosis from the total TB deaths are shown in table 10.

Table 10

Distribution of TB cases established post-mortem according to the studied periods

Period of study	TB deaths n = 1175	Post-mortem diagnosed TB	
		No	M ± m
I (2001-2003)	494	99	20,0 ± 1,8▪
II (2007-2009)	456	63	13,8 ± 1,6
III (2013-2014)	225	29	12,9 ± 2,2●

Note: ▪ – statistically significant difference between Period I and II, p<0.05; ● – statistically significant difference between Period I and III, p<0.05.

Comparing the results obtained in different periods, we pointed out that the number of deaths of TB detected post-mortem predominated in period I compared to period II and period III (p<0.05).

Analyzing the number of post-mortem deaths among new cases of TB we have identified a continuous decrease in the number of deaths among the new cases: 2324 cases – in the first period, 2126 cases – in the second period, and 1518 cases – in the third period. The percentage of cases detected post-mortem among new cases in the 1st period amounted to 4.3%, in the 2nd period – 3% and in the 3rd period – 1.9%.

By distributing the cases of deceased by gender we established the significant predominance of male compared to female in all three time periods (p<0.05): in the 1st period – 85 (85.9±3.5%) of men and 14 (14.1±3.5%) women, in the 2nd period – 47 (74.6±5.4%) and 16 (25.4±5.5%) women and in the 3rd period – 25 (86.2±6.4%) men and 4 (13.8±6.4%) women. The male / female ratio was 6: 1 in period I, 2.9:1 in period II and 5.0:1 in period III. Differences between the studied periods were not significant. Data are reported in table 11.

Table 11

Distribution of post-mortem TB cases by gender

Sex	Periods of study					
	I (2001-2003) n = 99		II (2007-2009) n = 63		III (2013-2015) n =29	
	No	M ± m	No	M ± m	No	M ± m
Men	85	85,9 ± 3,5▪	47	74,6 ± 5,4▪	25	86,2 ± 6,4▪
Women	14	14,1 ± 3,5	16	25,4 ± 5,5	4	13,8 ± 6,4

Note: ▪ – statistically significant difference between men and women, p<0.05.

Studying the age groups of the TB deaths detected post-mortem we established that in the first period the number of deaths predominated significantly in the 51-60 age group – 42 (42.4±4.9%) cases, followed by the age group 41-50 years – 26 (26.3±4.4%), then by age group 31-40 years – 14 (14.1±3.5%) cases, age group older than 60 years – 9 (9.1±2.8%) cases, (p<0.05) and age group 21-30 years – 8 cases (8.1±2.7%). Data are shown in table 12.

Table 12

Distribution of post-mortem TB deaths by age

Age groups years	Periods of study					
	I (2001-2003) n = 99		II (2007-2009) n = 63		III (2013-2015) n =29	
	No	M ± m	No	M ± m	No	M ± m
21-30	8	8,1±2,7	2	3,2 ±2,2	5	17,2±7,0*
31-40	14	14,1 ± 3,5	12	19,1±4,9	5	17,2 ±7,0
41-50	26	26,3±4,4	19	30,1 ±5,7	5	17,5 ±7,0
51-60	42	42,4±4,9	19	30,1±5,7	5	17,5 ±7,0 ▪
≥60	9	9,1± 2,8	11	17,5±4,7	9	31,0 ±8,5▪

Note: ▪ – statistically significant difference between period I and period III, p<0.05; ● – statistically significant difference between period II and period III, p<0.05.

In the second period, 41-50 years old age group and the 51-60 age group had a similar number of TB deaths – 19 (30.1±5.7%) cases, which predominated insignificantly from the group aged 31-40 years – 12 (19.1±4.9%) cases and the age group older than 60 years – 11 (17.5 ±4.7%) cases and significantly compared with the age group 21-30 years - 2 (3.2±2.2%) cases, (p<0.05). In period III in the 21-30 years, 31-40 years, 41-50 years and 51-60 years, 5 cases (17.5±7.0%) were recorded post-mortem, and in the age group older than 60 years – 9 (31.0±8.5%) cases. Comparing the studied periods, we pointed out that the deaths in the age group 51-60 predominated significantly in period I compared to period III (p<0.05), in the age group over 60 years deaths predominated in period III compared to period I (p<0.05) and in the age group 21-30 deaths predominated in period III compared to period II (p<0.05).

Table 13

TB deaths detected post-mortem according to the place of death

Periods of study	The place of death					
	Home		Somatic hospitals		Other places	
	No	M ± m	No	M ± m	No	M ± m
I (2001-2003), n = 99	50	50,5±5,0	23	23,2±4,2	26	26,3±4,4
II (2007-2009), n = 63	28	44,4±6,2	9	14,3±4,4	26	41,3±6,2 ▪
III (2013-2015), n = 29	15	51,7±9,2	9	31,0±8,5	5	17,3±7,0 *

Note: * – statistically significant difference between period III and II, p<0.05; ▪ – statistically significant difference between period II and I, p<0.05.

Analyzing the place of death, we established that in all three periods approximately 1/2 of the patients died at home: in period I – 50 patients (50.5±5.0%), in period II – 28 (44.4±6.2%) patients and in period III – 15 (51.7±9.2)

cases. In somatic hospitals died: in period I –23 patients (23.2±4.2%), in period II – 9 (14.3±4.4%) patients and in period III – 9 (31.7±8.5%) cases. In other places, died: in the 1st and 2nd periods – 26 patients (26.2±4.4% and 41.3±6.2% respectively) and in the 3rd period – 5 (17.3±7.0 %) cases, significantly less compared to period II, ($p<0.05$). Data are presented in table 13.

By evaluating the belonging to socially vulnerable groups, we established that among the cases of deaths with post-mortem TB 44 (44.4±4.9%) patients in period I, 26 (41.3±6.2%) patients in period II and 9 (31.0±8.6%) patients in period III were without stable living space (homeless). The distribution of TB deaths detected post-mortem according to the presence/absence of the place of residence is shown in figure 1.

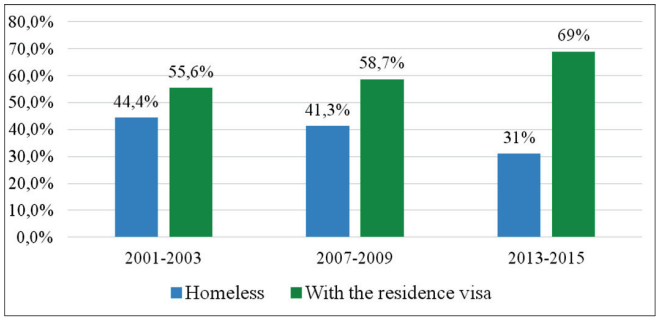

Fig. 1. Distribution of TB deaths detected post-mortem.

Thus, during the studied periods, we have determined the decrease of the number of patients' living places. This was done with the help of the non-governmental organization "AFI" through the early active detection of tuberculosis and the treatment in both phases in stationary conditions.

Conclusions

The number of deaths of pulmonary tuberculosis due to concomitant illnesses and other causes in the reference periods was rising as the number of deceased persons in suburbs increased. Male subjects predominated compared to females both in the group of deaths from pulmonary tuberculosis due to concomitant diseases and in post-mortem diagnosis of tuberculosis. Detection of deaths of tuberculosis patients by progression of associated diseases was predominantly realized by the passive method, with the predominance of pulmonary tuberculosis, with a high rate of infiltrative form in the tuberculosis process destruction phase in approximately half of cases.

Sputum microscopy at BAAR was negative in half of the deceased, during the last two periods the number of bacteriological examinations increased; the increase of MBT resistance to anti-tuberculosis drugs took place on the account of MDR resistance. Associated diseases that more frequently contributed to the death of the tuberculosis patient are: cancer of various organs, ischemic heart disease, cirrhosis, community pneumonia, alcoholism and other causes.

The number of deaths with post-mortem diagnosis of tuberculosis and their share among new cases has been decreasing in the studied periods. Half of the deaths with the post-mortem diagnosis of tuberculosis occurred at home, their number being stable in all studied periods, the number of deaths in the somatic stations increased during the third period, and the deaths in other places doubled during the period II and have been decreasing in the third period.

Approximately 1/2 of deceased individuals with post-mortem diagnosis of tuberculosis had no place of stable living, but there is a downward trend in the number of homeless deceased in the 3rd period.

References

1. Chou-Han Lin, Chou-Jui Lin, Yao-Wen KuoJann-Yuan Wang et al. Tuberculosis mortality: patient characteristics and causes. BMC Infectious Diseases. 2014; 14:5.
2. Didilescu C., Popescu G., Cioran N., et al. Tuberculosis mortality in Romania – a marker of endemic severity. 2012; 61 (3):150-152.
3. Global Tuberculosis Report 2016. WHO/HTM/TB/2016.13. Geneva: World Health Organization, 2016.
4. Haidarlî I., Sain D., Pisarenco, S., et al. Mortality by multidrug resistant tuberculosis in the Republic of Moldova in 2007, In: The 4th National Congress of Phthisiopneumology in Moldova. Actualities in etiology, pathogenesis, prophylaxis, diagnosis and treatment of tuberculosis and non-specific pulmonary disorders. Chişinău, 2009, p. 32-33.
5. Iavorschi C., Emilianov O., Bolotnicov V., et al. Mortality through Early and Tardive Pulmonary Tuberculosis. In: Bulletin of the Academy of Sciences of Moldova. Medical Sciences. Chişinău. 2012; 4 (36): 85.
6. Martinson N. A., Karstaedt A., Venter W. D., et al. Causes of death in hospitalized adults with premortem diagnosis of tuberculosis: an autopsy study. AIDS 2007; 21: 2043-2050.
7. Mathew T. A., Ovsyanikova T. N., Shin S. S., et al. Causes of death during tuberculosis treatment in Tomsk Oblast, Russia. Int J Tuberc Lung Dis. 2006; 10: 857-863.
8. Migliori GB, Zellweger JP, Abubakar I. et al. European Union Standards for Tuberculosis Care. European Respiratory Journal. 2012; 36: 807-819.
9. Popa V., Some aspects of tuberculosis mortality in the municipality of Chisinau in 2007-2009. Scientific annals of the 13th edition, volume 3, Chisinau. 2012, p. 235-238.
10. Popa V., A. Ustian, I. Haidarlî, et al. Lethality through Tuberculosis in The Municipal Clinical Hospital for Phthisiopneumology in Chisinau. Bulletin of the Academy of Sciences of Moldova. Medical Sciences. Chisinau, 2011; 4 (32): 44-49.
11. Roya Alavi-Naini, Ali Moghtaderi, Maliheh Metanat, et al.. Factors associated with mortality in tuberculosis patients Journal of Research Medical Science. 2013 Jan; 18(1): 52–55.
12. Sain D., I. Haidarlî, C. Palihovici, et al. Tuberculosis control management issues in the Republic of Moldova. Medical Clerk. 2012; 3 (327): 295-297.
13. Trends in Tuberculosis Morbidity and Mortality, American Lung Association Research and Health Education Epidemiology and Statistics Unit April 2013.
14. Tudor E., Haidarlî I., Groza G.,et al. Morphological features of pulmonary tuberculosis. Bulletin of the Academy of Sciences of Moldova Medical Sciences. 2011; 4(32):100.
15. Balas'janc T.S. Razvitie epidemiologicheskogo processa: vliyanie vneshnih I vnutrennih faktorov [Epidemiological process evolution: external and internal factors impact]. V: Medicinskiy akademicheskiy zhurnal [Medical Academical Journal]. 2014; 2: 55-59.
16. Baranova V.S., Odinec V.S., Fisher J. J. Osobennosti techeniya tuberkuleza, ne raspoznannogo pri zhizni bol'nogo [Particularities of TB evolution in alive patients]. Problemy tuberkuleza i boleznei legkih [Problems of tuberculosis and lung diseases]. 2011; 4: 49-50.
17. Gabbasova L.A. Experts WHO E. R. Global tuberculosis report (2015). World Health Organization Geneva, 2015: 192.

18. Kobeleva G. V., Grigor'eva E. A. Somaticheskie zabolevaniya kak prichina smerti bol'nyh aktivnym tuberkulezom [Somatic disease as a cause of death in active TB patients]. Problemy tuberkuleza i bolezni legchih [Problems of tuberculosis and lung disease]. 2001; 2: 47-49.
19. Kobeleva G.V., Kopylova I.F., Baiborodova T.I. Letal'nye ishody bol'nyh tuberkulezom v usloviyah ego epidemii [Fatal outcomes in TB patients in condition of epidemy]. Tuberkulez I bolezni legkih [Problems of tuberculosis and lung disease]. 2011; 4: 195-196.
20. Makarova V.N. Analiz sudebno-medicinskih issledovaniy trupov s diagnozom tuberkulez legkih i viyavliaemye pri etom defekty diagnostiki [Assay of medical examination of cadavers with pulmonary TB diagnosis and diagnostic mistakes detected]. Avtoref. Na soiskanie uchennoy stepeni kandidata medicinskih [PHD Thesis], Moskva, 2009.
21. Mario K. Ravil'one, A. A. Korobicyn. Likvidacia tuberkuleza – novaya strategiya VOZ v rusle ustoychivogo razvitiya, vklad Rossiyskoy Federacii [End TB – the new strategy in the era of stable development, Russian Federation contribution]. "Tuberkulyoz i bolezni liogkih" [Problems of tuberculosis and lung disease]. 2016; 94 (11): 7-15.
22. Parolina L. E., Morozova T. I. Otpushhennikova O. N. Rezul'taty sopostavleniya prizhiznennogo i posmertnogo viyavleniya tuberkuleza mnozhestvennoy lokalizacii u bol'nyh VICh-infekciey [Results of correlation between alive and dead patients detected with tuberculosis with multiple localization and HIV-patients]. Tuberkulyoz i bolezni liogkih» [Problems of tuberculosis and lung disease]. 2015; 93 (5): 135-136.
23. Ravil'one M.K., Korobicyn A.A. Likvidaciya tuberkuleza – novaya strategiya VOZ v rusle ustoychivogo razvitiya, vklad Rossiiskoy Federacii [End TB – the new strategy in the era of stable development, Russian Fedration contribution]. "Tuberkulioz i bolezni liogkih" [Problems of tuberculosis and lung disease]. 2016; 94 (11): 7-15.
24. Smetanina E. A. Prognosticheskoe lechenie faktorov, okazyvayushih vliyanie na formirovanie pokazateley smertnosti ot tuberkuljoza i zabolevaemosti tuberkulioza [Prognostic treatment of predictive factors with impact above mortality and prevalence of TB]. Avtoref. na soiskanie uchennoy stepeni kandidata medicinskih [Phd Thesis], Moskva, 2013, 242 p.
25. Frolova O.P., Shhukina I.V., Frolov I.G. et al. Analiz smertnosti ot tuberkuleza v sochetannii s VICh-infekciey [Assay of TB mortality in HIV-patients]. Tuberkulez i bolezni legkih [Problems of tuberculosis and lung disease]. 2014; 7: 32-36.
26. Cybikova, Je.B. O prichinah smerti vperviye viyavlennyh bolnyh tuberkuliozom liogkih [The death causes of pulmonary TB new cases]. Zdravoohranenie Rossiyskoy Federacii [Russian Federation Ministry of Health]. 2013; 1: 15-19.
27. Shilova M.V. Smertnost' naseleniya u bolnyh tuberkulezom ot tuberkuleza i drugih prichin i faktory, okazyvayushhie vliyanie na yego uroven' [Population mortality from TB and other causes and factors with impact on the level of mortality]. Poliklinika [The policlinica]. 2015; 2 (2): 32-37.
28. Shilova M.V. Tuberkulez v Rossii v 2012-2013 gg [TB in Russia in 2012-2013]. Moskow, 2014, 244 p.