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A study on demographic characteristics of drug resistant *Mycobacterium tuberculosis* isolates in Belarus

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ABSTRACT

Objective: A descriptive study of drug-resistance patterns by age group and among culture-positive pulmonary tuberculosis (TB) patients referred to the Research Institute for Pulmonology and Phthisiology of Belarus between January 2007 and January 2008.
Methods: Drug susceptibility tests were performed for first- and second-line anti-tuberculosis drugs. Patients were clustered into five resistance categories: mono-resistant (Mono); multi-drug resistant (MDR); all first-line drug resistance (MDR + ES); and extensively drug resistant (XDR). The patients were divided into primary and secondary and into six groups based on age in years (<15, 15–24, 25–44, 45–54, 55–65, and >65).
Results: An analysis was undertaken of information gathered from 934 TB patients, of whom 660 were men (70.67 ± 1.5%) and 274 were women (29.33 ± 1.5%) ($p < 0.001$). In the age group 25–65 years, men outnumbered women between 2.7 and 9.0 times higher. Cases of secondary TB totaled 414 (52.02 ± 1.77%), and primary cases totaled 382 (47.98 ± 1.77%) ($p > 0.05$); 756 of the patients were of working age, and 170 were of non-working age, of whom 570 men of working age (18–60 years) and 188 women of working age (18–55 years) participated. Males were significantly more likely to have MDR-TB than females. All cases with XDR-TB were older than 14 years old.
Conclusion: As Belarus is a high-burden MDR-TB country and treatment of drug-resistant TB is long and complicated, the findings of this study provided useful information to deliver effective community-based disease control measures and a proposed plane for the effective management of drug-resistant TB at the national level.

Introduction

Tuberculosis (TB) causes huge consequences in different societies. One out of every three individuals is infected with *Mycobacterium tuberculosis* (MTB), which means around 2 billion people total. Further, every second of every day a person is newly infected with MTB. There are more than 8 million new cases and 1.7 million deaths annually [1].

TB (all forms) accounts for 2.5% of the global burden of disease and is the most common cause of death in young women, killing more women than all causes of maternal mortality combined [1,2]; 75% of people with TB are within the

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economically productive age group of 15–54 [2,3]. Every year in Europe, 445,000 people become sick with TB and 8 people die because of TB every day; 75% of these deaths occur in Eastern Europe. Among the cases of those who registered for treatment and reported to the World Health Organization (WHO) in 2005, the ratio of men to women was 1:0.7.

Belarus is one of the 18 prior countries for TB control in the WHO European Region [4,5] and one of the 25 preceding multi-drug resistant-TB (MDR-TB) and extensively drug resistant-TB (XDR-TB) countries [5]. In 2007, the estimated total number of MDR-TB cases in Belarus was 707, and 579 MDR-TB patients were receiving treatment (including XDR). At the same time, 68 XDR-TB patients were under treatment [6].

Alternatives such as exposure, risk of infection, and progression from infection to disease are some epidemiological differences which will describe the reason for the higher rate of TB incidence in men. However, some researches reveal that women in their early reproductive ages may have higher rates of progression from infection to disease and case fatality as well [7].

In San Francisco, the male to female ratio was 2:1 (95% CI 1.9–2.3) in the year 2000. Analyses revealed differences in sex-specific rates after the age of 14 and the highest male/female ratios were seen in the American populations [8].

In almost all countries below the poverty line, twice as many men than women are reported with TB. Biological mechanisms might be one of the causes of this difference; however, socio-economic and cultural issues also influence the availability of health care, which leads to underreporting in females. Thus, gender needs to be considered as an effective factor in TB control programs [9].

Prevalent data and reporting from 29 surveys in 14 countries were used by Borgdorff [10]. Notification rates fluctuate dramatically in different countries, but the male/female ratio remains below 1 and declines owing to increasing age nearly in all countries. The female/male (F/M) prevalence ratio was less than 0.5 in surveys in South-East Asia and the Western Pacific Region, and was approximately 1 in the African Region.

MDR-TB is TB that is resistant to at least two of the best anti-TB drugs—Isoniazid (INH) and Rifampicin (RIF). These two drugs are known as first-line drugs and are prescribed in all TB patients' treatments [2,5]. MDR-TB has become a very serious problem in most countries of the Commonwealth of Independent States (CIS), more serious than in any other places in the world. This is mainly because present treatments are inappropriate, drug shortages occur intermittently and patients receiving treatments are being poorly monitored as well [11]. TB patients in parts of Eastern Europe and Central Asia are 10 times more likely to have MDR-TB than those in the rest of the world [12].

Another type of drug-resistant TB is called extensively drug resistant TB (XDR-TB), which is relatively rare. XDR-TB is defined as TB that is resistant to INH andRIF, along with resistance to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., Amikacin, Kanamycin, or Capreomycin). XDR-TB is resistant to both first- and second-line drugs; therefore, patients suffering from this kind of TB have no other choices except the much less effective treatment options. Individuals with HIV infection or any other conditions which may render the immune system weaker are more threatened by XDR-TB. These individuals are more likely to develop TB once they are infected, and they also have a higher risk of death once they develop TB [13]. According to reports from the WHO during 2000–2004, 20% and 2% of 17,690 TB isolates in the world were MDR and XDR, respectively [14].

The aim of this study was to determine high risk groups for MDR-TB and XDR-TB within different age and sex groups those TB patients in Belarus in a population study that included all cases of active culture-positive TB that have been referred to the National Reference Laboratory of the Research Institute for Pulmonology and Phthisiology from January 2007 to January 2008.

Material and methods

Study population and methods

The 934 culture-positive sputum samples referred to the National Reference Laboratory of the Research Institute for Pulmonology and Phthisiology in Minsk from January 2007 to January 2008 were analyzed; 40% of these samples were obtained from Minsk's patients (hospitalized in Minsk) and 60% from other regions (hospitalized in Minsk and other regions)—equal to patient's population in the regions.

Drug susceptibility testing

All 934 cases were subjected to a drug-resistance test. The anti-microbial drug susceptibility tests (DST) were performed using the WHO standard conventional proportional method.

The Preferable First Line Drugs were INH 1 mcg/ml, RIF 40 mcg/ml, Ethambutol (EMB) 2 mcg/ml, and Streptomycin (SM) 10 mcg/ml on slants with the H37Rv strain of MTB as the positive control. Furthermore, MDR isolates were tested for resistance to fluoroquinolones and three injectable drugs (Amikacin 8 mcg/ml, Kanamycin 30 mcg/ml, and Capreomycin 8 mcg/ml) for detection of XDR isolates.

Definitions

First- and second-line drugs are the two main categories of drugs used for TB treatment. Traditionally, there are five first-line drugs, including INH, RIF, Pyrazinamide (PZA), EMB and SM. Second-line drugs contain aminoglycosides, Kanamycin and Amikacin, the polypeptide Capreomycin, Phage antibiotic synergy (PAS), cycloserine, thioamides, ethionamide and prothionamide and several fluoroquinolones, such as ofloxacin, moxifloxacin, levofloxacin and gatifloxacin; SM has been reported as a second-line drug, though [1].

For drug resistance, the following terms were used as defined by the WHO [15]:

- MDR: multi-drug resistant tuberculosis (MDR-TB) is resistance to at least two of the best anti-TB drugs, INH and RIF.
- XDR: extensively drug resistant tuberculosis (XDR-TB) is resistance to: INH and RIF plus resistance to the best second-line medications: fluoroquinolones and at least one of three injectable drugs (i.e., Amikacin, Kanamycin, or Capreomycin).

- Susceptible: it means susceptibility to both INH andRIF.

In this study, the following terms were also used:

- Mono: it is resistant to at least INH or RIF.
- FLR: first-line drug-resistant isolates are MDR (resistant to INH and RIF), plus resistant to PZA, EMB, and SM.
- TMDR (Total MDR): in this study, as a clinical aspect based on clinical differences, MDR patients were divided into MDR and FLR. In some parts, the general term MDR was used as defined by the WHO. For this purpose, these two terms were combined and were named TMDR.
- Male/female ratio: male/female ratios were calculated for all groups, in terms of the total number of men to the total number of women in each group.
- Working age: all patients were divided into two groups: working age patients (18–60 for men and 18–55 for women) and non-working age patients (including men or women under 18, men over 60 and women over 55); *p*-values were used for evaluation of the significance of differences that have been found among the groups.
- Data analysis: the collected data were analyzed using Statistica and Microsoft Office Excel software programs. As a criterion, reliability differences indicators used the profile $p < 0.05$.

Results

During the research period, 934 pulmonary TB patients were studied, of which 274 (29.33 ± 1.5%) ($p < 0.001$) men in the age group 25–65 years outnumbered women between 2.7 and 9.0 times more (Table 1); 660 (70.66 ± 1.5%) of the TB cases were men.

In the age group <15–24, as well as in the age group over 65 years, the proportion of men and women were similar. In the remaining age groups, the proportion of men with TB was significantly higher than women. The total ratio of male TB patients among the female patients of all groups surveyed in 2007 was 2.4, which agrees with the WHO European Region. In the age group 45–54 the male to female ratio was the highest among patients with TMDR-TB.

Frequency of MTB isolates with different levels of resistance, depending on age and sex

Drug sensitivity of MTB of all 934 surveyed patients with TB in 2007 was studied by culture in the dilution of drugs in the growth medium.

From a clinical aspect, patients were divided into five groups based on levels of resistance of MTB to the primary anti-tuberculosis drugs. This idea was based on clinical differences over the course of the disease and resistance to anti-tuberculosis drugs. For example, to treat MDR-TB cases resistant to INH and RIF (but not to EMB, PZA and SM) and first-line-resistant TB (FLR-TB), cases were considered resistant to all first-line drugs.

Mono-resistance TB cases are treated separately from the drug-sensitive and MDR cases. Among patients with drug-resistant TB in different age groups, significant differences among men and women were noted. There were no differences by age group, when comparing male and female populations with XDR-TB ($p > 0.05$), MDR-TB ($p > 0.05$) and drug-sensitive TB ($p > 0.05$) (Table 2).

Drug susceptible group

This group is sensitive to INH, RIF and other drugs and is 26.5 ± 1.4% of all analyzed isolates; 32.26 ± 2.96% of them were isolated from female patients, and 67.74 ± 2.96% males ($p < 0.05$). This group includes the largest number of patients less than 15 years (16 people). In contrast to all other groups, among TB patients younger than 15 years, the number of girls (12.5 ± 3.69%) outnumbered boys (3.57 ± 1.43%) ($p < 0.05$). A similar trend was found in patients older than 65 years: women were 25 ± 4.84%, while men were 8.3 ± 2.1% ($p < 0.05$) (Table 2).

Mono-resistant group (Mono)

Patients suffering resistance to one of the major anti-tuberculosis drugs (INH or RIF) was 7.7 ± 0.87% of those surveyed, 69.4 ± 5.4% of them were men ($p < 0.05$). In this group, there were no girls under the age of 15 years (Table 2).

First-line resistant group (FLR-TB)

This group, which included 31.0 ± 1.51% of all surveyed consisted of patients infected with MDR-isolates (resistant to INH and RIF), which were also resistant to PZA, EMB and SM. The group with the FLR-TB treated 51.8% of patients with MDR-TB because they do not respond to treatment with INH, RIF and first-line drugs. The ratio of men and women in this group was 3.07; the difference in sex composition was observed in the range of 15–24 years (women 22.8 ± 4.6%, men 5.8 ± 1.6% ($p < 0.05$) (Table 2).

Multi-drug resistant group

MDR-isolates were resistant to both of the best anti-tuberculosis drugs: INH and RIF. Patients with MDR-TB accounted for 28.9 ± 1.5% of all patients. If, in accordance with the WHO requirements, patients with FLR-TB were added to this group,

Table 1 – A statistical characterization of the studied population of TB patients based on sex differentiation.

Sex	Number of men and women in age groups (number and %)						Total
	<15 (*n* = 28)	15–24 (*n* = 98)	25–44 (*n* = 400)	45–54 (*n* = 203)	55–65 (*n* = 125)	>65 (*n* = 80)	
Women	14 50.0 ± 5.3	47 47.9 ± 5.0	108 27.0 ± 2.2	34 16.7 ± 2.6	31 10.0 ± 2.7	40 50.0 ± 5.6	274 (29.3 ± 1.5)
Men	14 50.0 ± 5.3	51 52.1 ± 5.0	292 73.0 ± 2.2	169 83.3 ± 2.6	94 90.0 ± 2.7	40 50.0 ± 5.6	660 (70.66 ± 1.7)
P	>0.05	>0.05	<0.001	<0.001	<0.001	<0.05	934 (100%)

Table 2 – Frequency of MTB isolates from patients with different levels of drug resistance depending on age and sex.

Drug resistance group	Gender	Age ranges (year), as number(%)						Total as, number%
		<15	15–24	25–44	45–54	55–65	>65	
Susceptible	Women	10(12.5 ± 3.69)	6(7.5 ± 2.9)	27(33.7 ± 5.2)	9(11.25 ± 3.5)	8(10.0 ± 3.35)	20(25.0 ± 4.84)	80(32.26 ± 2.96)
	Men	6(3.57 ± 1.43)	15(8.9 ± 2.2)	55(32.7 ± 3.6)	44(26.2 ± 3.4)	34(20.2 ± 3.1)	14(8.3 ± 2.1)	168(67.74 ± 2.96)
	Total	16(6.45 ± 1.56)	21(8.4 ± 1.8)	82(33.0 ± 3.0)	53(21.3 ± 2.6)	42(16.9 ± 2.4)	34(13.7 ± 2.2)	248(26.5 ± 1.4)
Mono resistant (Mono)	Women	–	3(13.6 ± 7.3)	10(45.45 ± 10.6)	4(18.18 ± 8.2)	2(9.1 ± 6.1)	3(13.6 ± 7.3)	22(30.5 ± 5.4)
	Men	2(4.0 ± 2.7)	5(10 ± 4.24)	23(46.0 ± 7.0)	12(24 ± 6.0)	4(8 ± 3.8)	4(8 ± 3.8)	50(69.4 ± 5.4)
	Total	2(27 ± 1.90)	8(11.11 ± 3.7)	33(45.8 ± 5.8)	16(22.2 ± 4.9)	6(8.33 ± 3.2)	7(9.7 ± 3.4)	72(7.7 ± 0.87)
T MDR								
First-line resistant (FLR)		3(3.6 ± 2.0)	19(22.8 ± 4.6)	29(34.9 ± 5.2)	12(14.4 ± 3.8)	12(14.4 ± 3.8)	8(9.6 ± 3.2)	83(28.6 ± 2.6)	83(8.88%)
		2(0.96 ± 0.6)	12(5.8 ± 1.6)	101(48.7 ± 3.4)	53(25.6 ± 3.0)	29(10.4 ± 2.4)	10(4.8 ± 1.5)	207(71.3 ± 2.65)	207(22.16%)
		5(1.7 ± 0.75)	31(10.7 ± 1.8)	130(44.8 ± 2.9)	65(22.4 ± 2.4)	41(14.1 ± 2.0)	18(16.2 ± 2.3)	290(31.0 ± 1.51)	290(31.05%)
Multi-drug resistant (MDR)		1(1.35 ± 1.34)	17(22.9 ± 4.9)	34(45.9 ± 5.8)	7(9.4 ± 3.4)	8(10.8 ± 3.6)	7(9.4 ± 3.4)	74(27.4 ± 2.7)	74(7.93%)
		4(2.0 ± 1.0)	14(7.1 ± 1.8)	99(50.5 ± 3.5)	50(25.5 ± 3.1)	20(10.2 ± 2.16)	9(4.6 ± 1.5)	196(72.6 ± 2.7)	196(20.98%)
		5(1.85 ± 0.82)	31(11.5 ± 1.2)	133(49.2 ± 3.0)	57(21.1 ± 2.5)	28(10.3 ± 5.76)	16(5.9 ± 1.43)	270(28.9 ± 1.5)	270(28.9%)
Extensively drug resistant (XDR)	Women	–	2(13.3 ± 8.7)	8(53.3 ± 12.8)	2(13.3 ± 8.7)	1(6.6 ± 0.4)	2(13.3 ± 8.7)	15(27.78 ± 0.6)
	Men	–	5(12.8 ± 5.3)	14(35.9 ± 7.6)	10(25.6 ± 7.0)	7(17.9 ± 6.1)	3(7.7 ± 4.2)	39(72.22 ± 0.6)
	Total	–	7(12.9 ± 4.5)	22(40.7 ± 6.7)	12(22.2 ± 5.6)	8(14.8 ± 4.8)	5(9.2 ± 3.9)	54(5.7 ± 2.4)
	Sum	28 (2.99 ± 0.55)	98 (10.49 ± 1.0)	400 (42.8 ± 1.6)	203 (21.7 ± 1.3)	125 (13.4 ± 1.1)	80 (8.5 ± 0.9)	934 (100)

Table 3 – Treatment status of patients when admitted to hospital, based on resistance groups.

Status	Resistance groups					
	Susceptible	Mono	TMDR		XDR*	Total
			MDR*	FLR		
Secondary tuberculosis	184 (48.1 ± 2.55)	33 (8.6 ± 1.43)	63 (16.5 ± 1.89)	91 (23.8 ± 2.17)	11 (2.87 ± 0.85)	382 (100%)
Primary tuberculosis	36 (8.7 ± 1.38)	33 (7.9 ± 1.32)	202 (48.8 ± 2.45)	103 (24.8 ± 2.12)	40 (9.66 ± 1.45)	414 (100%)
Total	220 (27.6 ± 1.58)	66 (8.3 ± 0.97%)	265 (33.3 ± 1.6%)	194 (24.3 ± 1.5%)	51 (6.4 ± 0.86%)	796 (100%)

* $p < 0.05$.

the resulting aggregate, which can be designated as TMDR-TB will be 59.9 ± 1.6% of all patients enrolled in the study. In the age group 15–24 years, the proportion of women with MDR-TB was 22.9 ± 4.9%, while the proportion of men was 7.1 ± 1.8% ($p < 0,05$) (Table 2).

Extensively drug resistant group

XDR-TB is resistant to INH and RIF, as well as to any of the second choice of drugs: fluoroquinolones and at least one of three injectable drugs (i.e., Amikacin, Kanamycin and Capreomycin). During 2007, the lab was sent isolates from 54 patients (5.7 ± 2.4% of all surveyed) diagnosed with XDR-TB. Men accounted for 39 (4.1 ± 0.6%), and the women accounted for 15 (1.6 ± 0.4%) of them ($p < 0.05$); children in this group were not accounted for. The greatest number of patients was found in the age group 25–44 years (40.7 ± 6.7%) (Table 2).

Treatment status

From another aspect, all groups were divided into two categories based on treatment or non-treatment status when referred to hospital (see Table 3).

Patients with secondary TB totaled 414 (52.02 ± 1.77%), and patients with primary TB totaled-382 (47.98 ± 1.77%) ($p > 0.05$). Patients with primary TB were significantly more distinguished because MTB is sensitive to anti-tuberculosis drugs (48.1 ± 2.55%), while only 8.7 ± 1.38% of cases ($p < 0.05$) of patients with secondary TB were detected. The frequency of drug-resistant MTB in patients with secondary TB was 378 (47.48 ± 1.77%), which was significantly higher than in the group suffering from primary TB: 198 (24.8 ± 1.52%) ($p < 0.05$). It should be emphasized that a similar result was related to XDR patients ($p < 0.05$).

Characteristics of drug resistance in the working age group

The *p*-value was calculated for the evaluation of the significance of differences among age groups. In this way, all MDR patients were added to those with FLR. Subsequently, MDR patients in these sections include all patients that are resistant to all first-line drugs and ones that are resistant only to INH and RIF (as in TMDR). In Table 4, some groups with significant differences are shown.

Out of a total of 756 patients of working age, 570 (75.4 ± 1.56%) of them were men (working age 18–60 years) and 186 (24.6 ± 1.56%) were women (working age 18–55 years).

Study of some groups that show significant differences

Patients with MDR-TB and FLR were merged into one group renamed TMDR that included patients infected with strains resistant to all first-line drugs, and strains resistant only to INH and RIF. Men patients in mono-resistant, TMDR and XDR groups have a similar frequency ($p > 0.05$). In susceptible

Table 4 – Results of the comparison between the detection rate of MTB with different levels of resistance among patients and disabled working age.

Drug Resistance	Age	Sex	Patients, Number and%	P value
Susceptible	Non- working	Men	33 (46.4 ± 0.35%)	$p < 0.05$
		Women	38 (53.5 ± 0.35%)	
	Working	Men	127 (75.59 ± 3.3%)	$p < 0.05$
		Women	41 (24.4 ± 3.3%)	
Mono-resistant	Non- working	Men	6 (42,85 ± 13,2%)	$p > 0.05$
		Women	8 (57.15 ± 13,2%)	
	Working	Men	44 (70,96 ± 5.76%)	$p < 0.05$
		Women	18 (29 ± 5.76%)	
TMDR	Non- working	Men	39 (50 ± 5.66%)	$p > 0.05$
		Women	39(50 ± 5.66%)	
	Working	Men	364(75.5 ± 1.95%)	$p < 0.05$
		Women	118(24.48 ± 1.95%)	
XDR	Non- working	Men	4 (57.1 ± 18.7%)	$p > 0.05$
		Women	3 (42.8 ± 18.7%)	
	Working	Men	35 (76.0 ± 6.28%)	$p < 0.05$
		Women	11 (23.9 ± 6.28%)	

patients of working age, mono-resistance, TMDR and XDR were more prevalent in men ($p < 0.05$).

It should be noted that 560 (59.95 ± 1.6%) patients had MDR-TB and FLR-(TMDR), which is an isolated pathogen resistant to at least INH and RIF (51.78 ± 2.1% of all patients with TB TMDR-FLR-treated group). This means that approximately half of the TB patients at admission were not responding to therapy with INH, RIF or other first-line drugs, which greatly increases the importance of developing rapid and efficient methods for detection of resistant forms of the parasite.

Discussion

In this study, from a clinical aspect, the patients were divided into five groups based on resistance to principal anti-mycobacterium drugs. This idea was based on the clinical differences between, for example, an MDR case resistant to INH and RIF (but not to EMB, PZA, or SM) and an FLR case resistant to all first-line drugs. As recommended by the WHO, both of the FLR and MDR groups were treated as MDR. For this reason, these items were added. In this respect, mono-resistant cases differ from susceptible and MDR cases.

Out of 934 pulmonary TB patients, 660 (70.7%) were men. The gender differences were mainly seen in the age group 25–65; the largest differences were in the 25–44 age group, and the lowest differences were in the <15 and >65 age groups. The male/female ratio of above unity (>1) was the same in all groups except in the susceptible group (0.6 and 0.7 for <15 and >65, respectively).

The proportions of tuberculosis in ages <15 and >65 were 3% and 8.56%, respectively. The male/female ratio in these groups was equal. On the other hand, it was found that female patients in the susceptible group under age 15 and above age 65 were more than men in number. This situation was also seen in the 15–24 MDR age group, in contrast with all other groups. Interestingly, there was not a single patient <15 in the mono-resistant group (Mono).

Approximately 60% of all patients were MDR and FLR, at least to INH and RIF; 51.8% of all MDR patients were in the FLR group. It means that around half of the patients did not respond to INH and RIF or to the remaining choices of the first-line drugs, so more expensive and less effective drugs must be used.

After childhood, it was noted that the incidence of TB was consistently higher in males until after working age; 70% of cases occurred in males. The greatest difference in rates between the genders was in the 24–44 age groups. This observation provides compelling evidence of real sex differences rather than a bias in diagnosis and reporting, since this is a group where women are known to have greater health-seeking behavior.

Working age

In this study some paired groups were compared in working and non-working ages based on drug-resistant status. A total of 756 working age (18–60) patients were referred to this laboratory, including 570 males and 186 females.

There were no significant differences among susceptible women of working age (45 patients) and those with MDR (126 patients) ($p = 0.07$). This result was the same as the non-working age groups. That means women of working and non-working age in Belarus in 2007 were possibly equally at risk for MDR or a susceptible form of TB. For men, these results were the same. For example, there were no significant differences among men of working age with regard to susceptible forms of XDR or MonoTB ($p = 0.32$ and 0.07, respectively). Furthermore, no significant differences were detected among men in working age in MDR and XDR ($p = 0.7$), MDR and Mono ($p = 0.32$), etc.

A significant difference between susceptible men of working and non-working ages was found ($p = 0.00001$) (see Table 4). This result was also found for the other drug-resistant groups, like XDR and MDR ($p = 0001$ for both). There were significant differences among MDR men and women of working age ($p = 0.0001$) (see Table 4). This situation is the same as in the susceptible group ($p = 0.016$), but among XDR and Mono in the same groups (men and women of working age) there were no significant differences ($p = 0.28$ and 0.53, respectively). It was concluded that in Belarus in 2007, men rather than women were at higher risk for MDR or susceptible TB at working age (but not for XDR and mono forms of TB). On the other hand, there were no significant differences among men and women of non-working age with susceptible Mono resistance and XDR forms of TB ($p = 0.21$, 0.36 and 0.41, respectively).

Susceptible men of working age (127 patients) did not have significant differences with XDR patients (35 patients) ($p = 0.32$) and with Mono resistant patients (44 patients, $p = 0.1$). In other words, men of working age were possibly equally contracting any form of TB. Interestingly, a significant difference ($p = 0.016$) between groups of susceptible working men and susceptible working women was found. Based on the ages of patients, in the susceptible group, there was a higher risk of TB for men than for women.

This research searched for the existence of a correlation between “work and TB”. There were significant differences among susceptible non-working and working men and MDR and XDR non-working and working men ($p = 0.00001$, 0.0001 and 0.0001, respectively), but no correlation was found between women in such groups ($p = 0.07$, 0.22 and 0.1, respectively). It was concluded that tuberculosis in Belarus in 2007 was a disease that correlates to working status in men (but not for women). However, a significant difference was found between susceptible and MDR men based on age ($p = 0.01$). This means men in Belarus in 2007 were contracting MDR-TB rather than the susceptible form (based on ages of patients) ($p = 0.0001$). It was not seen between Mono in men ($p = 0.82$).

Male/female

TB patients are more commonly males than females in most countries. This difference is probably partly owing to the fact that women have less access to diagnostic facilities in some settings, but the broader pattern also reflects real epidemiological differences between men and women, both in exposure to infection and susceptibility to disease [10].

The results of this study show that the male/female ratio was >1 in almost all 15–65 age groups but differed in <15 and >65 groups. Overall, in 2007, the male/female ratio was 2.4 (see Table 4) for the referred patients. The male/female ratio for susceptible strains increased with increasing age, and its maximum was at 25–65, but it was unlike the ratio for XDR strains. The male/female ratio for XDR-TB was the highest for all age groups over 45.

Variety of social and economic roles and activities may cause differential exposure to bacilli responsible for TB. The rate of progression from infection to disease in TB-infected people is influenced by general health/nutritional condition. A number of studies suggest that responses to illness differ in women and men, and also barriers to early detection and treatment of TB vary (and are probably greater) more for women than for men. Gender differences also exist in rates of compliance with treatment. As children's health and welfare are in direct relation with that of their mothers, families and households can be influenced by women suffering from TB. Socio-economic and cultural factors may be important in two ways. First, they may play a role in determining overall gender differences in rates of infection and progression to disease, and secondly, they may lead to gender differentials in barriers to detection and successful treatment of TB [16].

Conclusion

TB is a matter of concern for all countries in Europe. The eastern part of the European Region and the former Soviet Union with higher notification rates of TB remains a priority for TB surveillance in the WHO European Region. The results illustrate the significance of national efforts to improve treatment and control of drug-resistant TB in Belarus by implementing evidence-based measures to regulate the monitoring of TB treatment and contact tracing. As Belarus is a high-burden MDR-TB country and treatment of drug-resistant TB is long and complicated, these findings suggest that the effective management of drug-resistant TB at the national level will positively influence national productivity. Further investigation is recommended via a representative survey of drug-resistant TB among all culture-positive TB patients notified in the country, with follow-up of their treatment outcomes.

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