

Nosocomial pseudo-outbreak of *Mycobacterium gordonae* associated with a hospital's water supply contamination: a case series of 135 patients

Marija Zlojtro, Mateja Jankovic, Miroslav Samarzija, Ljiljana Zmak, Vera Katalinic Jankovic, Mihaela Obrovac, Igor Zlojtro and Marko Jakopovic

ABSTRACT

Nontuberculous mycobacteria (NTM) are opportunistic pathogens found in natural and human-engineered waters. In 2009, a relative increase in the isolation of *Mycobacterium gordonae* from pulmonary samples originating from General Hospital Zabok was noted by the National Mycobacteria Reference Laboratory. An epidemiological survey revealed a contamination of the cold tap water with *M. gordonae* and guidelines regarding sputum sample taking were issued. In addition, all incident cases of respiratory infection due to NTM reported from 2007 to 2012 at General Hospital Zabok were included in a retrospective review. Out of 150 individual NTM isolates, *M. gordonae* was the most frequently isolated species ($n = 135$; 90%) and none of the cases met the criteria of the American Thoracic Society for pulmonary NTM disease. While concomitant *Mycobacterium tuberculosis* infection was confirmed in only 6 (4%) patients, anti-tuberculosis treatment was initiated for a significant portion of patients ($n = 64$; 42.6%) and unnecessary contact tracing was performed. This study points out the need to enhance the knowledge about NTM in our country and indicates the importance of faster NTM identification, as well as the importance of good communication between laboratory personnel and physicians when evaluating the significance of the isolated NTM.

Key words | *Mycobacterium gordonae*, nontuberculous mycobacteria, pseudo-outbreak, water contamination

Marija Zlojtro
Department for Respiratory Diseases,
General Hospital Zabok,
Bracak 8, 49210 Zabok,
Croatia

Mateja Jankovic (corresponding author)
Department for Respiratory Diseases,
University Hospital Centre Zagreb,
Jordanovac 104, 10000 Zagreb,
Croatia
E-mail: mateja.jankovic@gmail.com

Miroslav Samarzija
Marko Jakopovic
Department for Respiratory Diseases,
University of Zagreb Medical School,
University Hospital Centre,
Salata 3 10000 Zagreb,
Croatia

Ljiljana Zmak
Vera Katalinic Jankovic
Mihaela Obrovac
National Mycobacterial Reference Laboratory,
Croatian National Institute of Public Health,
Zagreb, Rockefellerova ulica 7, 10000 Zagreb,
Croatia

Igor Zlojtro
University of Zagreb Medical School,
Salata 3, 10000 Zagreb,
Croatia

ABBREVIATIONS

AECOPD	acute exacerbation of chronic obstructive pulmonary disease
AFB	acid-fast bacilli
ATS	American Thoracic Society
IDSA	Infectious Diseases Society of America
IGRA	interferon gamma release assay
IPF	idiopathic pulmonary fibrosis
MTB	<i>Mycobacterium tuberculosis</i>
NTM	nontuberculous mycobacteria
TB	tuberculosis

INTRODUCTION

Nontuberculous mycobacteria (NTM) encompass all *Mycobacterium* species other than *Mycobacterium tuberculosis* (MTB) complex and *Mycobacterium leprae*. Recently, these organisms have been coming into the limelight due to an increased isolation frequency of NTM as well as an increasing incidence of pulmonary NTM disease (Griffith *et al.* 2007; Marras *et al.* 2007; Martín-Casabona *et al.* 2004; Andréjak *et al.* 2010; Van Ingen *et al.* 2010). Unlike MTB, NTM are present in soil and water and infection is thought to be acquired from the environment rather than transmitted

person-to-person, with very rare exceptions (Aitken *et al.* 2012). Due to their ubiquitous presence in municipal water supplies, exposure to NTM is common (Von Reyn *et al.* 1994; De Groote *et al.* 2006; Falkinham *et al.* 2008; Feazel *et al.* 2009; Falkinham 2011), and NTM can colonize the respiratory tract without actually causing a disease.

Currently, rapid tests for identifying MTB are not routinely available in all laboratories included in the mycobacteria diagnostics network in Croatia, and identification of clinical isolates of mycobacteria at the species level is primarily based on the characteristics of the cultured bacteria, biochemical test results and, in some cases, identification using molecular methods. These test procedures are complex and laborious, and they are usually impeded by the slow growth of mycobacteria in culture (Bang *et al.* 2011). Clinical symptoms combined with acid-fast bacilli (AFB)-positive sputum smear or culture do not allow accurate differentiation between MTB, NTM infection or NTM environmental contamination. Since definitive identification of mycobacterial species can take several weeks, patients who have respiratory AFB-positive specimens present a public health dilemma. This is especially true for countries with a low incidence of NTM infections where clinicians rarely think about NTM as a disease causing pathogens. It is only recently that the first population-based study of NTM isolation frequency in Croatia has been published (Jankovic *et al.* 2013). This study showed that the number of NTM infections, in spite of an increase in the isolation frequency, was still remarkably low when compared to tuberculosis (TB). Thus, when a positive sputum smear microscopy result is reported to clinicians, they usually assume TB infection. This possible misdiagnosis can have serious consequences for both patients and their contacts.

The aim of this study was to describe the NTM isolation frequency at General Hospital Zabok, to confirm the presumed pseudo-outbreak of *M. gordonae* and to assess the impact of this outbreak on patients' treatment.

METHODS

Background

A relative increase in the isolation of *M. gordonae* from pulmonary samples originating from General Hospital

Zabok was noted by the National Reference Laboratory (NRL), at the Croatian National Institute of Public Health, Zagreb in 2009. An epidemiological survey was conducted to assess possible contamination of patients' samples with NTM from water supplies within the hospital. Moreover, all incident cases of respiratory infection due to NTM reported from 2007 to 2012 at General Hospital Zabok were included for retrospective review. This study protocol was approved by the Ethics Committee for the Protection of Human Subjects, by the General Hospital Zabok, Croatia (Protocol 4716, December 20th 2012).

Isolation and identification of the NTM

A total of 3903 pulmonary samples suspected of containing MTB or NTM were sent from General Hospital Zabok to the NRL, in the period 2007–2012. All samples were processed according to standard procedures as previously described. After discovering AFB in the sample, preliminary results were sent back to General Hospital Zabok, while the final result followed after identification of the species. The samples of cold tap water ($n=4$) were collected in 2009 from multiple sites within the hospital and sent to the NRL for isolation and identification of mycobacteria. All NTM were identified by biochemical and molecular methods (GenoType[®] CM/AS; Hain Lifescience, Nehren, Germany).

Data collection and clinical review

The records of all patients with NTM were reviewed. The following data were recorded from the patients' charts: age, specimen collection source, clinical presentation, underlying diseases, radiological data and treatment.

RESULTS

From January 2007 to December 2012, a total of 150 incident cases with pulmonary NTM isolates were identified at the General Hospital Zabok (Figure 1).

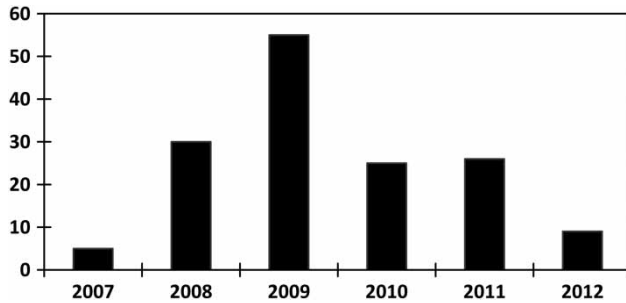


Figure 1 | Overall annual distribution of NTM isolated from pulmonary samples at General Hospital Zabok.

Distribution of patients with pulmonary NTM isolates

Distribution of patients with isolated NTM species throughout selected years is shown in Table 1. Out of 150 patients included in this study, 91 (60.6%) were men with median age of 70.2 years and 59 (39.3%) were women with median age of 74.1 years. Most of the isolated NTM species were those of little clinical significance, with *M. gordonae* being the most frequently isolated species ($n = 135$; 90%). Furthermore, *M. gordonae* was isolated from all cold tap water samples collected in different parts of the hospital. The incidence of NTM isolation peaked in 2009 when 55 patients were identified, out of which 96.4% had *M. gordonae* isolates. Out of 135 patients with *M. gordonae*, 10 (7.4%) patients had two or more *M. gordonae* isolates, while 92.6% had a single isolate.

After reviewing the medical records, we found that none of the 150 cases met the criteria of American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) for pulmonary NTM disease. The vast majority of patients had underlying pulmonary diseases with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) being the most common

one (Table 2). History of prior TB treatment was noted in 17 (11.3%) patients, while concomitant MTB infection was confirmed in only 6 (4%) patients. Still, in a significant portion of patients ($n = 64$; 42.6%), the anti-TB treatment was initiated. The majority of cases in which the treatment was initiated occurred in the period from 2008 throughout 2010 (Figure 2).

DISCUSSION

After observing increased *M. gordonae* isolation in patients' samples from the General Hospital Zabok in 2009, a pseudo-outbreak in a newly constructed hospital building was suspected; namely, the building where the Department for Respiratory Diseases is situated which was opened in February 2008. Epidemiological Service (part of the Croatian National Institute of Public Health) performed an inspection and confirmed contamination of cold tap water with *M. gordonae* in multiple sites throughout the plumbing system of the new building. Municipal water supplies have already been recognized as a major niche for NTM, as well as the major reservoir for most nosocomial outbreaks and pseudo-outbreaks caused by these organisms (Wallace et al. 1998; Philips & Fordham von Reyn 2001). NTM are tolerant to a much wider pH and temperature range than most other bacterial pathogens detected in municipal water supplies. Their general tolerance to chlorine makes them potentially more difficult to eliminate (Carson et al. 1978; Hall-Stoodley et al. 1999; Le Dantec et al. 2002). The presence of some of the nonthermophilic NTM, such as *M. kansasii*, in hospital water systems has been reported worldwide (Bailey et al. 1970; McSwiggan & Collins 1974; Picardeau et al. 1997). Conversely, *M. gordonae* has not

Table 1 | Number of patients with NTM isolated from pulmonary samples, hospitalized at General Hospital Zabok, from 2007 to 2012

NTM species	2007	2008	2009	2010	2011	2012
<i>M. gordonae</i>	1	29	53	23	24	5
<i>M. fortuitum</i>	1	0	2	1	1	3
<i>M. nonchromogenicum</i>	3	1	0	0	0	0
<i>M. terrae</i>	0	0	0	1	1	0
<i>M. xenopi</i>	0	0	0	1	0	1
Total n (%)	5 (3.3)	30 (20)	55 (36.6)	25 (16.6)	26 (17.3)	9 (6)

Table 2 | Distribution of underlying pulmonary diseases in patients with NTM isolated from pulmonary samples, hospitalized at General Hospital Zabok, from 2007 to 2012

Underlying disease	Number (%)
AECOPD	69 (46)
Pneumonia	40 (26.6)
Lung cancer	14 (9.3)
Inflamed bronchiectasis	12 (8)
Exacerbation of asthma	7 (4.6)
Active pulmonary TB	6 (4)
Aspergilloma	1 (0.6)
IPF	1 (0.6)

AECOPD – acute exacerbation of chronic obstructive pulmonary disease; IPF – idiopathic pulmonary fibrosis; TB – tuberculosis.

been studied extensively yet. Two recent studies from Turkey ([Genc et al. 2013](#)) and Korea ([Shin et al. 2008](#)) have shown the presence of *M. gordonae* in hospital tap water samples without consequences for staff or patients treated in those hospitals.

The tap water is potable in Croatia, hence it was presumed that drinking and/or gargling was the reason for the rise and pseudo-outbreak of *M. gordonae* infections in our patients.

Accordingly, guidelines for physicians, nurses and patients were issued, advising avoidance of drinking the tap water or even rinsing the mouth prior to giving the sputum sample. The potential weakness of the report was that the clonality of the isolates was not assessed but the implementation of measures was followed by a decreasing isolation trend of *M. gordonae* from respiratory samples with a steep decline achieved in 2012 and

maintained up to date. Even though TB was later confirmed in only 6 (4%) patients, in more than 40% of all patients, treating physicians initiated the anti-TB treatment immediately after notification of positive AFB in the specimen. This unnecessary drug administration could lead to potentially severe adverse reactions. According to standard procedure in our country, patients were mostly transferred to a hospital which specialized in treating TB for prolonged hospitalization and/or isolation. Furthermore, it can be assumed that contact tracing was carried out, including unnecessary physical exams, chest X-rays, interferon gamma release assay (IGRA) testing and preventive treatment, especially in children under 5 years of age. Moreover, a false diagnosis of TB infection could have delayed the recognition of the real underlying condition and postponed specific treatment for a number of patients.

Some of the reasons for such a great number of unnecessarily treated patients are: the burden of TB in Croatia; existing respiratory symptoms in patients (mostly due to other underlying diseases); and the lack of knowledge about the NTM, even among respiratory physicians. Croatia is a country that still has a medium TB incidence (23/100,000 in 2008). At the time, the incidence of NTM isolation was still considered quite low and there were only occasional reports regarding the significance of these pathogens ([Katalinic-Jankovic et al. 2007](#)). The percentage of treated patients was highest in the period from 2008 to 2010, whereupon both the number of *M. gordonae* isolates as well as the fraction of treated patients started to decline due to the raised awareness about this pathogen among physicians.

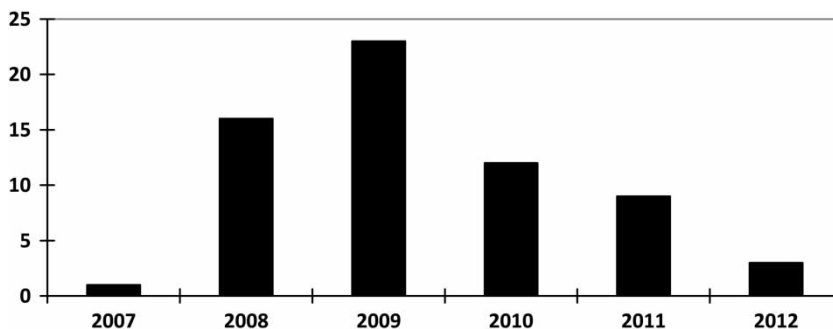


Figure 2 | Number of patients with NTM isolated from pulmonary samples that were started on anti-tuberculosis treatment.

CONCLUSIONS

We have confirmed a pseudo-outbreak of *M. gordonae* infection originating from a hospital's plumbing system and evaluated its impact on patients. This is a rare study of a large pseudo-outbreak of *M. gordonae* and its high influence on misdiagnosis of TB. The low awareness about the NTM in general, resulted in a significant number of inappropriately treated patients. TB treatment might have caused increased risk of drug-related adverse events but also unnecessary expense for the patient, hospital and the state. Moreover, patients' contacts were probably subjected to physical exams, laboratory analyses, and in some cases, prescribed with TB preventive medication. This study points out the importance of a faster NTM identification in patient samples as well as the importance of education and good communication between laboratory personnel and physicians when evaluating the significance of the isolated NTM.

CONFLICTS OF INTEREST STATEMENT

The authors whose names are listed certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript.

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