Multidrug-Resistant Tuberculosis in Poland: Results of a Nationwide Survey, 1997 To 2012

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Abstract

The knowledge of the prevalence of drug resistant tuberculosis in the population is important information about the epidemiology of the disease in the country. In Poland, the incidences of drug-resistant tuberculosis have been monitored since the early years of chemotherapy. In the period from 1997 to 2012 were four prospective studies covering the whole country.

The aim of this study was to determine the prevalence of primary and acquired drug resistance of M. tuberculosis strains isolated from patients in Poland in 2012, compared with the results obtained in previous studies (1997-2008).

Material and methods: The material for the work was taken from 4781 tuberculosis patients excreting susceptible and drug resistant bacilli during the 12-months from 1st January to 31st December 2012. Data about patients were collected based on the results of routine diagnostic tests carried out in tuberculosis laboratories. Division by age group, verification and analysis of data was performed according to WHO recommendations. Drug susceptibility testing was performed on solid medium (L-J) by proportion method and liquid medium using the Bactec MGIT 960 system.

Results: In this study we were included 4136 patients with tuberculosis (86.9% new and 13.1% treated cases). Among 3596 studied untreated patients 157 (4.4%) excreting drug resistant bacilli. MDR-TB was found in 12 (0.6%) patients and bacilli resistant to 4 drugs in 7 patients (0.2%). Among previously treated patients 63 (11.7%) excreting drug resistant bacilli. MDR-TB was found in 24 patients (4.4%), bacilli resistant to 3 drugs SM+INH+RMP (11 patients – 2.0%) and 4 drugs SM+INH+RMP+EMB (6 patients – 1.1%).

Conclusions: Among untreated patients 157 (4.4%) excreting drug resistant bacilli, in previously treated patients 63 (11.7%). Excreting drug resistant bacilli MDR-TB was more often in previously treated (4.4%) than untreated patients (0.6%).

ABBREVIATIONS

WHO: World Health Organization; RMP: Rifampicin; INH: Isoniazid; SM: Streptomycin; EMB: Ethambutol; MDR-Tb: Multidrug Resistant; CRG: Central Tuberculosis Register; NRL: National Reference Laboratory; IUATLD: International Union Against Tuberculosis and Lung Disease

INTRODUCTION

In Poland, the incidence rate of tuberculosis slightly decreasing every year. In 2012, the incidence rate of tuberculosis (19.6) was lower than that for 2011 (22.2), similar to that for 2010 (19.7). However, despite the significant improvement of the epidemiological situation in Poland, the incidence rate of tuberculosis is slightly higher than Western European countries (eg. The incidence rate of tuberculosis in Germany is 5.8 / 100.00, France 8.8 / 100.00, Sweden 7.2 / 100,000) [1].

In Poland in 2012 to the Central Tuberculosis Register (CRG) has reported 7542 cases of tuberculosis, including 6665 patients with newly detected, among which in 4284 the diagnosis was confirmed bacteriologically. According to the reports sent to the CRG in clinics p/tuberculosis in 2012 were registered 108 patients excreting bacilli resistant to drugs. Of these patients, 35 patients had MDR tuberculosis, among them was 13-year-old girl [2]. Among the 48 patients were registered foreigners, which accounted for 0.6% of all cases.

Factors affecting the unfavorable epidemiological situation of tuberculosis in the world are the existence of strains resistant to antimycobacterial drugs, the co-existence of HIV and M. tuberculosis complex, insufficient detection of the disease.

After the introduction in the second half of the twentieth century for the treatment of tuberculosis, TB drugs, many countries showed a decrease in incidence rates and mortality due to tuberculosis [3,4]. In the 80s, with the advent of the HIV virus was observed deterioration of the epidemiological situation.
of tuberculosis and the rapid growth of mycobacterial disease caused by MDR resistance [5,6]. The first global report on DRS was released in 1997. This report showed that drug resistance was ubiquitous.

Drug-resistance tuberculosis, and particularly multidrug-resistance tuberculosis is an increasing health problem and serious challenge to Tb control programmes. Information concerning susceptibility patterns of Mycobacterium tuberculosis isolates to tuberculosis drugs is an important aspect of tuberculosis control and surveillance. Analysis of local rates of tuberculosis drug resistance is helpful in the detection and monitoring of the predominance of MDR strains, indicating the quality of TB control in a country. Knowledge of the prevalence of primary drug resistance guides the selection of drugs used in initial treatment of tuberculosis.

The aim of the study was to report on the prevalence and patterns of antimycobacterial drug resistance among M. tuberculosis isolated in 2012 from new cases of tuberculosis (primary resistance) and from previously treated cases (acquired resistance) and compare its results to the results of the survey carried out 1997-2008 year.

MATERIALS AND METHODS

Patients isolates and study location

The M. tuberculosis strains analyzed in this study were collected from the patients whose specimens were positive in culture during 12-month period from January 2012 to December 2012. As in previous surveillance programmes the study was based on collaboration with all regional TB laboratories with National Reference Laboratory (NRL) in Warsaw. The detailed questionnaires consisted of two parts: the first included information about patients such as age, sex, place of residence, nationality, HIV status, past medical history of tuberculosis and treatment with antituberculosis drugs. The second part of questionnaire passed information about the type of specimen, status of microscopy examinations, morphology of the strains, time, and abundance of growth, results of identification and drug resistance. The strains from all TB patients participating in programme were collected in lyophilized form and were frozen at -75°C.

Quality control programmes

All TB strains were sent to NRL and declared as a resistant and 10 % of sensitive strains were restested to verify the pattern of drug resistance. In case of any discrepancies, the results of drug resistant test achieved in NRL were considered as corrected.

Definition of drug resistance

Primary resistance was defined as the presence of resistance to one or more antituberculosis drugs in strains obtained from patients who had never received treatment or less than 1 month after the beginning of treatment. Acquired resistance was defined as resistance to one or more antituberculosis drugs in strains recovered from patients who had received it at least 1 month prior to anti-tuberculosis treatment. Whereas multi-drug resistance was defined as resistance to at least INH and RMP, the two most potent drugs and the mainstay of antituberculosis treatment.

RESULTS AND DISCUSSION

Patient demography

The NRL in Warsaw received questionnaires for 4190 patients; 54 (1, 3%) were excluded from the survey because of a lack of full medical information, contaminated cultures or because mycobacterial other than tuberculosis strains were isolated. The study thus included 4136 tuberculosis patients with M. tuberculosis cultures isolated. No patient was identified as HIV positive. Among these 4136 Tbc cases 2951 (71,3%) were males and 1185 (28,7%) were females giving a sex ratio 2,5:1. The majority of the patients (68% of males and 66% of females) were over 45 years of age. Near 35% woman were over 65 with the oldest female 103 years old. Fifteen children (0-14 years) 5 boys and 10 girls were included in the study. Thirty individuals were foreign born patients. Concerning treatment, 3596 (86, 9%) patients had not received any previous treatment (new tuberculosis cases), while 540 (13, 1%) patients had received treatment (previously treated tuberculosis cases).

New cases of tuberculosis (n= 3596): The study covered 3359 cases (93, 4%) of pulmonary tuberculosis and 237 cases (6, 6%) extrapulmonary tuberculosis. Of the 3596 new tuberculosis cases, 3429 (95, 6%) excreted bacilli susceptible to all four drugs, while 157 patients (4, 4%) had strain resistant to one or more drugs. The most frequent was resistance to one drug 112 cases (3, 1%) and to two drugs 29 cases (0, 8%). In the group of monoresistance strains resistance to INH was found in 72 (2, 0%) cases, to SM in 38 (1, 1%) cases, to RMP in 2 (0, 06%) of cases, none was resistant to EMB. Twenty patients (0, 6%) were infected with MDR strains with the most frequent patterns, resistant to SM+INH+RMP in 7 (0, 2%) patients and resistant to four drugs in 7 (0, 2%) cases. Five patients (0, 1%) were resistant to INH+RMP, and one was resistant to INH+RMP+EMB. Among other patterns, the most common pattern of resistance to INH+SM was found in 22 cases (0, 6%). Of the 3359 pulmonary tuberculosis patients studies, 3211 (95, 6%) excreted bacilli susceptible to all four drugs, while 148 patients (4, 4%) had strain resistant to one or more drugs. The most frequent was resistance to one drug 106 cases (3, 2%) and to two drugs 27 cases (0, 8%). In the group of monoresistance strains resistance to INH was found in 67 (2, 0%) cases, to SM in 37 (1, 1%) cases, to RMP in 2 (0, 06%) of cases, none was resistant to EMB. Eighteen patients (0, 5%) were infected with MDR strains with the most frequent patterns, resistant to four drugs in 7 (0, 2%) patients and resistant to SM+INH+RMP in 6 (0, 2%) cases. Five patients (0, 1%) were resistant to INH+RMP. Among other patterns, the most common pattern of resistance to INH+SM was found in 20 cases (0, 6%). Of the 237 extrapulmonary tuberculosis patients studies, 228 (96, 2%) excreted bacilli susceptible to all four drugs, while 9 patients (3, 0%) had strain resistant to one or more drugs. The most frequent was resistance to one drug 6 cases (2, 5%) and to two drugs 2 cases (0, 8%). In the group of monoresistance strains resistance to INH was found in 5 (2, 1%) cases, to SM in 1 (0, 4%) cases, none were resistant to EMB or RMP. One patient (0, 4%) was infected with MDR strains with the most frequent pattern...
Previously treated cases (n=540): The study covered 529 cases (98, 0%) of pulmonary tuberculosis and 11 cases (2, 0%) extrapulmonary tuberculosis. In total 63 (11, 7%) of the 540 cases were resistant to one or more drugs. Thirty one patients (5, 7%) excreted strains resistant to one drug, fourteen (2, 6%) excreted strains resistant to two drugs; 12 patients (2, 2%) to three drugs and six patients (1, 1%) excreted strains resistant to four drugs. Among the monoresistant strains, 19 patients were found resistant to INH (3, 5%), 10 (1, 9%) to SM and 2 (0, 4%) to RMP and none was resistant to EMB. Twenty four (4, 4%) patients were infected by MDR strains, 11 (2, 0%) of who were resistant to SM+INH+RMP, 6 (1, 1%) had resistance to all four drugs, 6 patients (1, 1%) had the strains resistant to two drugs: INH+RMP and one patients (0, 2%) had the strain resistant to INH+RMP+EMB. Among other patterns resistance to INH+SM was found in 8 (1, 5%) patients.

Of the 529 pulmonary tuberculosis patients studies, 467 (88, 3%) excreted bacilli susceptible to all four drugs, while 62 patients (11, 7%) had strain resistant to one or more others. The most frequent was resistance to one drug 31 cases (5, 9%) and to two drugs 14 cases (2, 6%). In the group of monoresistant strains resistance to INH was found in 19 (3, 6%) cases, to SM in 10 (1, 9%) cases, to RMP in 2 (0, 4%) of cases, none was resistant to EMB. Twenty three patients (4, 4%) were infected with MDR strains, 11 (2, 0%) of who were resistant to SM+INH+RMP, 6 (1, 1%) had resistance to all four drugs, 6 patients (1, 1%) had the strains resistant to two drugs: INH+RMP and one patients (0, 2%) had the strain resistant to INH+RMP+EMB. Among other patterns resistance to INH+SM was found in 8 cases (1, 5%).

Of the 11 extrapulmonary tuberculosis patients studies, 10 (90, 9%) excreted bacilli susceptible to all four drugs, while 1 patient (9, 1%) had strain resistant to SM+INH+RMP.

Comparison of the results of drug resistance of 2012 with the results obtained in 1997-2008: Acquired drug resistance occurred more often than primary one in all five research editions. Also, patients excreting MDR resistant strain were more likely to remain sources of infection longer than those with drug-susceptible organisms.

CONCLUSION

Drug resistant tuberculosis including MDR are an actual occurrence in Poland both in treated and untreated patients. Acquired drug resistance occurred more often than primary one in all five research editions. Preventing drug resistance type in both groups of patients was single-drug resistance to INH while among MDR strains it was triple-drug resistance RMP+INH+SM. Multidrug resistance occurred more often in previously treated patients (6,8%) than in new cases (0,6%).

Table 1: Drug-resistant tuberculosis in Poland in 2012; comparison with the 1997-2008 survey.

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<tbody>
<tr>
<td>Number of patients</td>
<td>2976</td>
<td>994</td>
<td>3037</td>
<td>668</td>
<td>2716</td>
<td>552</td>
</tr>
<tr>
<td>Any resistance %</td>
<td>106/3,6</td>
<td>169/17,0</td>
<td>116/11,6</td>
<td>111/16,6</td>
<td>152/5,6</td>
<td>94/18,0</td>
</tr>
<tr>
<td>Total MDR %</td>
<td>18/0,6</td>
<td>70/7,0</td>
<td>35/1,15</td>
<td>57/8,5</td>
<td>8/0,3</td>
<td>43/7,8</td>
</tr>
<tr>
<td>Resistant to 4 drugs</td>
<td>0/0,0</td>
<td>15/0,5</td>
<td>14/1,4</td>
<td>14/2,1</td>
<td>2/0,1</td>
<td>7/1,3</td>
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REFERENCES