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Drug-resistant tuberculosis in Naples, 2008-2013

Annalisa Del Giudice[1], Alessandro Mustazzolu[2], Angelo Iacobino[2], Rossella Perna[1], Riccardo Smeraglia[1], Rachele Marino[2], Lanfranco Fattorini[2] and Giulia Santoro[1]

[1]*Laboratorio di Microbiologia e Virologia, Ospedali dei Colli, Naples, Italy*
[2]*Dipartimento di Malattie Infettive, Parassitarie e Immunomediate, Istituto Superiore di Sanità, Rome, Italy*

Abstract

Background. Drug-resistant tuberculosis (TB) is a serious threat in industrialized countries, but information from Southern Italy is lacking. Here, we present the results of a retrospective study of TB cases diagnosed in 2008-2013 in Naples, the largest city in Southern Italy.

Methods. Six hundred ninety *Mycobacterium tuberculosis* strains were isolated at the Ospedali dei Colli of Naples, and resistance to first-line and second-line drugs was determined.

Results. Multidrug-resistant (MDR) TB increased from 2008 to 2013, with 77.4% of strains isolated from migrants from 41 countries. Overall, 4.5% of strains were MDR: Italian-born persons, 2.2%; Romania, 7.5%; Former Soviet Union countries (Ukraine, Russia, Armenia, Georgia), 22.4%; all other foreign countries, 2.0%. Resistance of MDR strains to second-line drugs was high against kanamycin, ofloxacin, capreomycin.

Conclusions. MDR-TB in Naples increased in 2008-13 and was observed predominantly in migrants, indicating the need to intensify diagnosis and treatment of these populations in this town.

Key words

- tuberculosis
- *Mycobacterium tuberculosis*
- drug resistance
- migrants
- Naples
- Italy

INTRODUCTION

Tuberculosis (TB) still remains a major infectious disease worldwide. In recent years, TB caused by multidrug-resistant (MDR) *Mycobacterium tuberculosis* strains (*i.e.* resistant to at least isoniazid, H, and rifampin, R) and extensively drug-resistant (XDR) strains (*i.e.* MDR strains resistant to any fluoroquinolone and to at least one injectable drug: kanamycin, KM; capreomycin, CM; amikacin, AK) is becoming a public health concern in all industrialized countries due to increasing migration from regions where TB is endemic [1]. Fifteen of the 27 high MDR-TB burden countries worldwide are in the European Region [2]. Population mobility is a main factor in globalization of several drug-resistant organisms and plays an important role in TB epidemiology in the EU/EEA [3]. The highest proportions of MDR-TB cases and the most severe drug-resistance patterns were observed in the countries of the Former Soviet Union (FSU). From 2008-2014, 2.6% of a total of *M. tuberculosis* strains in Italy were isolated from patients whose country of birth was in the FSU [4, 5].

In our country, the number of reported TB cases decreased from 4246 in 1990 to 3153 in 2013, corresponding to 5.3 cases per 100 000 population, but the proportion of notifications from people born abroad consistently increased in the last decades from 22% in 1999 to 46% in 2008 and 63% in 2013 [6, 7]. In 2008, almost two-thirds of TB cases in foreigners occurred in Northern Italy [8]. Less information is available from Southern Italy [9], with lower data for this part of the country likely due to under-notification [10]. Only one study reported the TB incidence in 1996-2000 for migrants living in Naples, the largest city in Southern Italy and county seat of the region of Campania [10]. In 2008, the incidence of TB in Italian-born (IB) and foreign-born (FB) persons in Campania was about 2 and 42 cases per 100 000 people, respectively [7]. In 2013, 989 111 people lived within the Neapolitan administrative limits [11] and the metropolitan area had a population of more than 3 million inhabitants.

The aim of the present study was to perform a retrospective investigation of microbiologically-confirmed TB cases diagnosed in 2008-2013 in a laboratory covering a part of the metropolitan area of Naples, to provide updated information on drug-resistance proportions and drug-resistance profiles of *M. tuberculosis* strains circulating among IB and FB patients.

MATERIALS AND METHODS

The study was conducted at the Laboratory of Microbiology and Virology of the Ospedali dei Colli, Naples. The Ospedali dei Colli is a consortium of three public

Address for correspondence: Giulia Santoro, Laboratorio di Microbiologia e Virologia, Ospedali dei Colli, Via L. Bianchi 5, 80131 Naples, Italy. E-mail: giulia_santoro@hotmail.com.

hospitals (Monaldi, Cotugno and CTO) with 14 beds for TB patients in the Cotugno hospital. Demographic data of patients were obtained from medical records. Any case with a positive culture for *M. tuberculosis* was considered microbiologically-confirmed TB. Specimens collected from patients admitted to the hospital were routinely examined from 1 January 2008 to 31 December 2013 by smear microscopy, and cultured using solid media (Löwenstein-Jensen, Becton Dickinson, Sparks, MD, USA) and liquid media (MGIT 960; Becton Dickinson), according to known guidelines [12]. Identification of *M. tuberculosis* strains was performed by the GenoType *Mycobacterium* CM molecular genetic assay (Hain Lifescience, Nehren, Germany) and/or the BD MGIT TBc Identification assay (Becton Dickinson). Drug susceptibility testing (DST) to first-line drugs (FLD) streptomycin (S), H, R, ethambutol (E), and second-line drugs (SLD) KM, AK, CM, ofloxacin (OFL) was performed by the MGIT 960 system (Beckton Dickinson), using the following critical concentrations: 1.0, 0.1, 1.0, 5.0, 2.5, 1.0, 2.5, 2.0 µg/ml, respectively [13]. In case of *M. tuberculosis* strains identified as MDR or XDR by the MGIT 960 system, resistance to H and R was confirmed by the GenoType MTBDR*plus* assay (Hain) and resistance to aminoglycosides/cyclic peptides, fluoroquinolones and E by the MTBDR*sl* assay (Hain).

The Laboratory of Microbiology and Virology participated in the drug susceptibility proficiency testing of the Istituto Superiore di Sanità, Rome [14] and ≥ 90% agreement for FLD and SLD was achieved in 2010 and 2013.

RESULTS

In the period 2008-2013, 690 *M. tuberculosis* strains (115.0 ± 9.5 per year) were isolated from primary cultures from 690 different patients (76.4% of new cases and 23.6% of previously treated cases) and characterized for resistance to FLD and SLD.

The age of patients was as follows: mean, 41.9 ± 17.3 years; median, 37 years; range, 1-89 years. In the six years of the study, 482 TB cases occurred in males (69.9 ± 2.3%: 262 FB and 220 IB persons) and 208 in females (30.1 ± 2.3%: 100 FB and 108 IB persons) *(Figure 1A)*. Three hundred and twenty-two cases (46.7%) were diagnosed in IB persons and 368 (53.3%) in FB persons (Europe: 27.4%, Africa: 16.1%; Asia: 7.6%; the Americas: 2.2%). The top-five countries contributing to the FB group were Romania (32.7%), Ukraine (11.2%), Morocco (10.3%), Nigeria (4.7%), Pakistan (4.2%). The FB persons were younger than IB persons (33.7 ± 10.6 *versus* 49.5 ± 19.7 years; $P < 0.001$, Student's *t* test) and arrived from 41 countries. Tuberculosis in children (≤ 5 years) occurred in 9 cases including 6 in IB persons (1, 1, 1, 2, 5, 5 years) and 3 in children (2, 5, 5 years) born in Italy from FB parents. The latter cases were included in the FB group due to the close contacts with their parents.

As to drug resistance, out of 690 strains tested 144 (66.9% of new cases and 33.1% of previously treated cases) showed resistance to FLD *(Table 1)*. While the rate of MDR strains isolated in 2008-2013 *(Figure 1B)* from IB patients remained stable at around 1% of the cases, in the same period the rate of MDR strains isolated from FB patients increased from about 2% to 4%. To evaluate drug-resistance proportions and profiles, we stratified data of *M. tuberculosis* strains isolated from FB patients in three groups including Romania (the largest group from a single country), FSU countries (the highest MDR-TB group) and all other foreign countries, in comparison with data of IB strains *(Table 1)*. The proportion of strains resistant to FLD isolated from patients born in the FSU countries (44.9%, 22 strains) was higher than that observed in IB persons and in the other two FB groups. The FSU countries of origin of the 22 FLD resistant strains were: Ukraine, 15; Russia, 4; Georgia, 2; Armenia, 1. In the FSU-group the rates of resistance to S (32.7%) and H (36.7%) were higher

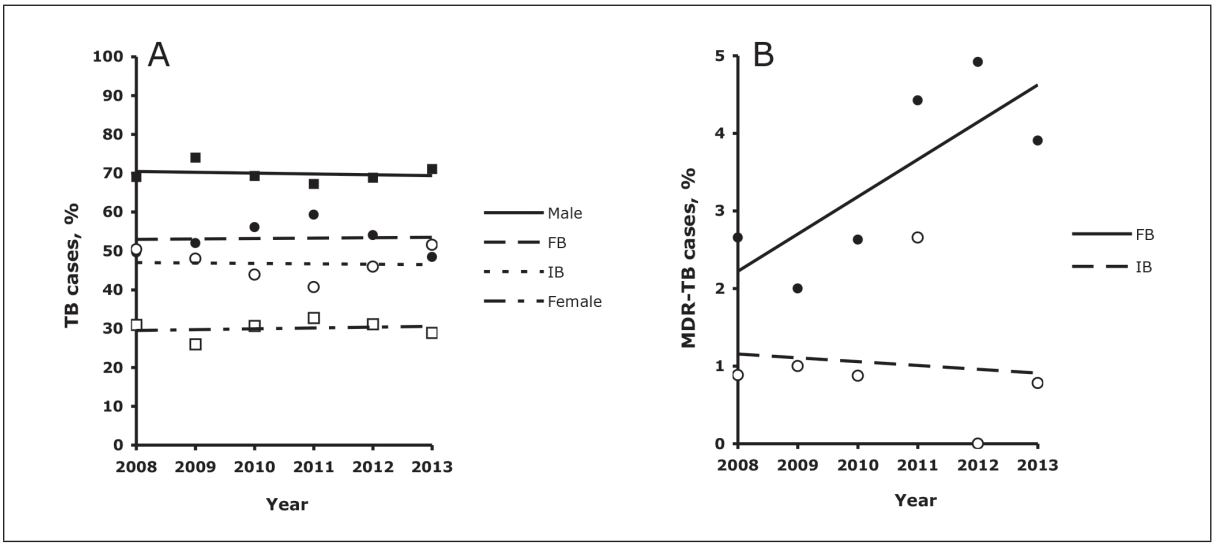

Figure 1
Trend of TB cases in male, female, foreign-born (FB) persons, Italian-born (IB) persons (A), and of MDR-TB cases in FB and IB persons (B) in Naples, in the period 2008-2013.

Table 1
Antituberculosis drug resistance in 690 *Mycobacterium tuberculosis* strains isolated in Naples from Italian-born (IB) and foreign-born (FB) persons in the period 2008-2013

	IB	FBs from:			Total no.
	(%)	Romania (%)	FSU[a] (%)	All other foreign countries (%)	(%)
Total tested	322 (100.0)	120 (100.0)	49 (100.0)	199 (100.0)	690 (100.0)
Resistance to FLD[b]	65 (20.2)	15 (12.5)	22 (44.9)	42 (21.1)	144 (20.9)
Monoresistance					
S	30 (9.3)	2 (1.7)	2 (4.1)	15 (7.5)	49 (7.1)
H	9 (2.8)	4 (3.3)	0 (0.0)	13 (6.5)	26 (3.8)
R	1 (0.3)	0 (0.0)	2 (4.1)	0 (0.0)	3 (0.4)
E	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any resistance					
S	50 (15.5)	11 (9.2)	16 (32.7)	29 (14.6)	106 (15.4)
H	33 (10.3)	13 (10.8)	18 (36.7)	27 (13.6)	91 (13.2)
R	9 (2.8)	9 (7.5)	13 (26.5)	4 (2.0)	35 (5.1)
E	4 (1.2)	0 (0.0)	12 (24.5)	4 (2.0)	20 (2.9)
MDR[c]	7 (2.2)	9 (7.5)	11 (22.4)	4 (2.0)	31 (4.5)
SHRE	2 (0.6)	0 (0.0)	7 (14.3)	2 (1.0)	11 (1.6)
SHR	1 (0.3)	9 (7.5)	3 (6.1)	2 (1.0)	15 (2.2)
HRE	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)	1 (0.2)
HR	4 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.6)
Other resistances					
HS	15 (4.7)	0 (0.0)	3 (6.1)	8 (4.0)	26 (3.8)
HSE	1 (0.3)	0 (0.0)	1 (2.0)	2 (1.0)	4 (0.5)
HE	1 (0.3)	0 (0.0)	3 (6.1)	0 (0.0)	4 (0.6)
RE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RS	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
RES	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Resistance of MDR strains to SLD[d]	7 (100.0)	9 (100.0)	11 (100.0)	4 (100.0)	31 (100.0)
KM	2 (28.6)	6 (66.7)	5 (45.5)	2 (50.0)	15 (48.4)
OFL	3 (42.9)	1 (11.1)	7 (63.6)	1 (25.0)	12 (38.7)
CM	3 (42.9)	0 (0.0)	4 (36.4)	4 (100.0)	11 (35.5)
AK	0 (0.0)	0 (0.0)	2 (18.2)	2 (50.0)	4 (12.9)

[a]FSU: Former Soviet Union countries (Ukraine, Russia, Armenia, Georgia).
[b]FLD: first-line drugs. S, streptomycin; H, isoniazid; R, rifampin; E, ethambutol.
[c]MDR: multidrug-resistant (resistant to at least H and R).
[d]SLD: second-line drugs. KM, kanamycin; OFL, ofloxacin; CM, capreomycin; AK, amikacin.
Values in parenthesis are the percentages of MDR strains.

than those to R and E. Monoresistance of FSU-strains to S and R was 4.1% and no monoresistance to H and E was seen.

Out of the 690 *M. tuberculosis* strains examined, 31 (4.5%) were MDR strains, including 24 (77.4%) from FB persons. Large differences among the three groups were observed, with a very high MDR rate in people coming from the FSU countries (22.4%) and lower levels in the other groups. Eleven MDR strains were isolated from FSU countries (Ukraine, 6; Russia, 3; Armenia, 1; Georgia, 1) and 20 from other countries (Romania, 9; Morocco, 2; Sri-Lanka, 1; India, 1; Italy, 7). The FB persons with MDR-TB were younger than IB persons [26.8 ± 12.1 (median 27.5) years *versus* 49.7 ± 19.3 (median 47) years; $P < 0.001$]. As to FLD combinations, 27 out of 31 MDR strains were resistant to three drugs. The MDR strains isolated from the FSU countries were more resistant to SHR and SHRE than to HR and HRE.

Among MDR strains tested for susceptibility to SLD (7 from IB and 24 from FB patients), a high proportion (48.4%) of strains were resistant to KM, followed by OFL (38.7%), CM (35.5%), AK (12.9%). Five MDR isolates (16.1%) were XDR strains (2 each from Ukraine and IB patients, and 1 from Morocco).

DISCUSSION

Tuberculosis is slowly declining globally at about 1.5% per year [4] but in industrialized countries a decreasing incidence in the native population is often associated

with an increase of TB notifications in FB patients [5, 8, 15-17].

Our study is the first report on the microbiological and epidemiological trends of drug-resistant TB in Naples, the largest city in Southern Italy. It is known that FB residents in Naples and in the region Campania were 1.7% and 1.6% of the total populations in 2005, 2.5% and 2.3% in 2008, 3.5% and 4.8% in 2013, respectively [11] but a consistent rate of illegal migrants was also reported [10]. In 2013, the top-five native countries of FB residents in Naples were Sri-Lanka, Ukraine, China, Romania and Philippines, and in Campania were Ukraine, Romania, Morocco, Sri-Lanka and China. Overall, in 2008-2013 the number of *M. tuberculosis* strains annually isolated in our laboratory from IB and FB patients was quite stable. As previously reported for TB patients at a national level [5, 15], FB persons at Naples were significantly younger that IB persons. The observation that microbiologically-confirmed TB cases occurred mostly in migrants from Romania, Ukraine and Morocco is in keeping with nationality rates of FB residents in Naples/Campania and consistent with a high prevalence of TB in their native countries (*e.g.*, Romania, 99; Ukraine, 114; Morocco, 137 cases per 100 000 population) [18].

Our data showed that the MDR-TB increase in the FB patients paralleled the increase in immigration rate reported for Naples and Campania [11] in the six years of the study. Over 60% of MDR-TB cases occurred in young male migrants coming from the FSU countries (Ukraine, Russia, Armenia, Georgia) and Romania. These FSU countries are all included in the WHO list of 27 high MDR-TB burden countries [4]. The contribution of FSU countries to MDR-TB in Naples/Campania was higher (11/31 strains, *i.e.* 35.5%) than that observed at national level (29.8%) in 2008-2014 [5]. The high MDR-TB prevalence in FB patients was also consistent with that of their native countries (*e.g.* in 2013: Ukraine, 21.8%; Russia, 33.5%; Armenia, 15.0%; Georgia 17.7%; Romania, 7.8%) [6]. The low proportion of African-born persons with MDR-TB (2 out of 31 cases from Morocco) is also in keeping with recent national observations [5], likely due to the fact that for many years Africa was neglected and TB was not treated, and that fixed-dose combinations were widely used in that continent [5, 19, 20]. The contribution of MDR *M. tuberculosis* strains isolated from IB patients was relatively low (2.2%) but higher than that seen at national level (1.2% in 2008-2014 [5]).

When MDR *M. tuberculosis* strains were tested for susceptibility to SLD, the percentages of resistance to the injectable drugs KM and CM and the fluoroquinolone OFL were very high while resistance to AK was low, but the number of strains examined was small, making it difficult to draw conclusions. It is important to point out that five MDR were XDR strains and that two of them were isolated from IB patients. These observations indicated that in Naples TB is an ongoing threat and that we must not lower our guard against this difficult-to-treat disease.

Overall, our data indicated that in 2008-2013 more than half of patients with TB belonged to the FB group. This pattern is different from that previously reported in Naples in 1996-2000 [10]. In that study FB notifications were 14.3% of total cases, with Africans being the largest group (9.4%) and people from East Europe the smallest one (1.4%). Now, after more than ten years from that investigation, the proportions of TB patients substantially changed, with Africans being 16.1% of cases and Europeans 27.4%, mostly arriving from Romania. Furthermore, large differences in MDR-TB rates between IB patients (2.2%) and people coming from FSU countries (22.4%), particularly Ukraine, were observed. A possible limit of this study is the fact that the diagnostic coverage of the large metropolitan area of Naples by our laboratory was partial. We tried to control the bias by stratifying TB cases in different groups. In 2014, ECDC stated that the odds of harboring MDR-TB in FB patients in the WHO European Region was greater than that of natives, and in ten countries including Italy this was statistically significant [21]. As observed at the national level [5], migrants from countries with medium and high risk of TB retained their risk of developing MDR disease even after moving to low endemic areas. Thus, our observations are in keeping with national and European data and strongly indicate the need to intensify efforts to make local TB diagnosis and treatment services more and more accessible to migrant populations living in Naples together with IB persons. It is also important to understand how migrants perceive TB and the specific obstacles they face when accessing the health systems, seeking a diagnosis and adhering to a treatment programme. In Italy, several types of accomodation centres for migrants have been recently created for screening TB and other infectious diseases [22, 23].

CONCLUSIONS

Overall, our data showed that in Naples the MDR-TB increased from 2008 to 2013 and that it occurred at rates reflecting those in the countries of origin. These epidemiological observations need to be taken into account in order to use all available tools to rapidly identify drug-resistant *M. tuberculosis* strains and begin treatment of TB patients. This approach will decrease transmission of the disease in a city with known socio-economic problems and a high population density [10, 11], under the WHO vision of improving TB control and eventually eliminating it as a public health problem by 2035 [1].

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Conflict of interest statement

There are no conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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REFERENCES

1. Lönnroth K, Migliori GB, Abubakar I, D'Ambrosio L, de Vries G, Diel R, Douglas P, Falzon D, Gaudreau MA, Goletti D, González Ochoa ER, LoBue P, Matteelli A, Njoo H, Solovic I, Story A, Tayeb T, van der Werf MJ, Weil D, Zellweger JP, Abdel Aziz M, Al Lawati MR, Aliberti S, Arrazola de Oñate W, Barreira D, Bhatia V, Blasi F, Bloom A, Bruchfeld J, Castelli F, Centis R, Chemtob D, Cirillo DM, Colorado A, Dadu A, Dahle UR, De Paoli L, Dias HM, Duarte R, Fattorini L, Gaga M, Getahun H, Glaziou P, Goguadze L, Del Granado M, Haas W, Järvinen A, Kwon GY, Mosca D, Nahid P, Nishikiori N, Noguer I, O'Donnell J, Pace-Asciak A, Pompa MG, Popescu GG, Robalo Cordeiro C, Rønning K, Ruhwald M, Sculier JP, Simunović A, Smith-Palmer A, Sotgiu G, Sulis G, Torres-Duque CA, Umeki K, Uplekar M, van Weezenbeek C, Vasankari T, Vitillo RJ, Voniatis C, Wanlin M, Raviglione MC. Towards tuberculosis elimination: an action framework for low-incidence countries. *Eur Respir J* 2015;45:928-52.
2. Lange C, Abubakar I, Alffenaar JW, Bothamley G, Caminero JA, Carvalho AC, Chang KC, Codecasa L, Correia A, Crudu V, Davies P, Dedicoat M, Drobniewski F, Duarte R, Ehlers C, Erkens C, Goletti D, Günther G, Ibraim E, Kampmann B, Kuksa L, de Lange W, van Leth F, van Lunzen J, Matteelli A, Menzies D, Monedero I, Richter E, Rüsch-Gerdes S, Sandgren A, Scardigli A, Skrahina A, Tortoli E, Volchenkov G, Wagner D, van der Werf MJ, Williams B, Yew WW, Zellweger JP, Cirillo DM, TBNET. Management of patients with multidrug-resistant/extensively drug-resistant tuberculosis in Europe: a TBNET consensus statement. *Eur Respir J* 2014;44:23-63.
3. European Centre for Disease Prevention and Control. *Assessing the burden of key infectious diseases affecting migrant populations in the EU/EEA*. Solna, Stockholm: ECDC; 2014. DOI 10.2900/28792
4. World Health Organization. *Global tuberculosis report 2014*. Geneva: WHO; 2014.
5. Fattorini L, Mustazzolu A, Borroni E, Piccaro G, Giannoni F, Cirillo DM, Italian Multicentre Study on Resistance to Antituberculosis Drugs Group. Tuberculosis in migrants from 106 countries to Italy, 2008-2014. *Eur Respir J* 2016;47:1273-6.
6. European Centre for Disease Prevention and Control/ World Health Organization Regional Office for Europe. *Tuberculosis surveillance and monitoring in Europe, 2015*. ECDC/WHO; 2015. DOI 10.2900/666960
7. Ministero della Salute. *La tubercolosi in Italia*. Available from: www.salute.gov.it/imgs/C_17_pubblicazioni_1472_allegato.
8. Ingrosso L, Vescio F, Giuliani M, Migliori GB, Fattorini L, Severoni S, *et al.* Risk factors for tuberculosis in foreign-born people (FBP) in Italy: a systematic review and meta-analysis. *PLoS One* 2014;9(4):e94728.
9. Gillini L, Centis R, D'Ambrosio L, Fedele A, Aprile V, Pasanisi G, *et al*. Is Europe ready to reach tuberculosis elimination? An outbreak report from Southern Italy. *Eur Respir J* 2015;46:274-7.
10. Ponticiello A, Sturkenboom MC, Simonetti A, Ortolani R, Malerba M, Sanduzzi A. Deprivation, immigration and tuberculosis incidence in Naples, 1996-2000. *Eur J Epidemiol* 2005;20:729-34.
11. Comuni-Italiani.it. Available from: http://www.comuni-italiani.it/index.html.
12. Della-Latta P. Mycobacteriology and antimycobacterial susceptibility testing. In: Isenberg HD (Ed). *Clinical microbiology procedures handbook*. Washington DC: ASM Press; 2004.
13. World Health Organization. *Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis*. Geneva: WHO; 2014.
14. Fattorini L, Migliori GB, Cassone A, Mustazzolu A, Piccaro G, Filippini P, *et al.* Proficiency testing of first- and second-line anti-tuberculosis drugs in Italy. *Eur Respir J* 2012;39:1263-6.
15. Lombardi G, Dal Monte P, Denicolò A, Tadolini M, Martelli G, Bacchi Reggiani ML, *et al*. Trend of microbiologically-confirmed tuberculosis in a low-incidence setting with high immigration rates. *BMC Public Health* 2014;14:340.
16. Aldridge RW, Zenner D, White PJ, Muzyamba MC, Loutet M, Dhavan P, Mosca D, *et al.* Prevalence of and risk factors for active tuberculosis in migrants screened before entry to the UK: a population-based cross-sectional study. *Lancet Infect Dis* 2016;16:962-70.
17. Pareek M, Greenaway C, Noori T, Munoz J, Zenner D. The impact of migration on tuberculosis epidemiology and control in high-income countries: a review. *BMC Med* 2016;14:48.
18. World Health Organization. *Tuberculosis country profiles*. Geneva: WHO; 2016. Available from: www.who.int/tb/country/data/profiles/en/
19. Lukoye D, Ssengooba W, Musisi K, Kasule GW, Cobelens FG, Joloba M, Gomez GB. Variation and risk factors of drug resistant tuberculosis in sub-Saharan Africa: a systematic review and meta-analysis. *BMC Public Health* 2015;15:291.
20. Ben Amor Y, Nemser B, Singh A, Sankin A, Schluger N. Underreported threat of multidrug-resistant tuberculosis in Africa. *Emerg Infect Dis* 2008;14:1345-52.
21. European Centre for Disease Prevention and Control/ World Health Organization Regional Office for Europe. *Tuberculosis surveillance and monitoring in Europe, 2014*. ECDC/WHO; 2014. DOI 10.2900/1956
22. Crepet A, Repetto E, Al Rousan A, Sané Schepisi M, Girardi E, Prestileo T, Codecasa L, *et al*. Lessons learnt from TB screening in closed immigration centres in Italy. *Int Health* 2016;8:324-9.
23. Germinario C, Gallone MS, Tafuri S. Migrant health: the Apulian model. *Epidemiol Prev* 2015;39(Suppl 1):76-80.