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Medicine

CLINICAL IMPORTANCE OF NONTUBERCULOUS MYCOBACTERIA IN CHRONIC PULMONARY LUNG DISEASES.

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ABSTRACT

Introduction: The isolation of non - tuberculous mycobacteria (NTM) from clinical specimens is becoming common in mycobacteriology laboratories. Globally, the NTM' s are perceived as a contaminant only. Concomitantly NTMs are observed to be another major causative agent of pulmonary and extrapulmonary diseases in immunocompetent patients. It calls for a different line of diagnosis. To complement the paradox on role of NTM, its isolation, identification and diagnosis, a study was carried out in symptomatic patients attending OPD of NITRD New Delhi.

Materials & Methods: The study was conducted on the patients whose first sputum culture report was positive for NTM in the microbiology laboratory. At the time of enrollment, second sputum sample was collected along with patient's clinical data and radiological finding. The results of 2 sputum culture along with clinical & radiological features were recorded and co-related. During the study, tracing of the patients was done mainly through 3 different methods (i) Patients were traced during the report collection in microbiology laboratory by clinical microbiologist, (ii) Through laboratory records registration number address and/or phone number iii)By the help of field worker of the DOTS Centre. Cultures were done in MGIT 960 automated bacterial culture system and identification was done through routine biochemical character.

Results : As per protocol, during the 12 months of study period, 2285 sputum samples were processed for liquid culture using MGIT-960 system(BD) for routine culture and DST. 77 (3.36%) patients showed their 1st sputum was positive for NTM. Culture on 2nd sputum sample of 77 patients showed positive growth in 36/77 (46,75%) cases. The 36 positive patients were analyzed further in this study. The age distribution of 36 patients showed that 61% NTM were isolated from patient's age group 20-45 years. Male : female ratio was 2:1. The common symptoms were cough (36), fever (28), hemoptysis (24), weight loss (23), sputum production (10), and loss of appetite (24). Lungs were involved in all 36 cases with bilateral involvement in 20/36 and unilateral lunginvolvement in 16/36 cases.. Radiological findings showed cavity in 31/36 (86.11%) patients. Among these patients 11 different species of NTM were identified with five rapid growers; *M.kansasii*(11), *M.chelonae*(06),*M.terrae complex* (05), *M.avium complex* (05), *M.fortuitum*(02), *M.vaccae*(02), *M.abscessus*(1), *M.haemophilum*(1), *M.gastri*(1), *M.xenopi*(1)*and M.intracellularae*(1),.

Conclusion : It is imperative on the part of microbiologist to carry out identification tests on all culture isolates before DST is done as 50 % of the laboratory isolates were positive for NTM in repeat samples. Any of the standard tests for M. Tb complexes turn out to be negative;microbiologist shall look for NTM's. For this purpose a checklist to be developed to avoid delay in diagnosis of NTM related diseases.

KEYWORDS :

INTRODUCTION:

Nontuberculous Mycobacteria (NTM) are widespread environmental organisms capable of causing infection in immunocompromised and immunocompetent hosts. Presently 125 different types of NTM exist in the environment, amongst them 40 species are seen to be involved in human disease (1).

Clinical practitioners normally opinethat NTM are typically environmental and poorly pathogenic for humans. However, NTM may be responsible for opportunistic diseases in subjects resenting with various predisposing conditions is well versed understanding.

Indeed, NTM are being identified as causative agents of human disease with increasing frequency in pulmonary and extra-pulmonary infection involving lymph nodes, skin, soft tissues, bones and joints like any other diseases.NTM can produce nonspecific symptoms with clinical manifestations ranging from asymptomatic to fatal diseases. These signsand symptoms are often indistinguishable clinically and radiographically from those caused by Mycobacterium tuberculosis (2,3). The laboratory report of growth of Nontuberculous Mycobacteria often causes anxiety to patient and a poser for the clinician, as the significance of infection is often difficult to determine in patients with chronic pre-existing lung disease.

The isolation of nontuberculous mycobacteria (NTM) from clinical specimens is frequent these days. The increased incidence of NTM disease is attributed to improved diagnostic techniques, increasing life expectancy and increased number of elderly patients.

Clinical assessment and identification of species is important because it has different antimicrobial susceptibility pattern and treatment options. The present study was undertaken to assess the frequency of NTMs among TB suspects. The assessment of the clinical significance of NTM, along with a consideration of the more frequent NTM pathologies, was also studied.

MATERIALS & METHODS:

This was a prospective study pertaining to clinical and radiological profile of NTM during June 2014 to May 2015, in the Santosh Med Colege, Santosh University and NITRD, New Delhi. It was approved by ethical and research committees of the National Institute of Tuberculosis and Respiratory Diseases. Patients were selected on the basis of mycobacterial culture report that identifiedthe MOTT. This was done because the clinical presentation of tubercular and non tubercular disease was almost same.All the patients whosefirst sputum sample positive for Mycobacterium other than tuberculosis (MOTT) were enrolled in the study. In the case when reports were not delivered directly to patients, they were contacted on phone as recorded in the OPD slip or admission paper. In absence of phone numbers, patients were contacted through the help of field worker of the DOTS Centre. Once the patient contacted through any of above means, the enrollment of the patients was done by filling the proforma and getting the consent form signed for the study. At the time of enrollment 2nd sputum sample of patients were collected for repeat culture examination, their clinical profile and radiographic results were recorded in a pre-designed proforma.

Clinical evaluation

The patients were evaluated for NTM infection on the basis of following criteria as described by Griffith et al (4)

Clinical criteria :

Signs/symptoms; cough, fatigue, fever, weight loss, hemoptysis, dyspnea, deterioration in clinical status if an underlying condition is present

Radiographic criteria

Infiltrates with or without nodules persistent for more than 2 months or progressive, cavitation, single or multiple nodules.

HRCT abnormalities
Multiple small nodules, multifocal bronchiectasis with or without small lung nodules.

Bacteriologic criteria : At least three available sputum/bronchial wash samples within 1 year; three positive cultures with negative AFB smears or two positive cultures and one positive AFB smear or Positive culture result from at least one bronchial wash or lavage.

The outcome of the second sputum sample culture result, the clinical & radiological features were recorded and co-related with the first sputum sample report.

RESULTS

During study the microbiology laboratory has processed 2285 sputum samples. Out of the total processed samples 77 (3.36%) patients showed their 1st sputum positive for NTM. Second sputum of these 77 patients when subjected to re-culture 36 (1.57%) were positive for NTM. In total 36 true NTM were followed further in detail. The age distribution study showed that mean age was 41.12 years and out of 36 patients 22/36 (61%) NTM were isolated from patient's age group 20-45 years. (Table 1). In this study NTM isolated from male patients were 24 (66.66%) and 12 (33.33%) were female patients. The common symptoms were cough (36) followed by fever (28), hemoptysis (24), weight loss (23), sputum production (10) and loss of appetite (24). Lung was involved in all 36 patients. The radiological finding in NTM group of patients showed that bilateral lung was involved in 20/36 patients and unilateral lung was involved in 16 patients. Other important radiological observation in this study was cavity in lung which was seen in 31/36(86.11%). Pleural effusion and lymphadenopathy was uncommon finding in NTM group. The species identification of result showed that the 11 different types of NTM were identified. The species identified were *M.kansasii*(11), *M.chelonae* (06),*M.terrae complex* (05), *M.avium complex* (05), *M.fortuitum*(02), *M.vaccae* (02), *M.abscessus*(1), *M.haemophilum*(1),*M.gastri*(1), *M.xenopi* (1) *andM.intracellularae*(1), In this study it has been observed that among the 36 NTM 5 were from the rapidly growing mycobacterial group.

DISCUSSION:

In this study we found that 1.5 % of NTM isolated in the laboratory during the routine culture are well correlated with clinical presentation in tertiary care institute. Matos et al has observed that the prevalence of NTM isolated from the sputum of patients from the specialized MRTB clinic in Brazil was significant (8.2%), taking into account the high prevalence of TB in that region which was higher than our observation (5). In contrast to our study Shanker et al from India observed a 7.9% prevalence of NTM in 604 mycobacteria positive cultures from patients at a TB clinic (6). However, these differences may be attributed to the geographic distribution of NTM which vary from one place to another. Age distribution of NTM disease in our study was similar to Dias et al where NTM isolates in MRTB Center in Bahia, Brazil was 48.8 ± 13.8 years by Matosh et al (5). This study revealed that NTM is preponderance in male patients in comparisons to female cases. The male dominance of NTM cases were also described by O'Brien et al (7).

The most frequent symptoms were respiratory (60.9%), but 30.5% of the total patients had both respiratory and systemic symptoms, including cough, dyspnea, hemoptysis, thoracic pain, fever, weight loss, and night sweats was described by Couto deMello et al from Brazil (8). In our study also cough and sputum were the commonest manifestation along with others non respiratory manifestations. In our study 55.6% showed bilateral lung involvement and 86% showed cavitary lesion which was comparable to the study of Couto de Mello et al whose results showed bilateral lung involvement in 23/77 (29.87%) and cavitary lesion in 43/73 (55.84%) (8).

In this study the most common NTM isolated was *M.kansasi* but many western literature showed *M. avium-intracellular* as the most frequently found NTM.M.kansasi as a commonest isolate has been discussed by Corbett et al from South Africa in gold miner population (9). This similarity may be correlated with similarity of climate in the two countries. However, some studies have found a higher frequency of other NTM species, such as *M. gordonae (10*), *M. xenopi (*11), *M. fortuitum*, and *M. chelonae (*12).

CONCLUSION :

This study, in true sense, is an eye opener in countries like India where the NTM is silently present and mimics as pulmonary tuberculosis. One should carefully lookout and identify the culture positive isolates before starting the treatment. This study merited that NTM exist in general population as a cause for chronic lung infection. Such chronic lung infections should be carefully examined for NTM infection before TB treatment. Continued monitoring of pulmonary NTM is desirable and more detailed information should be obtained on pulmonary disease in order to strengthening the data of NTM infection and their regional distribution and species prevalence.

TABLE- 1: Demographic profile of patients (n=36)

Sr. no.	Parameters		
1	Age	Mean age (years)	41.12
		Adolescence (10-19 yrs)	1 (2.7%)
		Adults (20-45 yrs)	22 (61.11%)
		Elderly (46-60 yrs)	9 (25.00%)
		Old-age group (≥ 61) yrs)	4 (11,11%)
2	Sex ratio (M:F)		2:1
3	Education	Basic education (primary and above)	21
		Illiterate	15
4	Employment status	Unemployed	14
		Regular	14
		Daily wager	08
5	Average weight (Kg)		47.33
6	Average height (centimetres)		172.83
7	Basal metabolic index (BMI)		19.39
		Total	36

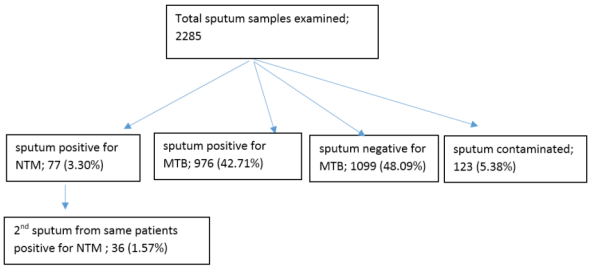

Figure 1. Distribution of NTM amongst the total processed sputum samples (N=2285)

TABLE-2: Clinical Manifestations of NTM Pulmonary disease

Symptoms	NTM (n=36)	
	Present	Absent
Fever	28 (77.8 %)	8 (22.2%)
Cough	36 (100.0%)	0 (0.0%)
Sputum	19(52.8%)	17(47.2%)
SOB	10 (27.8%)	26 (72.2%)
Haemoptysis	24 (66.7%)	12 (33.3%)
Weight loss	23 (63.9%)	13 (36.1%)
Loss of appetite	24 (66.7%)	12 (33.3%)

TABLE-3: Chest X- ray finding of NTM disease patients (n=36)

Sr.no	Finding	Sites	Total number
1	Lung involvement	Unilateral	16/36 (44.4%)
		Bilateral	20/36 (56.6%)
2	Cavity	Present	31/36 (86.1%)
		Absent	5/36 (13.9%)

TABLE 4: Species of nontuberculous mycobacterium identified from sputum specimen

NTM species	NTM (n=36)	
	Total number	percentage
M.kansasii	11	30.55%
M.chelonae	06	16.66 %
M.terrae complex	05	13.88%
M.avium complex	05	13.88%
M.fortuitum	02	5.55%

M.vaccae	02	5.55%
M.abscessus	01	2.77%
M.haemophilum	01	2.77%
M.gastri	01	2.77%
M.xenopi	01	2.77%
M.intracellularae	01	2.77%
Total	36	

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