

DOI: 10.5281/zenodo.3556469
UDC: 616.24-002.5-085.33(478-25)



Eligibility criteria for video-observed anti-tuberculosis treatment at patients from Chisinau city

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Manuscript received September 02, 2019; revised manuscript December 02, 2019

Abstract

Background: It is known that the main barriers in the anti-tuberculosis treatment delivery are social, economic, educational and psychological issues. According to the estimations the Republic of Moldova (RM) remains a high risk zone showing an inadequate concern regarding social determinants that represent the risk factors for achieving high treatment outcome. Tuberculosis is concentrated in areas with high density of the population, poor environmental and sanitation conditions: poverty, food insecurity, low living conditions.

Material and methods: A retrospective selective, descriptive study of socioeconomic, epidemiological peculiarities, case-management, diagnosis and microbiological characteristics of 693 patients with tuberculosis registered in Chisinau in 2016 was performed.

Results: Despite the fact that criteria for selection of patients for video-assisted anti-tuberculosis treatment (VOT) were defined, a range of risk factors can endanger treatment performing, such as: deep social economic vulnerability, comorbidities associated or not with psychic impairment, disease related characteristics, such as extensiveness, severity, duration of the tuberculosis evolution, positive microbiological state and multi-drug resistance are conditions which can exclude the ambulatory treatment and VOT. The low treatment outcome shows the limited potential of VOT to improve the epidemiological indices due to the complexity of patient's risk factors.

Conclusions: VOT can be implemented in the management of tuberculosis patients in the actual epidemiological state of the RM, if a complex of patients supporting measures are performed.

Key words: tuberculosis, treatment, outcome.

Introduction

Tuberculosis is one of the 10 causes of death worldwide [1]. The lack of an appropriate and adequate treatment according to the drug resistance profile contributes to the death in a couple of years [2]. The main objectives of the anti-tuberculosis treatment constitute: 1. To cure the patient; 2. To prevent the death from active disease or its late effects; 3. To prevent relapse of tuberculosis; 4. To decrease the risk of the mycobacteria transmission to others; 5. To prevent the development of the acquired drug resistance [1, 2].

According to the World Health Organization guideline "Treatment of tuberculosis" and TB report drug susceptible tuberculosis is treated with the first-line anti-tuberculosis drugs: isoniazid, rifampicin, ethambutol, pirazinamide and streptomycin [1, 2]. Tuberculosis determined by the multi-drug resistant strains (MDR-TB) is treated during 18-24 months with 2nd line antituberculosis drugs according to the drug susceptibility test [3]. The standard treatment for MDR-TB consists in injectable antibiotics – aminoglycosides (kanamycin, amikacin or capreomycin) and orally administrated anti-tuberculosis drugs: fluoroquinolones (levofloxacin, moxifloxacin or gatifloxacin), ethionamide, prothionamide, paraaminosalicylic acid and cycloserine [1, 2]. There are 3 types of the anti-tuberculosis treatment administration options: 1. Community or home-based directly observed treatment (DOT) when the treatment is

delivered in the community close to the patient's home or work [1, 2]; 2. DOT administered by specialised healthcare providers such as in the hospitals or specialised services [1, 2]; 3. Video-observed treatment (VOT), based on the principle when the staff involved in its performing can observe the administration of the anti-tuberculosis drugs using electronic devices (personal computer, notebook, smartphone with Android system) through a web camera [3, 4, 5].

The technology required for VOT are broadband Internet and availability of an electronic device connected to a specialised in VOT platform. The option for VOT is real-time communication or recorded video. VOT can replace the DOT when video communication technology is available and the healthcare providers and the patients are well trained. VOT allows to observe adherence to treatment from distance, avoiding the direct contact of the patient with the healthcare worker. VOT is more flexible for patients, achieves a higher level of interaction between patients and medical staff and probably has a lower cost than DOT [6]. There were performed cohort studies in high income countries and no data were found from low and middle income countries which compared the treatment effectiveness of DOT compared with VOT [3, 4]. The studies showed that there is no statistical difference in the treatment completion and mortality among the groups treated through DOT and VOT [2, 3, 4].

In the Republic of Moldova the methodology of the VOT was established by the law no. 153-XVI of 4.07.2008 related to the control and prevention of tuberculosis, recommendations of the National Tuberculosis Control Program for 2016-2020, approved by the decision no. 1160 of 20.10.2016, the objective of the Strategic Program for the Technological Upgrade of the Government (E-Transformare) approved by the decision no. 710 of 10.09.2011 and the National Clinical Protocol "Tuberculosis in adults" 123 approved by the decision no.1081 of 29.12.2017. The regulation established that the responsibility for the initiation of the VOT lies on the pulmonologist specialised in tuberculosis and the primary healthcare worker responsible for the case management in the outpatient settings. In the Republic of Moldova the VOT facilitates the interaction between the healthcare worker and the patient; however, it does not replace the DOT. The including criteria for video-observed treatment (VOT) in the RM are: 1) The patient has an available electronic device (personal computer, notebook, smartphone with android system) and a web camera through which the medical staff involved in its performing can observe the administration of the anti-tuberculosis drugs; 2) The patient is residing in the RM. 3) the patient can administrate independently the anti-tuberculosis treatment [7, 8, 9, 10, 11, 12]. The technologies required for VOT to be available for the patient are: broadband Internet and availability of an electronic device connected to a specialised in VOT platform. The option for VOT according to the actual regulation is the recorded video available to be sent for validation through the VOT platform.

The steps to be performed by the trained in VOT healthcare worker are:

1. Before the initiation of the anti-tuberculosis treatment the patient must be informed by the healthcare worker about the possibility to accomplish it using the video-assistance.

2. To create an account on the site www.vot.tuberculosis.md on E-Sanata platform on the page "Medici".

3. Before the initiation the VOT the healthcare worker should identify if the patient is eligible according to the including criteria established in the "Eligibility Checklist for Including in VOT".

4. If the patient accomplishes 14 days of 100% treatment compliance the healthcare worker will appreciate him eligible according to the evaluation form "Eligibility Checklist for Including in VOT".

5. After the patient's assessment through the "Eligibility Checklist for Including in VOT" the pulmonologist will decide to include or exclude the patient from VOT.

6. The VOT will be monitored and followed-up according to the recommendations of the National Clinical Protocol No 123 "Tuberculosis in adults" [7, 11].

The trained patient will receive the anti-tuberculosis drugs for 14-30 days confirmed by the signature in the TB01 register. Before the video recording the patient must prepare the drugs on a white paper visible in the webcam and a transparent glass with water in an illuminated place. After the onset of the video recording the patient has to pres-

ent himself and to enumerate the drugs prepared and the number of the pills. The patient should be placed in front of the webcam and to swallow the drugs one by one with the water prepared in the transparent glass. The patient has to open the mouth and to show the tongue after the swallowing of the pills. At the end of the administration the patient will stop the video recording and will send to validation. The healthcare worker must assess and validate the video recording from 1 to 3 points. The value 1 means the treatment was administrated and the dose was validated. The value 2 means that there is no certainty that the pills were swallowed. The value 3 means that the treatment was not administrated or the dose of a drug was not swallowed. The patient is responsible for the storing the anti-tuberculosis drugs in special conditions such as dry and dark place, far from children.

The regulation establishes excluding from VOT criteria or criteria which cannot allow the patient to be enrolled in VOT. The patient should be treated using the DOT instead of VOT if: a) he refuses to sign the informed consent for VOT; b) the therapeutic regimen includes injectable drugs; c) the patient has no available electronic device (personal computer, notebook, smartphone); d) the electronic device has no Internet connection or the connection has a low speed; d) the patient is unable to take independently the anti-tuberculosis drugs, e) the patient is diagnosed with mental disorders.

There are several criteria which ensure the transfer of the patient from VOT to DOT: a) the patient's requirement; b) the patient fails to transmit for validation the recorded video for at least 2 days; c) the patient does not answer the telephone; d) the hospitalisation in the emergency department; e) imprisonment; f) the patient left the Republic of Moldova for more than 1 month; g) the patient has a low tolerance of the anti-tuberculosis drugs or experiences adverse drug effects; h) the referral pulmonologist decides to stop the VOT.

Before the initiation of the VOT the healthcare worker must register the patient on the site www.vot.tuberculoza.md and complete the electronic file of the health state ("Dosarul electronic de sănătate") with the patient's data about diagnosis and treatment. Special duties are attributed to the nurse specialized in the case management, such as:

1. Supporting the patient in the creating the account on www.vot.tuberculoza.md,

2. To explain what means VOT and its principles;

3. To establish the number of the doses, the frequency of the administration, the modality of the video recording and sending for validation, the steps to be followed in different issues (technical problems, lack of electricity, low Internet speed).

4. To receive and to validate the video files and to confirm the administration of the anti-tuberculosis drugs according to the recommended regimens.

5. To complete the treatment register TB01 after the VOT video files validation.

6. To explain and ensure that the patient could recognize

the clinical signs of the adverse drug reactions and declare them.

However, the main barriers in the anti-tuberculosis treatment delivery are social, economic, educational and psychological issues [7, 9, 13, 14, 15]. According to the estimations the Republic of Moldova (RM) remains a high risk zone showing an inadequate concern regarding social determinants, that represent the risk factors for achieving high treatment outcome. Tuberculosis is concentrated in areas with high density of the population, poor environmental and sanitation conditions: poverty, food insecurity, low living conditions. The most affected groups, being assessed as hard-to-reach groups, are homeless, migrants, individuals living with HIV, drug injected users, alcohol abusers. Accumulated evidence suggested that not only the deficiencies in performing an effective antituberculosis treatment is a problem for the public health care system, but also the lack of intervention to resolve social and economic problems of tuberculosis patients. All factors that diminish the treatment success rate could be assessed as excluding criteria from the VOT. In this paper we evaluated tuberculosis patients diagnosed in Chisinau according to the social, demographic and economic characteristics for identifying target groups for VOT. So, the aim of the study was to assess the including and excluding criteria from VOT in a cohort group of tuberculosis patients from Chisinau city. The objectives were: 1. Assessment of the socioeconomic and epidemiological risk factors of patients with tuberculosis distributed in including and excluding for VOT criteria. 2. Evaluation of the case management, diagnosis, radiological patterns and microbiological characteristics of tuberculosis patients distributed in including and excluding for VOT criteria.

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 693 patients registered with tuberculosis in Chisinau in 2016. 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" and F090/e "Declaration and follow up of multidrug-resistant tuberculosis". The inclusion criteria were: age more than 18 years old, tuberculosis diagnosed by the specialist and signed informed consent. All patients with tuberculosis were investigated and treated according to the National Clinical Protocol 123 "Tuberculosis in Adults" [8]. Statistic analysis was carried out using the quantitative and qualitative research methods [16].

Results and discussion

According to the data obtained from the monitoring and follow-up of the cases during the period of 2016, were regis-

tered 693 tuberculosis cases among all residents of Chisinau, which included 581 (84%) patients from the urban sectors and 112 (16%) from rural communes. So, the VOT could be implemented mainly in patients from urban sectors where broadband Internet and electronic devices connected to specialize in VOT platform are more available than in rural regions. While distributing selected patients according to the sex, it was established the statistical predominance of men 474 (68%) compared with women 219 (31%), with a male/female rate 2.1/1 (fig 1).

Repartition of patients into age groups, according to the WHO recommendation identified that the largest subgroups were between 25 and 34 years old, and also between 35 and 44 years old, respectively 173 (25%) and 162 (23%) patients. Less numerous were patients from the subgroups 45-54 years old – 116 (17%), 55-64 years old – 100 (14%), 18-24 years old – 78 (11%) and older than 65 years – 64 (9%) patients. The total number of young patients who were between 18 and 44 years old constituted 413 (60%), which showed that VOT should target young patients (fig. 2).

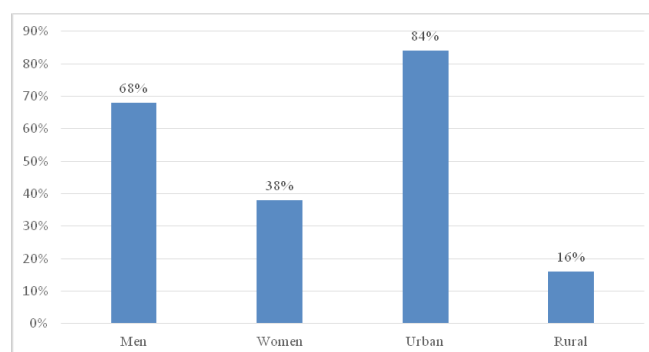


Fig. 1. Distribution of patients by sex and demographic residence (%).

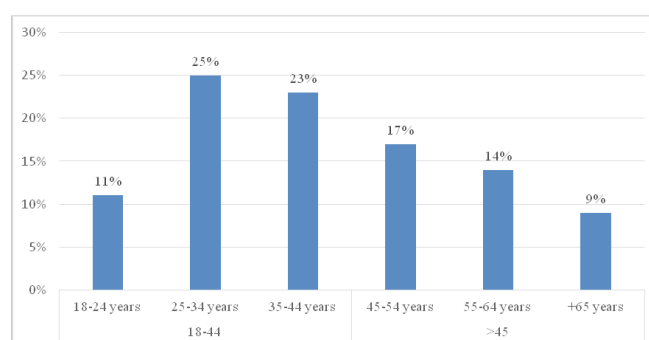


Fig. 2. Distribution of patients by age (%).

When distributing patients, according to the economic status, it was established that there were 158 (23%) employed persons, contributing to the health budget by paying taxes. So, according to the economic segregation of the patients, the financial capacity for supporting the VOT by acquiring electronic devices, such as personal computer, notebook, smartphone connected to a broadband Internet could have only one fourth. 82 (12%) patients were retired. Older than 65 years were 83 (12%) patients, being eligible for VOT, however, they are less likely to use electronic devices connected to a broadband Internet. 61 (9%) patients were

disabled, which have a high risk to be excluded due to the incapacity to take the pills independently. Unemployed patients made up the majority of the group – 377 (54%) cases, which can also be excluded due to the economical incapacity. There were 14 (2%) pupils and students. Most of them should be excluded due to the age criteria and the fact that they form infectious clusters made up preponderantly by children (fig. 3).

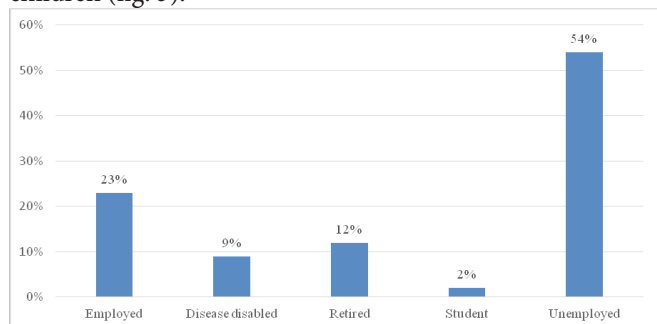


Fig. 3. Distribution of patients in economic subgroups (%).

Assessing the educational level, we established that most of the patients had secondary education – 291 (42%) cases. Technical vocational education had 181 (26%) and bachelor studies – 49 (7%) patients. So, according to the educational level, 521 (75%) could be eligible to perform VOT, considering their intellectual ability to use electronic devices (personal computer, notebook, smartphone). Lack of studies, only primary and incomplete secondary education were established in each fourth patient – 172 (25%) and could not be eligible for VOT (fig. 4).

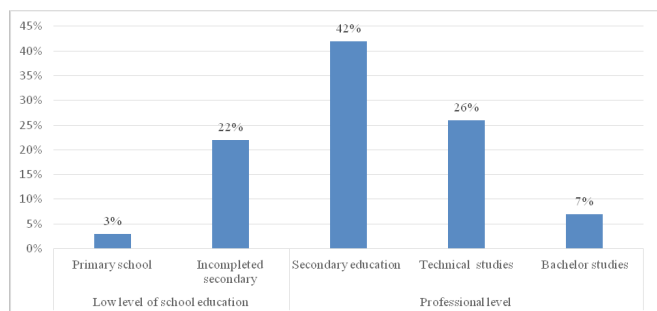


Fig. 4. Distribution according to the last graduate level (%).

The extreme poverty, caused by homelessness or lack of the demographic registration was identified in each fourth patient – 147 (21%). So, certainly every fourth patient will not be eligible for VOT. Migrants were defined persons who left the Republic of Moldova for more than 3 months during the year of the tuberculosis diagnosis. One of excluding criteria for VOT is the situation when the sick person leaves the Republic of Moldova for more than 1 month. The data confirmed that 70 (10%) patients are not eligible for VOT because they could be lost from follow-up due to their absence in the Republic of Moldova. The history of detention during the last year was identified in 38 (5%) cases. This type of patients is not eligible for VOT according to the regulation establishing the conditions for VOT (fig. 5).

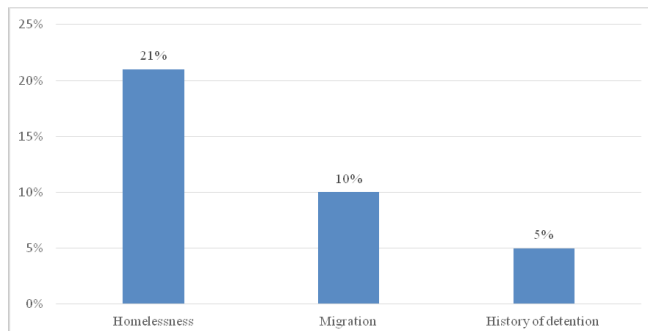


Fig. 5. Excluded from VOT patients.

Close infectious contact with a member of a family who was previously diagnosed with tuberculosis was established in 70 (11%) patients. The ambulatory treatment of the patients from infectious clusters makes the video-assistance a challenge. The VOT of patients with associated diseases raises big issues due to frequent severe adverse drug effects, incapacity to recognize them and to perform independently the treatment. Hospitalization in other departments than those specialized in the treatment of tuberculosis is a criteria which stops VOT and starts the DOT. There were 225 (32%) comorbid patients, which shows that each third case has a high risk to be transferred from VOT to DOT or to be illegible for video-assistance. Among comorbidities predominated HIV-infection – 62 (9%). The co-infection TB-HIV raises the rate of severe and disseminated forms with high risk of death. Those conditions make impossible the treatment in ambulatory conditions and make the patients not eligible for VOT. In a high proportion were diagnosed patients with chronic alcoholism – 59 (8.5%). Drug users were 10 (1.4%) patients. Psychiatric diseases were diagnosed in 12 (5%) patients. Numerous mental disorders were diagnosed in 81 (12%) and constitute certain exclusion criteria from the VOT. Diabetes mellitus was diagnosed in 11 (5%) cases. Due to a high rate of adverse drug effects diabetic patients have a high risk to be excluded from VOT. Immune suppressive conditions such as neoplastic diseases, treatment with corticosteroids and chronic renal failure were diagnosed in 15 (2%) cases (fig. 6). Due to frequent hospitalizations of immune suppressed patients they will be excluded from VOT.

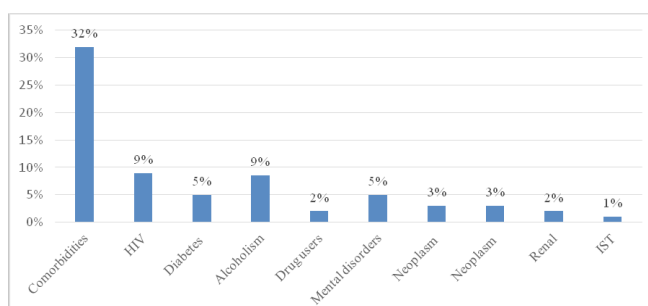


Fig. 6. Distribution according to the risk groups. Note: IST-immune suppressive treatment.

Studying case-management, it was identified that the general practitioners were involved in the detection of the most of the patients – 299 (43%) and the specialists detected 210 (30%) patients. Screening of the patients from high risk groups performed by the general practitioners detected 82 (12%) cases and through the investigation of the symptomatic cases were detected 217 (31%) cases. Pulmonologists detected 167 (24%) symptomatic patients and 43 (6%) from high risk groups. 43 patients (6%) came directly for hospitalization into a specialized institution and were hospitalized due to the personal requirement. Most of those patients were not admitted for the ambulatory treatment and could not be eligible for VOT.

While distributing patients, according to the registered case type, it was identified that the new cases, never treated cases, predominated – 425 (61%) compared with the relapses – 165 (24%) cases. New cases and relapses are eligible for VOT and their number constituted 590 (85%) with other excluding criteria will not be identified. Patients recovered after a previous “loss to follow-up” made up 69 (10%) and treatment failure – 31 (5%). The total number of the patients previously treated and not allowed for VOT due to the therapeutic incompliance was 100 (15%) cases (fig. 8).

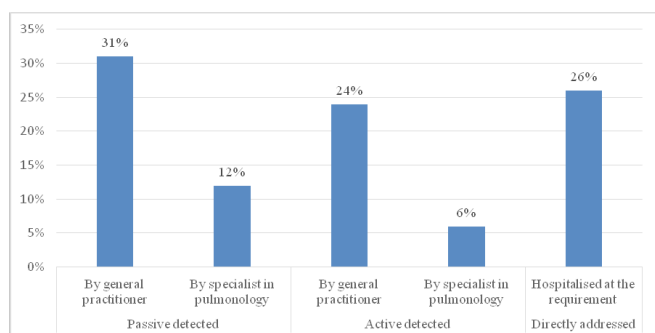


Fig. 7. Distribution according to the medical staff involved in the case detection.

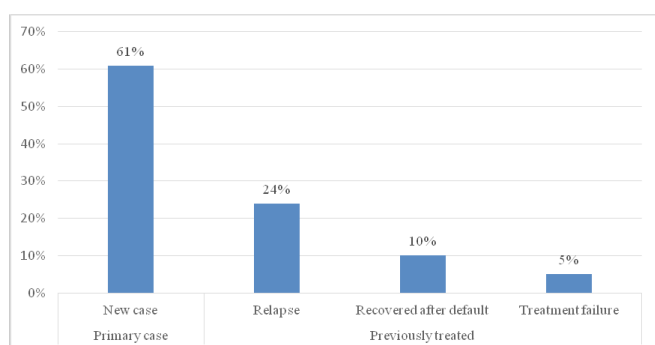


Fig. 8. Distribution according to the case type.

While identifying the clinical, radiological forms of tuberculosis, it was established that pulmonary forms were diagnosed in a higher proportion 656 (94%) cases. Extrapulmonary forms of tuberculosis were diagnosed in 34 (5.4%) patients. Generalised tuberculosis was diagnosed in 3 (0.4%) cases. Severe with extensive destructions pulmonary infiltrative tuberculosis – caseous pneumonia was

diagnosed in 41 (6%) cases. Disseminated tuberculosis and fibro-cavernous tuberculosis were diagnosed in 60 (8%) patients. Severe, disseminated, generalised and chronic forms of tuberculosis can not be treated in ambulatory conditions due to the risk of death and were diagnosed in at least 104 (15%) patients. Extended tuberculosis in both lungs was diagnosed in two thirds of patients – 484 (70%), which can raise difficulties for ambulatory treatment.

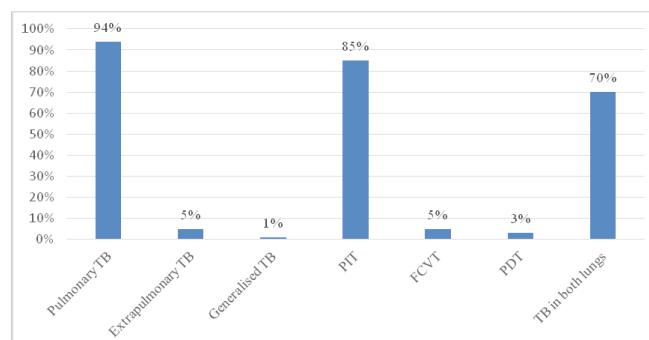


Fig. 9. Distribution according to the clinical radiological forms.

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

When assessing the laboratory features of the enrolled pulmonary tuberculosis patients, it was identified that one third of the entire sample was microscopic positive for acid-fast-bacilli, 200 (29%) patients. Microscopic positive patients are non-eligible for ambulatory treatment due to epidemiological threat, which they expose on the family and social community. A lower proportion of patients were identified to have positive bacteriological results at cultivation on solid Lowenstein-Jensen ether liquid MGIT BACTEC media: 144 (21%) patients. The molecular genetic assay was performed in all cases, but positive results were obtained in 278 (40%) cases, including rifampicine sensitive were 179 (26%) and resistant 99 (14%) cases. Microscopically positive for AFB and cultivation on the conventional media established Mycobacterium tuberculosis (MTB) in 104 (15%) being assessed as non-eligible for the ambulatory treatment. Patients with MDR-TB should be treated compulsory during the intensive phase, for 6 months, in the hospital due to the therapeutic regimen, which includes injectable drugs. So, 116 (17%) of patients were not allowed for VOT for the treatment in ambulatory conditions and VOT during the intensive phase (fig. 10).

The standard treatment for the new drug-susceptible tuberculosis in the RM has been used since 2000, lasts 6 months and consists of two phases with four first-line drugs: isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z) in the intensive phase and two first-line drugs: isoniazid and rifampicin in the continuation phase. For previously treated cases was used a regimen which lasts 8 months: 2 months with H, R, E, Z, S and 1 month with H, R, E, Z and 5 months with H, R and E. Patients with rifampicin-resistant or MDR-TB were treated with second-line drugs for 18 months or more divided in two phases The regimen com-

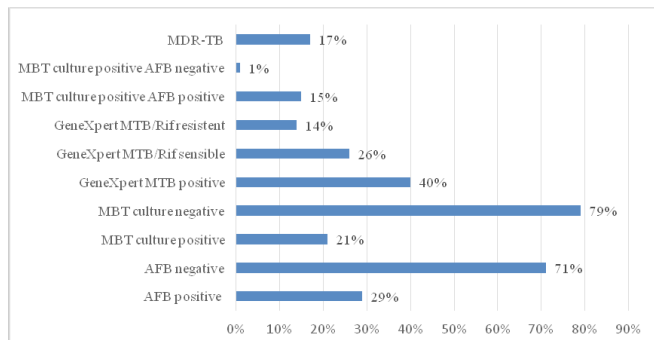


Fig. 10. Distribution according to the microbiological characteristics.

Note: MBT – Mycobacteria tuberculosis, AFB – acid fast bacilli, Rif – rifampicine.

position during the intensive phase lasts 6 months and included kanamycin (Km) or capreomycin (Cm), levofloxacin (Lfx), para-amino salicylic acid (PAS), ethionamide (Eto), cycloserine (Cs) and pyrazinamide (Z) and for continuation phases during 12-18 months of Lfx, PAS, Etho, Cs and Z. The standard treatment for drug susceptible tuberculosis with first-line anti-tuberculosis drugs was used for the treatment of 577 (83%) cases and for MDR-TB with second-line anti-TB drugs were treated 116 (17%), of which 7 (1%) patients with extensive drug resistance (XDR-TB) should be treated in specialized service.

All the patients were managed and treated with the standard treatment for tuberculosis. First-line anti-tuberculosis drugs were used in 577 (83%) patients from urban groups vs. 13 (11.7%) patients from the rural group. Successfully treated were 450 (65%) cases, failed the treatment – 9 (1%), were lost to follow-up – 51 (7%) cases and died 81 (12%) patients. 61 (9%) patients were still continuing the treatment and not available data was established in 41 (6%) cases, which are the candidates for lost to follow – up. So, the low therapeutic outcome, which included therapeutic failure, lost to follow-up and patients without available outcome was established in every third case – 182 (26%). Information is exposed in the figure 11.

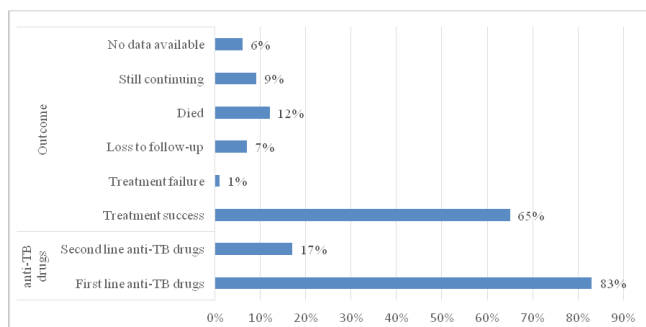


Fig. 11. Treatment outcome of tuberculosis patients.

An important research outcome represents the groups of patients in which the priority interventions for implementation of VOT are most suitable and the groups of patients which the excluding criteria will not allow to start the VOT.

It was established that the risk factors which contribute to the excluding from VOT or the transfer from VOT to DOT were linked with the sociovulnerability: unemployment, low level of the school education, homelessness or lack of the residence visa, harmful habits, migration, present imprisonment or history of imprisonment. Medical biological conditions which contribute to the excluding or lack of eligibility for VOT are: comorbidities, mental disorders and harmful habits with mental impairment. Epidemiological risk factors which arise challenges for the ambulatory treatment were close contact and clusters composed by children. Disease related characteristics which make non-eligible patients for ambulatory treatment are severe, extended, disseminated and chronic evaluated tuberculosis. Every tenth patient could not be allowed for VOT due to the enumerated conditions. One third of the groups were microscopic positive for AFB, which exclude the possibility for the ambulatory treatment and VOT as well. Second-line anti-tuberculosis treatment with injectable drugs in the intensive phase was used for the treatment of 17% of patients which make them non-eligible for the video-assistance. Generally, the treatment outcome did not achieve the 85% of success, as recommended by WHO [1]. The final results were diminished by a high proportion of patients, which had a low outcome due to therapeutic incompliance, severe forms of tuberculosis and comorbidities.

The relation between tuberculosis indices and treatment delivery was widely studied [1, 2]. Globally, the epidemic of tuberculosis is much higher in socially vulnerable subpopulations [1, 2]. It can be explained by the complexity of risk factors, which reflects the barriers for accessing the healthcare services and to achieve the treatment completion [3, 4, 5]. In the RM the specialised institutions offer a standard approach, which corresponds to the international recommendation and national regulations [10, 11]. The actual international recommendation imposes the ambulatory treatment of tuberculosis patients and implementation of VOT instead of DOT. Our research established increased rate of socially vulnerable patients (unemployed, homeless, migrants, patients with history of imprisonment) with low degree of school education which can reduce the effectiveness of the VOT implementation. No similar studies assessing the impact of social vulnerability on VOT were identified. Tuberculosis indices are linked with overcrowding, low level of sanitation and infectious clustering, which also endanger the treatment results; however, no studies assessed these conditions. Disease related characteristics, such as extensiveness, severity, duration of the tuberculosis evolution, drug resistance spectrum were not included as conditions with high impact on the treatment outcome in the international papers.

Conclusions

VOT represents a modality for the anti-tuberculosis treatment delivery in high income countries. VOT facilitates the interaction between the healthcare worker and the

patient, however, it does not replace the DOT in tuberculosis treatment.

The including criteria for video-observed treatment (VOT) in the RM are: 1) the patient has an available electronic device 2) the patient is residing in the RM. 3) the patient can administrate independently the anti-tuberculosis treatment.

The informal excluding criteria from VOT were deep social economic vulnerability, associated or not with migration, homelessness, detention and infectious clustering.

Associated diseases, which can reduce the VOT effectiveness are those which reduce the immune resistance (TB-HIV, diabetes mellitus, immune suppressive treatment, neoplastic diseases) and which exclude patients due to psychic impairment (psychiatric disorders, harmful habits such as chronic alcoholism and drug use).

Disease related characteristics, such as extensiveness, severity, duration of the tuberculosis evolution, positive microbiological state and multi-drug resistance are conditions which can exclude the ambulatory treatment and VOT as well.

The low treatment outcome during DOT shows indirectly that VOT will not improve the outcome due to the complexity of patient's risk factors.

VOT can be implemented in the management of tuberculosis patients in actual epidemiological state of the RM, if a complex of patients supporting measures is performed.

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