

The Incidence of *Mycobacterium* Other than Tuberculosis Isolated in Specimens Suspected of Tuberculosis in a Tertiary Hospital in the Philippines: A Retrospective Study

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Abstract

Introduction: In the Philippines, a diagnosis of pulmonary tuberculosis is very common especially in the presence of sputum findings positive for Acid Fast Bacilli (AFB). But it should be kept in mind that not all *Mycobacterium* are tuberculosis (TB). A previous study done at the University of Santo Tomas (UST) Hospital from 2003 to 2009 showed a 2.17% incidence of *Mycobacterium* other than tuberculosis (MOTT). However, due to its growing correlation with the Human Immunodeficiency Virus (HIV), updated incidence rates are warranted. Likewise, the importance of culture in the right diagnosis of diseases should always be emphasized.

Objectives: The study aimed to determine the incidence of MOTT in a tertiary hospital in Manila among patients suspected of having TB.

Materials and Methods: This is a retrospective study done at the UST Hospital, a quality-assured referral center for TB in Manila, with a TB Directly Observed Short Course (TB-DOTS) Clinic. Laboratory records of specimens submitted for culture and sensitivity studies for *Mycobacterium*

tuberculosis (MTB) for which isolates of MOTT grew, using BACTEC™ (Becton-Dickinson) method and *Mycobacteria* Growth Indicator Tube (MGIT™), from January 2003 to December 2014, were reviewed.

Results: A total of 6,886 specimens were submitted for MTB culture and sensitivity studies. Results showed 157 cases of MOTT with an incidence of 2.28%. Majority of the specimens with MOTT were from pulmonary sources (85%), most common of which was from sputum. Non pulmonary sources (15%) were mostly from urine, cerebro-spinal, and gastrointestinal tract. These findings are consistent with the previous local available data. Correct identification of this organism influence eventual decisions for treatment.

Conclusion: The incidence of positive culture for MOTT in our institution remains to be low. However, there is an increasing trend in the number of specimens which are turning out to be positive for MOTT. A future study on the correlation with the patients' clinical profile is recommended.

Key words: mycobacterium, University of Santo Tomas Hospital, TB, mycobacterium tuberculosis

Introduction

The genus *Mycobacterium* contains several species, many of which cause human illness. Infections from *Mycobacterium* species have a variety of clinical presentations. The most notorious species of this genus is *Mycobacterium tuberculosis* (MTB), which is responsible for many cases of tuberculosis (TB) worldwide.¹ Particularly in the Philippines, a diagnosis of pulmonary tuberculosis is very common especially in the presence of sputum findings positive for Acid Fast Bacilli (AFB). But again, it is important to note that not all *Mycobacterium* are TB. Less well known, but equally important in terms of causing illness are the *Mycobacterium* other than TB (MOTT).

MOTT are mycobacterial species that are ubiquitous in the environment. They are species other than those belonging to the MTB complex and *Mycobacterium leprae*. First identified in the late 19th century, they were documented to cause diseases in humans in the 1930's. But it was not until the 1950's that pulmonary disease due to these organisms became more recognized.²

Determining the number of environmental mycobacterial infections, particularly in the United States, is difficult because reporting these infections to public health departments is not required. Survey data from state laboratories in the early 1980's estimated the prevalence of MOTT infections to be only one to two cases per 100,000 population.² Locally, prevalence and incidence studies are focused on *Mycobacterium tuberculosis*. According to the Second National Drug Resistance Survey on TB,³ 558 out of 3,508 patients had MOTT, or were culture negative. In another study done by Visperas and Morfe, there was a 2.17% incidence of positive cultures for MOTT at the University of Santo Tomas (UST) Hospital from January 1,

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2003 to June 30, 2009.⁴

Recently, the unprecedented high level of interest in MOTT disease is the result of two major recent trends: the association of MOTT infection with Acquired Immune Deficiency Syndrome (AIDS) and recognition that MOTT lung disease is encountered with increasing frequency in the non-AIDS population.⁶

MOTT is not commonly known as compared with MTB. However due to the increasing trend of Human Immune Deficiency Virus (HIV)/AIDS cases, an increase in the incidence of MOTT, such as Disseminated *Mycobacterium* Avium Complex (MAC) infection, which affects 20-40% of all HIV/AIDS patients in several reported series,⁵ might be observed because these are potential complications of late stage HIV disease. In a local study⁷ describing the profile of TB of current HIV positive patients, one out of the 28 patients had *Mycobacterium* other than TB. In line with this, the importance of updated incidence rates for MOTT is warranted. Likewise, the importance of culture in the right diagnosis of diseases should always be emphasized.

Objectives

To determine the incidence of MOTT in specimens submitted at the UST Hospital among patients suspected of having TB and demonstrate the trend by comparing them with data from January 2003 to June 2009 by Visperas and Morfe³.

To determine the number of specimens submitted for *Mycobacterium* culture and sensitivity studies that were positive for MOTT.

To determine the types of specimens, and their frequencies, that yielded positive isolates for MOTT.

Methodology

This is a retrospective study done at the UST Hospital, a quality-assured referral center for TB in Manila, with a TB Directly Observed Short Course (TB-DOTS) Clinic. Records of specimens submitted for culture and sensitivity studies for MTB for which isolates of MOTT grew, using BACTEC™ (Becton Dickinson) method and *Mycobacteria* Growth Indicator Tube (MGIT™), from January 2003 to December 2014, at the hospital laboratory were reviewed. The records did not provide the patients' clinical profiles nor indications for TB culture requests. A letter of request for permission was sent and approved by the medical director and head of the UST Hospital Department of Clinical Pathology to access these results. Institutional Review Board (IRB) approval was granted after review. Data that was gathered from the logbook included the specimen number, date

of examination, type of specimen, and culture result. No sensitivity testing for MOTT were done. No informed consent was necessary since the study involved review of laboratory records. No interventions were carried out and all information obtained in this study remained confidential.

Results

Overall, a total of 6,886 specimens were submitted to the laboratory for *Mycobacterium* culture and sensitivity studies. Results showed a total of 157 cases (44 specimens from January 2003 - June 2009 and 113 specimens from July 2009 - December 2014) of MOTT with an incidence rate of 2.28%. Comparing July 2009 - December 2014 data, with that from January 2003 - June 2009, there were more number of cases from the former. Year 2003 had the least number of cases for MOTT, with only one specimen being positive, while 2010 registered the most cases for MOTT with 32 specimens being positive. (Table I)

Table I. Specimens that yielded positive for MOTT at the UST Hospital from January 2003 – June 2009³, July 2009 – December 2014.

Year	Total (%)
2003	1 (0.64%)
2004	3 (1.91%)
2005	9 (5.73%)
2006	9 (5.73%)
2007	8 (5.09%)
2008	9 (5.73%)
Jan to June 2009	5 (3.18%)
July to Dec 2009	15 (9.55%)
2010	32 (20.38%)
2011	27 (17.20%)
2012	7 (4.46%)
2013	9 (5.73%)
2014	23 (14.65%)
2003 - 2014	157 (100%)

Majority of the specimens with MOTT were from pulmonary sources (85%), most common of which is from sputum. Non pulmonary sources (15%) were mostly from urine, cerebrospinal fluid, and the gastrointestinal tract. Comparing the two study periods, there was noted increase in the number of cases from non pulmonary sources. (Table II)

Table II. Sources of specimens yielding MOTT at the UST Hospital from January 2003 – June 2009³, July 2009 – December 2014

	January 2003 – June 2009 ³ n = 44	July 2009 – December 2014 n = 113	Total (%) n = 157
Pulmonary	40 (90.91%)	93 (82.30%)	133 (85%)
Sputum	36 (81.82%)	85 (75.22%)	121 (77.07%)
Bronchial washing	3 (6.82%)	7 (6.19%)	10 (6.37%)
Bronchial aspirate	1 (2.27%)	0 (0.00%)	1 (0.64%)
Lung mass	0 (0.00%)	1 (0.88%)	1 (0.64%)
Non Pulmonary	4 (9.09%)	20 (17.70%)	24 (15%)
Gastrointestinal Tract	0 (0.00%)	4 (3.54%)	4 (2.55%)
Urine	1 (2.27%)	3 (2.65%)	4 (2.55%)
Cerebrospinal Fluid	1 (2.27%)	3 (2.65%)	4 (2.55%)
Wound Tissue	0 (0.00%)	3 (2.65%)	3 (1.91%)
Blood	0 (0.00%)	2 (1.77%)	2 (1.27%)
Pleura (Mass and Fluid)	0 (0.00%)	2 (1.77%)	2 (1.27%)
Subcutaneous Tissue	1 (2.27%)	0 (0.00%)	1 (0.64%)
Foot Debridement	1 (2.27%)	0 (0.00%)	1 (0.64%)
Brain Abscess	0 (0.00%)	1 (0.88%)	1 (0.64%)
Submandibular Mass	0 (0.00%)	1 (0.88%)	1 (0.64%)
Lumbar Mass	0 (0.00%)	1 (0.88%)	1 (0.64%)

Discussion

Specimens for mycobacterial identification and susceptibility testing may be collected from almost any area of the body. The American Thoracic Society and Infectious Disease Society of America's Diagnostic Criteria for MOTT pulmonary infections include clinical findings, imaging studies consistent with pulmonary disease and recurrent isolation of mycobacteria from sputum (at least two) or isolated from at least one bronchial wash in a symptomatic patient.⁵ The three most common pulmonary syndromes due to MOTT are caused by MAC, *Mycobacterium kansasii*, and *Mycobacterium abscessus*. It is emphasized that making the diagnosis of MOTT lung disease does not necessitate the institution of therapy. The decision is based on the potential risks and benefits of therapy for individual patients.⁴ Treatment of MOTT infection of the lung, as in other body site, is dependent upon the species of the infecting organism.⁵

The diagnosis of MOTT is essential for proper management of the disease. Likewise, differentiation from MTB and speciation for the different species of MOTT is important. Results of this study are consistent with a similar research by Visperas and Morfe⁴, wherein out of 2,714 specimens submitted for *Mycobacterium* culture and

sensitivity studies from January 2003 to June 2009, 59 (2.17%) were isolated for MOTT.

MOTT has been seen in most industrialized countries, where incidence rates vary from 1.0 to 1.8 cases per 100,000 persons. But studies suggest that incidence is much higher. In Ontario, Canada the isolation prevalence of pulmonary MOTT from 1997 - 2003 has significantly and rapidly increased from 9.1/100,000 in 1997 to 14.1/100,000 in 2003, with a mean annual increase of 8.4%, and a sizeable proportion of patients are likely to have disease.⁶ In another study by Gopinath and Singh⁷, MOTT is believed to be grossly underreported, especially in TB endemic countries. Possible factors for underreporting include the following: MOTT infections are not reportable in any country, including the Philippines, there is still a lack of awareness among treating physicians and microbiologists, laboratory infrastructure is lacking for culture and identification of MOTT, standardized or accepted criteria to define MOTT respiratory disease are lacking, and lastly, the high burden of MTB and HIV becomes more the priority in the health care system,⁸ and thus the focus in health programs. But as previously mentioned, MOTT has likewise been seen more commonly, especially in HIV/AIDS patients. As of December 2014,

the Department of Health AIDS registry in the Philippines reported 22,527 people living with HIV/AIDS.⁹ This would bring about new challenges in the diagnosis and treatment of diseases unique to this population, including MOTT.

Since, the data was extracted from the hospital laboratory records with a combination of inpatients and outpatients from the private and charity division, patients' clinical profiles, including demographics, signs and symptoms and indications for TB culture requests, were not all accessible, therefore not included in the study. However, our institution routinely requests for TB cultures in retreatment and treatment failure cases, multidrug (MDR) TB suspects and contacts, HIV contacts, and smear negative TB symptomatic with MDR risk, in compliance with the 2016 local guidelines.¹⁰ A future research on the clinical correlation with laboratory findings of MOTT is recommended, since positive cultures for MOTT may not necessarily indicate actual disease, as contamination is common. Laboratory limitations for further speciation studies should also be noted.

Conclusion

The incidence of positive culture for MOTT in our institution remains to be low. However, there is an increasing trend in the number of specimens which are turning out to be positive for MOTT, becoming more relevant, coinciding with the increasing HIV/AIDS rates. An addition of the review of patients' records on future studies is recommended to provide clinical correlation.

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