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Clinical presentation, risk factors and outcomes of tuberculosis in military recruits

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Abstract

Background: Tuberculosis represents the major threat for the health protection in the military forces**.** The aim of this retrospective and descriptive study was the evaluation of risk factors, clinical presentation and treatment outcomes of tuberculosis in military recruits.
Material and methods: 51 military recruits with tuberculosis diagnosed during 01.01.2010-31.12.2015 in Chisinau military quarters and managed in the Hospital of Pneumophtysiology were assessed.
Results: Most of military recruits aged 18-22, were residents of the rural localities, graduated incomplete general school or lyceum and were economically vulnerable. One half of the group consisted of active smokers and every tenth patient abused alcohol. Every fourth patient had tuberculosis in childhood and every tenth had family contact with a tuberculosis-affected person. Disease's insidious onset was established in one half of the group and the acute onset in every fourth patient. Every tenth patient was diagnosed with tuberculosis within the first 6 months after the enrollment. Only one half of the groups were symptomatic patients, who complained of cough, asthenia and loss of weight. Pulmonary infiltrative tuberculosis predominated among recruits. Extensive infiltrates and involvement of both lungs were identified in a lower proportion. The high rate of successful treatment outcome was endangered by the high rate of lost to follow-up patients, demonstrating poor evaluation and follow-up after the discharging from the hospital.
Conclusions: The epidemiological studies among military recruits are limited. The high rate of young, economically vulnerable men with risk factors demonstrates their priority for active screening. Treatment outcomes must be improved by the implementation of the adequate follow-up after hospital discharging.

Key words: tuberculosis, military, risk groups.

Introduction

Tuberculosis (TB) represents a major threat for health protection in the military forces worldwide [3]. The incidence of TB in the military forces is unknown. Military life consists in living, training, fighting in close quarters [14]. Military recruits are deliberately physically and mentally stressed during the training [1]. Continuous stress and associated harmful habits (e.g. tobacco smoking) could endanger the recruit's healthy state and contribute to the illness development [3]. In the United States (U.S.) military population's risk to develop tuberculosis was established eight times higher than in the general population [14]. Although, the estimated incidence of tuberculosis is unrecognized, the late detection and inadequate treatment put the members of the military forces at high risk [15]. World Health Organization (WHO) recommends stratifying the population according to the country specific profile for a better disease control [16]. The typical risk stratification is based on several criteria differentiated in low, mean and high impact risk factors, which should be used in the evaluation of each person before recruiting or each suspected case for tuberculosis [17]. The major risk factor identified in the (U.S.) military forces represents the recruits born in a high tuberculosis burden country or immigration from burden regions within 5 years from the arrival, and thus their health surveillance is important [15]. One of the most important factors associated with recrudescence of tuberculosis represents the latent tuberculosis infection (LTBI) assessed through the tuberculine skin testing (TST). The rate of positive TST was established two times higher in the American militaries than in the general population and higher in the American naval forces than in the army and air forces [14]. For improving the LTBI diagnosis there were recommended several commercially available interferon-gamma releasing assays (IGRAs): QuantiFERON-TB Gold and T-Spot TB test. However, the high rate of false-positive IGRAs results limits the usefulness in the LTBI and disease diagnosis [5, 20]. Other high risk factor for tuberculosis in military personnel is the HIV-infection or other immunocompromising conditions. According to the Moldovan national regulation the candidates for the incorporation in the military service should be investigated by clinical (physical examination) and laboratory methods during the health expertise performed by the medical military commission (MMC) [12]. The tuberculosis screening in military personnel is standardised and consists in medical history, physical examination and chest radiography [8, 12]. The capacity to perform military service is given by the excluding of well specified chronic diseases: HIV-infection, tuberculosis, diabetes, conditions requiring long-lasting immune suppressive treatment, cardiac diseases, arterial hypertension, renal diseases, central and peripheral nervous system diseases, psychiatric disorders, gastrointestinal disorders (chronic hepatitis, chronic malabsorption syndrome, chronic pancreatitis), low body weight and injection drug use [12]. Comparing the regulation papers, in the U.S. the militaries are investigated annually and are asked to answer some questions about: a) the face-to-face contact with someone sick with tuberculosis, b) place of birth and the presence of the family members outside the U.S., c) if the person had positive TST results or was previously treated for tubercu-

losis, d) if the persons worked or lived in a detainee facility, prison, homeless shelter, refugee camp or drug treatment facility, d) if the persons had an organ transplant, requires immunosuppressive medication (immune modulators or prednisone), had cancer of the head and neck, Hodgkin's disease, leukemia, end-stage renal disease, intestinal by-pass or gastrectomy [15]. A major attention is paid to the disease control among U.S. military health care workers. The U.S. health care workers caring the militaries are compulsory investigated if they: a) have the following symptoms: cough more than 2 weeks, fever more than 2 weeks, night sweats and weight loss; b) were working in an emergency room, inpatient hospital settings, mycobacteriology laboratory or other settings where tuberculosis patients are investigated and treated; c) had face-to-face contact with a sick person with tuberculosis and d) had written documentation of a prior positive TST, tuberculosis diagnosis and treatment [15].

Standard methods are used worldwide to detect tuberculosis in military population. Acid-fast bacilli sputum smear staining and culture on the conventional liquid or solid media are performed to each suspected person. This requires collecting at least two sputum samples in 8-24 hour intervals and one of which should be an early morning specimen [11]. However, the poor sensitivity (<30% in MD, <50% in the U.S.) of smear staining and delay of culture results (requires at least 120 days for providing a positive result) endanger the disease control in a military population [17]. Close contact between military personnel and their high receptivity to the infection make compulsory the performing the nucleic acid amplification testing in the frame of the case investigation. GeneXpert MTB/Rifampicine (Cepheid, California) represents a method extremely useful with a rapid capacity (2 hours) to detect *Mycobacterium* DNA and Rifampicin resistance mutations of the *rpoB* gene. It plays a decisive role in the treatment, allowing the onset of the treatment for multidrug-resistant infection before the results of the drug sensitivity test are available [7]. The U.S. Centre for Disease Control (CDC) recommends the use of IGRAs and TST for LTBI diagnosis. However, CDC requires that the results should be evaluated according to the patient's risk factors for infection and for developing the active disease. In the U.S. military settings several epidemics of TST conversions (prior negative than positive TST) were reported, but were attributed to the errors in the administration and reading of TST and cross-reactivity with non-tuberculosis mycobacteria [14].

The WHO's guideline for the treatment of tuberculosis is strongly recommended to be used in the settings caring sick military personnel [15]. The treatment must be performed as directly observed therapy (DOT) only in health care settings and the sick military person should be isolated until they have met the following criteria: 1) treatment with an effective regimen for at least 2 weeks; 2) two negative sputum smear at the end of the treatment's intensive phase; 3) clinical improvement during the treatment. The sick military personnel should be isolated in a negative pressured room and all infection control measures used [6, 15, 18].

The standard treatment for new patients presumed or known to have drug-susceptible tuberculosis is performed since 1993 and lasts 6 months [18]. It consists in a two phase regimen with four first-line drugs: isoniazid (H), rifampicine (R), ethambutol (E) and pyrazinamide (Z) used in the intensive phase and two first-line drugs: isoniazid and rifampicine used in the continuation phase. Previously sick patients have to be treated during 8 months with the same two phase regimen consisted of five first-line drugs: H, R, E, Z and streptomycine (S) in the intensive phase for 3 months followed by the continuation phase with H, R and E during the next 5 months. One of the emerging challenges in the treatment of tuberculosis in military forces is the epidemic extension of drug-resistance strains of *Mycobacterium.* Multidrug-resistant tuberculosis (MDR-TB) means the resistance to at least two of the most powerful first-line bactericidal drugs: isoniazid and rifampicine. An associated resistance to second-line drugs such as aminoglicozides (amikacyne, kanamycin and capreomycine) and any fluoroquinolone (levofloxacine or moxifloxacine) associated with multidrug-resistance was called extensively drug-resistant tuberculosis [22]. Military members are at a greater risk to become infected with drug-resistant strains circulating within the outbreaks from the quarters, but higher during the military service or overseas travel in the TB-endemic countries [10]. Usually patients identified with rifampicine-resistant strains or MDR-TB are treated with the standard combination of the second-line drugs for 18- 24 months (DOTS-Plus regimen) or different combinations (individualized regimens). The MDR-TB treatment success rate is low. It is associated with significant adverse events and poor treatment compliance [22]. In the Republic of Moldova the anti-tuberculosis treatment in military personnel is performed in specialized clinical departments during the intensive phase and in ambulatory at the home residence conditions in the continuous phase [4].

Reviewing exposed information it can be proved that tuberculosis, as a communicable, infectious disease is endangering the health protection in military forces all over the world. The rate of tuberculosis among millitary personnel is unknown, but the risk of infection and disease developing is much higher than in the general population. Reactivation of the latent tuberculous infection represents one of the most important factors for tuberculosis development in foreign born or immigrated persons from endemic countries; however, infection with drug-resistant strains is higher in outbreaks and during overseas military service. Case-management could be improved by performing cohort investigations, education of the military population about the clinical signs, detection procedures and using molecular genetic assays in all suspected cases. Treatment outcome could be improved by implementing an adequate patient's follow-up and evaluation.

The aim of the study was the assessment of the risk factors, clinical presentation and treatment outcome of tuberculosis in military recruits. The established objectives were: 1. assessment of social, economical and epidemiological risk

factors for tuberculosis in military recruits; 2. evaluation of the case-management, clinical and radiological aspects, microbiological results and treatment outcomes in military recruits.

Material and methods

According to the regulatory documents the military service of the Moldovan citizens in the National Armed Forces is performed in the frame of the National Army and Carabineer Troops during a limited period of time. The military service is performed compulsory by the citizens enlisted into the military service in term during 3 months (short contract), one year or more as specified time in the contract (variable contract).

It was performed a retrospective selective, descriptive study targeting risk factors, clinical aspects, laboratory results and treatment outcome of 51 patients – military recruits from the Chisinau Carabineer Troops diagnosed with tuberculosis in the period 01.01.2010-31.1201.2015. The inclusion criteria were: young age (18-24 years old) and signed informed consent. The study schedule included demographic, social, economical and epidemiological data, clinical features and laboratory results. All selected patients were diagnosed and managed according to the National Clinical Protocol 123 "Tuberculosis in adults". Statistic assessment was carried out using the quantitative and qualitative research methods. Statistical survey was performed using Microsoft Excel XP soft.

Results and discussion

All patients enrolled in the study were men. When distributing patients in age groups was established that the youngest group (18-20 years old) was the largest – 45 (88.23%) patients. Assessing the patients' residence was established that most of them were from the rural localities of the republic– 46 (90.19%) cases. No homeless patients were identified among selected cases. Distributing patients according to the educational level, it was determined that low level of school education (incomplete secondary school) was identified in every fourth case (13 (25.49%) patients), graduated lyceum one half of the group [25 (49.02%) patients], professional or superior studies had 9 (17.64%) patients.

Distributing patients according to the economical status it was established that the rate of employed patients before the recruitment was very low [4 (7.84%) patients]. History of migration in the last year was established in 2 (3.92%) patients. Every third patient [38 (74.51%) patients] was living under the standard of minimum consumption basket. Assessing the marital status it was identified that the majority of the patients [47 (92.16%) patients] were single-state persons due to their young age. Harmful social habits such as active tobacco smoking was established in one half of the group (25 (49,02%) patients) and alcohol abusers were 6 (11.76%) patients. No drug users were identified.

The proportion of patients with epidemiologic risk factors was low. Only 8 (15.68%) patients were from family infectious clusters, among them, 4 (7.84%) patients were in contact with drug-resistant tuberculosis family members and 3 (5.88%) patients were from clusters where a dead person due to tuberculosis was registered. Were previously treated for tuberculosis 12 (23.53%) patients and were diagnosed with post-tuberculosis lung changes 2 (3.92%) cases.

The rate of uninsured patients before recruitment was high [47 (92.16%) cases]. Diagnosis of tuberculosis was delayed for more than 60 days from the onset of the symptoms in 22 (43.14%) cases. Acute onset of tuberculosis was identified in 14 (27.45%) patients. 27 (52.97%) patients complained of the symptoms of the intoxication syndrome. Asthenia and loss of weight were identified in 27 (52.97%) patients, night sweats in 25 (49.02%) cases, fever in 4 (7.84%) cases, headache in 4 (7.84%) cases, loss of consciousness in 2 (3.92%) cases. Bronchopulmonary signs were established in 28 (54.91%) cases: cough for more than 3 weeks in 28 (45.91%) cases, thoracic pain in 5 (9.81%) cases, dysphagia in 2 (3.92%) cases and heamopthysis in 1 (1.96%) case. Associated diseases were diagnosed in 3 (5.88%) patients. No HIV infection, diabetes, immunosuppressive treatment and psychiatric disorders were identified.

Within the first 3 months after the enrollment 10 (19.61%) recruits developed tuberculosis and after the next three months – 16 (31.37%) recruits. During the first three months of the second semester 12 (23.53%) recruits developed active tuberculosis and three months later – 25.49%) patients (fig.).

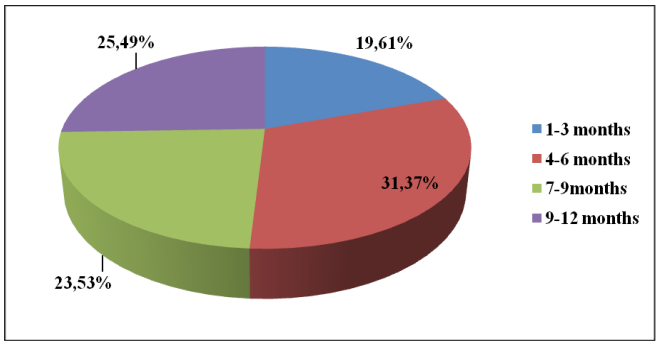

Fig. 1. Duration between enrollment and disease diagnosis (%).

The large spectrum antibiotherapy was initiated before tuberculosis treatment in 11 (21.57%) patients. When assessing the high risk factors, their hierarchy was established: patient's rural residence, unemployment before recruiting and harmful habits. The epidemiological risk factors such as household tuberculous contact and history of recent migration were identified in a low proportion, but it is important to emphasize the role of such factors in the infection and disease progression. Patients with comorbidities were in a limited number due to clear prohibiting conditions for the enrollment specified in the national regulatory documents (fig. 2).

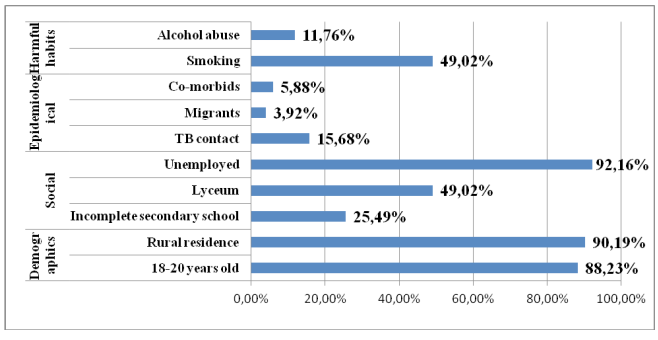

Fig. 2. Distribution of military recruits in risk groups (%).

Evaluating the laboratory features of the selected patients it was identified that 9 (17.64%) patients had positive results at the microscopic testing for acid-fast-bacilli and 8 (15.67%) had positive culture on solid Lowenstein-Jensen or liquid media (MGIT BACTEC). The first-line anti-tuberculosis drugs susceptibility was established in 6 (11.76%) cases, mono-resistance in 2 (3.92%) cases and multidrug-resistance in 1 (1.96%) case.

When assessing the radiological features of selected patients it was established that the patients with one affected lung outnumbered those with both involved lungs [38 (74.51%) vs. 13 (25.49%) cases, p<0,001]. Right superior lobe was affected in 21 (41.18%) cases and left superior lobe in 14 (27.45%) cases. Tuberculosis of the right lung was diagnosed more frequently than in the left lung: 29 (56.86%) patients compared to 22 (43.14) patients. Extensive infiltrates involving more than 3 segments were established in 12 (23.53%) cases and lung destruction was identified in 9 (17.64%) cases. The greatest part of the group was diagnosed with infiltrative form of pulmonary tuberculosis – 43 (84.31%) patients. Limited forms, recognized as nodular tuberculosis were diagnosed in 5 (9.81%) cases. It is important to note the absence of cases with severe forms, such as disseminated or fibro-cavernous tuberculosis. Secondary localizations were diagnosed in a low proportion: pleurisy – 3 (5.88%) patients and tuberculosis of the bronchus – 2 (3.92%) patients. Extrapulmonary form, such as tuberculosis of intrathoracic lymph nodes was diagnosed in 2 (3.92%) patients. Data were revealed in the figures 3 and 4.

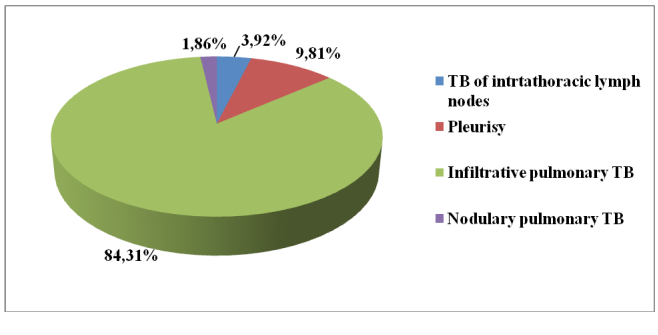

Fig. 3. Established clinical diagnosis in military recruits (%).

Comparing obtained results with previously published studies in the national journals it can be demonstrated that pulmonary tuberculosis was established in a similar rate as in the general population [9]. However, the rate of extensive infiltrates associating lung destruction and involvement of both lungs was much lower than in the general population.

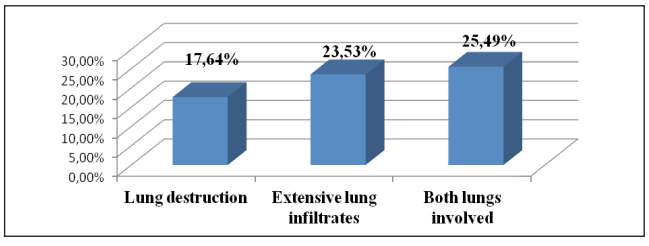

Fig. 4. Radiological features of pulmonary tuberculosis in military recruits (%).

As a consequence the proportion of positive microbiological results, which included smear microscopy and culture in the conventional media, was very low (fig. 4).

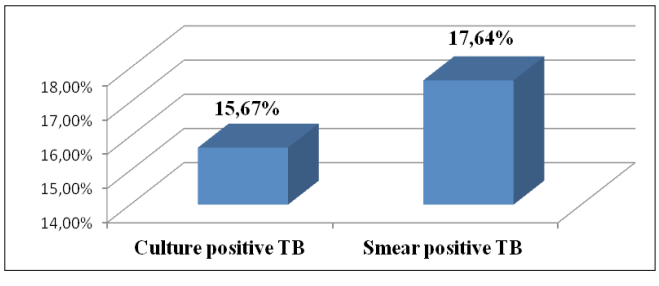

Fig. 5. The proportion of microbiological positive results.

All patients were treated during the intensive phase in the Chisinau Municipal Hospital of Pneumophtysiology. One half of the group [25 (49.02%) patients] was hospitalized for 2 months in the Municipal Hospital of Tuberculosis, 7 (13.72%) patients were hospitalized on average 3 months and 19 (37.25%) patients – more than 3 months. Treatment for MDR-TB was performed in 3 (5.88%) patients. Successfully treated according to the national policy criteria were 41 (80.39%) patients, that included 18 (35.29%) cured and 23 (45.10%) with completed treatment, 9 (17.64%) were lost to follow-up and 1 (1.96%) patient failed the treatment. The follow-up till 2016 of the selected group identified that 14 (27.46%) patients were included in retreatment regimens (fig. 3).

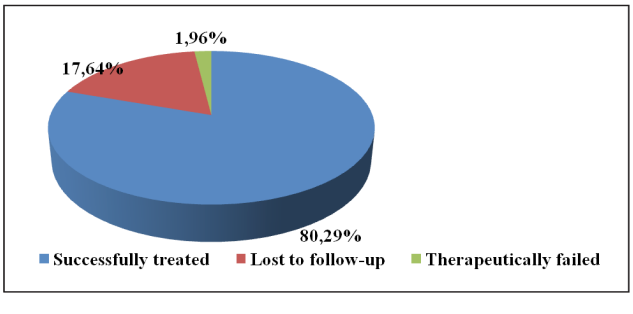

Fig. 6. Final treatment outcomes (%).

Conclusions

Moldovan citizens perform military service in the National Army or Carabineer Troops during different periods, specified in the contract.

In the Chisinau Municipal Clinical Hospital were diagnosed and treated 51 military recruits in the period 2010-2015.

All were men. Most of them were aged between 18-22 years old and were from rural localities of the republic. Every fourth had low level of the school degree and one half graduated the lyceum.

Before recruiting most of the patients had an economical vulnerable state, lacked the health insurance and were single-state persons. Obtained results demonstrated that military recruits had low accessibility to health care services due to their social vulnerability.

One half of the group comprised active smokers. Every fourth patient had tuberculosis in the childhood. Family contact with a sick person and the history of migration were established in a small number of cases.

Disease's insidious onset was established in one half of the group and acute onset in every fourth patient. Every tenth patient was diagnosed with tuberculosis within the first 6 months after the enrollment in the military service.

Cough, asthenia and loss of weight were established in all symptomatic cases, which constitute one half of the group.

Pulmonary forms of tuberculosis were the most prevalent, although extrapulmonary forms as pleurisy and tuberculosis of intrathoracic lymph nodes were diagnosed as well. Extensive infiltrates and involvement of both lungs were identified in a lower proportion than in the general population. No severe forms were diagnosed. Comorbidities were diagnosed in a limited number of cases at the same time with tuberculosis.

High rate of successfully treated militaries was endangered by a high rate of the lost to follow-up patients, demonstrating poor control after the discharging from the hospital and the military service.

The epidemiological data on tuberculosis among Moldovan military forces is unknown. The high rate of young, economically vulnerable men with risk factors demonstrates their priority for active screening.

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