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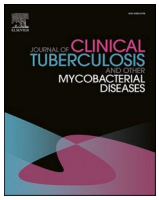

The epidemiology, demographics, and comorbidities of pulmonary and extra-pulmonary non-tuberculous mycobacterial infections at a large central Florida Academic Hospital

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ABSTRACT

Rationale: In the United States, non-tuberculous mycobacterium (NTM) infections are considered an important cause of morbidity and mortality, especially in people with progressive lung disease. The state of Florida has an extremely high incidence and prevalence of NTM disease which is likely a rapidly emerging infection in the state due to environmental and demographic factors.

Objectives: Adjemian et al. [1] To determine the burden of NTM disease of patients admitted to a large Central Florida academic center, Falkinham [2] to identify the most common risk factors associated with developing NTM disease in this area, and Sfeir et al. [4] to categorize antimicrobial susceptibilities and genetic resistance markers.

Methods: We conducted a retrospective case review from January 1, 2011 to December 31, 2017 in a large university-associated metropolitan hospital in west-central Florida. NTM infections were identified using TheraDoc® during the study period with the inclusion criteria of any inpatient admission, culture confirmed NTM at any site, and age $\geq$ 12 years. Demographic variables (including residential zip code) and comorbidity data (including solid organ transplant status, HIV status and subsequent testing results, intrinsic pulmonary disease, and cancer diagnosis of any site) were collected for each patient. Microbiologic data collected included NTM species/subspecies, anatomic location of specimen collection, antimicrobial susceptibility including minimum inhibitory concentration (MIC). All collected data were analyzed within Stata/IC14.2. Geospatial relationships between zip codes, diagnosis type, and co-morbidities were computed using Arc GIS Pro.

Results: Our results demonstrated that a substantial number of our inpatient cases with NTM were of the *M. abscessus* group, and with *M. avium* complex and *M. fortuitum* also representing the pathogen in numerous cases. Novel findings included compilation of the first hospital wide comprehensive NTM resistance plot to our knowledge. Our results did show a concordance with previous data with expected predominance of NTM inpatient cases in Caucasian males with pre-existing pulmonary disease, though additional work could be done with isolates within the transplant and immunosuppressed populations.

Conclusions: Our data set demonstrates the most common species/subspecies of NTM infections and their associated conditions seen at our central Florida hospital, and includes an antimicrobial sensitivity analysis in toto. This could be insight into the possible prevalence of NTM in the area, and provides the foundation for future studies on both the acquisition and prevention for NTM infections in central Florida.

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1. Introduction:

Non-tuberculous mycobacteria (NTM) are weakly Gram-positive bacteria with a lipid rich cellular membrane, which confers the ability to be ubiquitous in the environment [2]. The most common species of NTM are those within the *Mycobacterium avium* complex group [5] (*M. avium*, *M. chimaera*, *M. intracellulare*) [3,4] and those within the *Mycobacterium abscessus* group (subspecies; abscessus, bolletii, massiliense) [4]. All humans are exposed over time due to inhalation of the organisms from fresh water or aerosolized municipal water sources such as while showering. Thus, most cases are pulmonary in origin and are in patients with intrinsic pulmonary disease. However, extrapulmonary NTM often can present as isolated integumental infection via direct inoculation or disseminated disease via the bloodstream, especially in the presence of a cell mediated immunodeficiency such in severe HIV/AIDS infection. Municipal water sources have a greater bacillary load of NTM due to a decrease in competition from other organisms which are eliminated via the chlorination treatment process [5] to which NTM are mostly resistant [6].

The prevalence of NTM has increased globally, thought to be due to the increased diagnostic testing and availability of population-based studies. Some studies have suggested that the possible increase is due to the increasing co-morbidities, general NTM diagnosis awareness, aging population demographics, and immunosuppression [7–9]. However, there are still some areas within the United States (U.S.) and other countries where prevalence and epidemiological characteristics of NTM are unclear. A recent review from four separate data analyses of NTM cases across the United States (U.S.) noted that the range of persons infected varied from 1.4 to 6.6 per 100,000 people [10]. Interestingly, a higher rate was noted in both the U.S. state of Hawaii and the U.S. states on the coast of the Gulf of Mexico, including the state of Florida. A more recent review by Winthrop and colleagues noted that both incidence and prevalence were increasing in the U.S., and that the states of Florida, Texas and California now had the highest number of new diagnoses of pulmonary NTM disease [11]. A central challenge with management of NTM infection are the numerous and complex intrinsic resistance mechanisms, making antibiotic susceptibility interpretation often subjective and inconsistent due to reliance on individual reference laboratory interpretation. Due to the complex nature of NTM treatment, many clinicians in the U.S. refer complicated patient cases to the National Institutes of Health or the National Jewish Hospital. More information is needed on regional susceptibility patterns in order to have a more coordinated approach to diagnosis and treatment. This is especially true for the organisms of the *Mycobacterium abscessus* group (subspecies; abscessus, bolletii, massiliense), that have a prevalence in Florida and Hawaii, yet are not reportable to most local health departments nor to the U.S. Centers for Disease Control and Prevention (CDC). Since NTM are a rapidly emerging infection, we aim to discover the true burden of NTM disease seen at an academic tertiary Central Florida medical center through a retrospective case review study in order to determine the most common risk factors associated with developing NTM disease. The authors conducted a comprehensive, retrospective chart review of culture confirmed NTM disease within the past ten year.. The overall goal of this study was to determine both the 1) NTM prevalence at this academic tertiary Central Florida medical facility and 2) the susceptibility patterns for these organisms. Lastly, as Florida has one of the areas with the highest prevalence of persons living with HIV, co-infection with one of the *M. avium* complex group is common, and it is important to review this emerging data.

2. Methods

A retrospective case review study was conducted from January 1, 2011 to December 31, 2017 at one of the largest academic tertiary acute care medical centers in central Florida. Tampa General Hospital located in Tampa, Florida serves as the primary teaching hospital for the University of South Florida Morsani College of Medicine. The TheraDoc® Clinical Surveillance System (Premier Inc., Charlotte, NC) was used to identify all NTM infection cases during the study period with the inclusion criteria of any inpatient admission, culture confirmed NTM at any body site, and age $\geq$ 12 years. Excluded from the analysis were outpatient only encounters or patients less than 12 years of age. Demographic variables collected via electronic medical record review were: date of birth, sex at birth, race, ethnicity, and residential zip code. Comorbidity data included solid organ transplant status, HIV infection status by serum antibody-antigen testing or known prior confirmed diagnosis, pulmonary disease (COPD, asthma, pulmonary fibrosis, bronchiectasis, or cystic fibrosis), and cancer diagnosis of any site (i.e., lung, pancreatic, renal, or hematologic cancer). Microbiology data collected included NTM species and subspecies, anatomic location of specimen collection, antimicrobial susceptibility including minimum inhibitory concentration (MIC), if available, and name of reference lab. All data was originally collected into Microsoft Office Excel then converted and analyzed within Stata 14.2/IC (StataCorp LLC, Copyright (1985–2015). STATA 14.2. College Station, TX, USA).

Geospatial relationships between zip codes, diagnosis type, and comorbidities were computed using Arc GIS Pro 2019 as part of the University of South Florida licensed software. (Environmental Systems Research Institute (ESRI). (2019). ArcGIS Release 10.1. Redlands, CA, USA).

3. Results

Of a total of 831 cases identified, 507 NTM total isolates were identified among 361 unique individuals that met criteria for inclusion with complete microbiological data. Of the 361 unique patients, the average age was 59.2 years, with 47.6% (n = 172) $\geq$ 65 years, with 57.9% (n = 208) recorded as male (Table 1). The majority of cases were in Caucasians at 75.1% (n = 265), then in African Americans 16.7% (n = 59), and those of Latinx heritage 6.8% (n = 24). Most cases were from individuals referred from outside the Tampa Bay Metropolitan area at 81.2% (n = 293) and outside the county of referral hospital 52.4% (n = 189). Of the total 361 individuals, 271 (75.1%) had pulmonary NTM involvement, and 90 (24.9%) had only extra-pulmonary involvement.

Notable co-morbidities included chronic obstructive pulmonary disease at 23.0.% (n = 83), cystic fibrosis (11.1%; n = 40), diabetes mellitus type I or II (11.6%; n = 42), lung transplant recipient (11.1%; n = 40), living with HIV (12.2%; n = 44), and lung malignancy (7.8%; n = 28) (Table 2 and Fig. 1). Of a total of 145 individuals receiving HIV testing during the course of hospitalization, 39 of the 44 reactive individuals hada new diagnosis (39/145 = 26.9%), indicating the high prevalence of HIV and NTM co-infection in the region.

Of the 50 total NTM isolates, *Mycobacterium abscessus* group was the most common (45.4%; n = 230), comprised of *M. abscessus* subsp. *abscessus* (34.5%; n = 175), *M. abscessus* subsp. *massilense* (8.7%; n = 44), and *M. abscessus* subsp. *bolletii* (1.18%; n = 6) (Fig. 3 and Table 3). Other rapid growers isolated were *M. fortuitum* species (6.9%; n = 35) and *M. chelonae* (2.56%; n = 13). Of the slower growers, *M. gordonae* (19.9%; n = 101) and *M. avium* complex (8.28%; n = 42) were the most common. Of the *M. avium* complex pathogens, *M. chimaera* was most common (4.9%; n = 25). (Table 3).

Mycobacterium abscessus subsp. *abscessus* was the most prevalent NTM species not only in pulmonary disease (n = 155; 30.5%) but also within extra-pulmonary disease (n = 75; 14.7%), of which were mostly skin and soft tissue infections and bacteremias. (Figs. 2 and 3)

The lesser known NTM species were seen in 19 isolates, of which 14 out of 17 unique patient cases were identified in the respiratory tract from sputum or bronchoalveolar lavage. These included *M. interjectum, M. triplex, M. parascrofulaceum, M. arupense, M. yongonense, M. arupense, M. lavum, M. gastri, M.phocaicum, M. stomatepiae,* and *M. septicum*.

Of the 507 isolates from 361 unique individuals, 259 isolates had drug susceptibility reports found from chart reviews. After eliminating

Table 1
Demographics of inpatients with culture confirmed pulmonary, integumental and sites of dissemination/bloodstream infection sites of non-tuberculosis mycobacteria (NTM) Infection, Tampa General Hospital, Tampa, Florida (January 1, 2011 to December 31, 2017), N = 361.

	Pulmonary Involvement n (% of total)	Extra-Pulmonary only n (% of total)	N = 361 (% of total)
TOTAL INPATIENTS	n = 271 (75.1)	n = 90 (24.9)	N = 361 (100.0)
Age (years) (12 to 95 years)			
Mean (years)	60.5	55.4	59.2 years
less than 18 years	2 (0.6)	1 (0.3)	3 (0.83)
18–44 years	58 (16.1)	24 (6.6)	82 (22.7)
45–64 years	68 (18.8)	36 (10.0)	104 (28.8)
>= 65 years	272 (75.3)	89 (24.7)	172 (47.7)
Sex at Birth			
Male	168 (46.5)	40 (11.1)	208 (57.6)
Female	103 (28.5)	50 (13.9)	153 (42.4)
Race			
Caucasian	206 (57.1)	59 (16.3)	265 (75.1)
African American	38 (10.5)	21 (5.8)	59 (16.7)
Asian	6 (1.7)	1 (0.3)	7 (2.0)
Native American	0	0	0
Pacific Islander	0	0	0
Unspecified	21 (5.8)	9 (2.5)	30 (8.5)
Ethnicity [a]			
Hispanic	17 (4.7)	7 (1.9)	24 (6.8)
Non-Hispanic	250 (69.3)	82 (22.7)	332 (94.1)
Geography by County			
Hillsborough County	130 (36.0)	42 (11.6)	172 (47.7)
Non-Hillsborough County	141 (39.1)	40 (11.1)	189 (52.4)
Geography by City			
Tampa Metro Area	55 (15.2)	13 (3.6)	68 (18.8)
Outside Tampa Metropolitan Area	216 (59.8)	77 (21.3)	293 (81.2)

[a] Five patients did not disclose ethnicity.

repeating isolates in the same patient, 170 isolates on first case presentation were included in creating the antibiogram for each species. Of the two cases of pulmonary *Mycobacterium tuberculosis* complex and NTM co-infection, one of which had *Mycobactrium fortuitum*, the other with *Mycobacterium gordonae* (Supplemental Figs. E1–E7). Of note, there were six additional cases of individuals with NTM pulmonary infection who had recently treated *Mycobacterium tuberculosis* complex infection (culture negative on admission), three (50%) of which had *Mycobacterium gordonae* pulmonary infection. All NTM isolates were found to be susceptible to clofazimine with the exception of one isolate of *M. chimaera,* which was found to have intermediate susceptibility. Rapid growers (with the exception of *M. fortuitum*) were found to be susceptible to macrolides (>60%). *M. fortuitum* isolates were more susceptible to fluoroquinolones (ie ciprofloxacin and moxifloxacin) than to macrolides. Slow growers were also susceptible to macrolides but with intermediate range susceptibilities to rifampin/rifabutin.

Geospatial distribution of pulmonary and non-pulmonary NTM isolates based on residential zip code showed a diverse geographical sampling within the region that was distributed along areas of fresh, brackish, and salt water bodies of water (Fig. 4).

4. Discussion

Findings of our investigation are consistent with published literature regarding epidemiology of NTM disease being more common among

Table 2
Comorbidities of inpatients with isolates of pulmonary (bronchoaveolar lavage, and extra-pulmonary infection Non-tuberculosis Mycobacteria (NTM) Infection, Tampa General Hospital, Tampa, Florida (January 1, 2011 to December 31, 2017), N = 361 unique individuals.

Medical comorbidity with ntm infection (% of total)	Pulmonary Involvement	Extra-Pulmonary Only	N = 361
Pulmonary Comorbidities	271 (75.1)	90 (24.9)	361 (100.0)
Chronic Obstructive Pulmonary Disease (COPD)	75 (20.8)	8 (2.2)	83 (23.0)
Cystic Fibrosis (CF)	40 (11.1)	0	40 (11.1)
COPD and CF	1 (0.3)	0	1 (0.3)
Pulmonary Fibrosis	12 (3.3)	0	12 (3.3)
Asthma	10 (2.8)	0	10 (2.8)
Bronchiectasis without COPD diagnosis	8 (2.2)	0	8 (2.2)
Alpha-1 anti-trypsin deficiency	2 (0.6)	1 (0.3)	3 (0.8)
Bronchitis	2 (0.6)	0	2 (0.6)
Interstitial Lung Disease	1 (0.3)	1 (0.3)	2 (0.6)
Immotile Cilia syndrome	1 (0.3)	0	1 (0.3)
Persons Living with HIV	35 (9.7)	9 (2.5)	44 (12.2)
Reactive Ab/Ag test [b]	30 (8.3)	9 (2.5)	39 (10.9)
Non-reactive Ab/Ag test	79 (21.9)	28 (7.8)	107 (29.6)
Not tested	160 (44.3)	52 (14.4)	212 (58.7)
Malignancy	50 (13.9)	15 (4.2)	65 (18.0)
Lung	27 (7.5)	1 (0.3)	28 (7.8)
Breast	3 (0.8)	8 (2.2)	11 (3.1)
Gastrointestinal	6 (1.7)	1 (0.3)	7 (1.9)
Hematologic	4 (1.1)	3 (0.8)	7 (1.9)
Prostate	4 (1.1)	0	4 (1.1)
Hepatobiliary	2 (0.6)	1 (0.3)	3 (0.8)
Renal	2 (0.6)	0	2 (0.6)
Female Reproductive	1 (0.3)	1 (0.3)	2 (0.6)
Skin	1 (0.3)	0	1 (0.3)
Solid Organ Transplant	53 (13.6)	14 (3.6)	64 (17.7)
Lung	42 (11.6)	0	42
Heart	7 (1.9)	5 (1.4)	12 (3.3)
Renal	1 (0.3)	6 (1.7)	7 (1.9)
Heart and Renal (Double Transplant)	1 (0.3)	2 (0.6)	1 (0.3)
Liver	2 (0.6)	0	3 (0.8)
Corneal	0	1 (0.3)	1 (0.3)
Diabetes Mellitus (Type I or II)	28 (7.8)	12 (3.3)	42 (11.6)

[b] Total persons living with HIV was 44, with 39 with newly reactive confirmatory testing during January 2011-December 2017.

older age (above 50 years old), Caucasians, and in patients with COPD co-morbidity. [1,12–14] Our data however showed slightly more male predominance and *Mycobacterium abscessus* subsp. abscessus as the most common species causing NTM pulmonary and extra-pulmonary disease in our catchment area. This is in contrast to several other studies that have shown *Mycobacterium avium* complex [14] to be the most commonly isolated in pulmonary NTM infections, not just in the United States but in other countries as well. [9,15–17] A similar epidemiologic study in the U.S. state of Oregon, also observed a female predominance and MAC as the most common species causing NTM pulmonary and extra-pulmonary disease [18].These differences could be due to ecologic

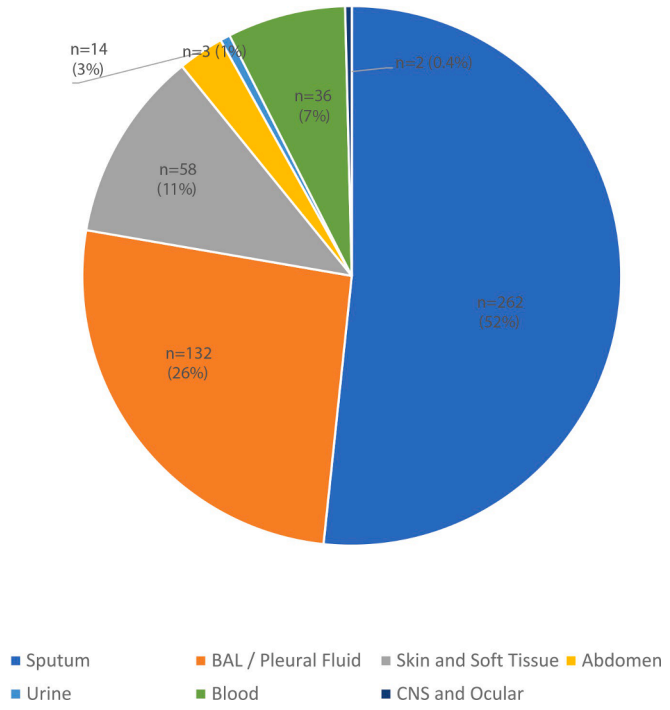

Fig. 1. Distribution of co-morbidities of inpatients with culture confirmed pulmonary, integumental and sites of dissemination/bloodstream infection sites with Non-tuberculosis Mycobacteria (NTM) Infection, Tampa General Hospital, Tampa, Florida (January 1, 2011 to December 31, 2017), N=361.

factors such as differences in soil and water composition between the states of Florida and Oregon in addition to differences in temperature or climates, even though Florida population statistics show a higher female to male ratios for age groups above 40 years of age [13]. Florida may have a higher prevalence of males having preexisting lung conditions such as COPD from prior tobacco or occupational exposure that account for slightly more severe NTM infections warranting hospitalization. Also, our data in the cystic fibrosis population from our facility is similar to other studies, which demonstrated higher incidence of *M abscessus* group infection in those from Florida compared to other NTM such as *M avium* Complex [23,24]. The concept of regional NTM susceptibility should be further explored given the differences in environmental exposure and municipal water treatment practices.

Secondly, our study included 11 additional lesser known NTM species isolated on routine inpatient samples seen more in tropical and subtropical climates. These rare species reflect the diversity of NTM in Florida likely related to both climate and water treatment practices.

Thirdly, geospatial mapping of NTM showed unique cases predominantly residing around bodies of fresh water which again verifies the predilection of non-tuberculous mycobacteria for moist and humid environments. This outcome, however, is limited in that data was acquired from only one acute care center in the region. A larger and more complete sample size that includes other healthcare centers in the area would be warranted to extrapolate more generalizable information.

The antimicrobial susceptibility patterns in this study contribute valuable information to the general knowledge base and treatment of NTM in the state of Florida. It serves as a starting reference in designing an empiric antibiotic regimens for treatment of NTM disease until receipt of susceptibilities from reference laboratories. Rapidly growing NTM were found to be mostly susceptible to macrolides with the exception of *M. fortuitum* for which identified isolates were more susceptible to fluoroquinolones [20]. The understanding of macrolide resistance of *M. fortuitum* complex remains limited at this time with most recent studies exhibiting common mutations of *erm* 39 [19,21]. It is unclear if an environmental milieu such as climate, and/or co-

Table 3
Culture confirmed isolates of pulmonary (bronchoaveolar lavage, and extra-pulmonary infection Non-tuberculosis Mycobacteria (NTM) Infection, Tampa General Hospital, Tampa, Florida (January 1, 2011 to December 31, 2017), N = 507, with 2 myobacterium tuberculosis co-infections in this population panel, N = 509.

Non-tuberculous Mycobacteria	Pulmonary (BAL, Pleural Fluid, or Sputum)	Extra-Pulmonary	Total Number of specimens isolated (%)
TOTAL UNIQUE ISOLATES	396 (77.8)	113 (22.2)	509 (100.0)
Rapid-Growers			
M. abscessus (total)	**155 (30.5)**	**75 (14.7)**	**230 (45.2)**
M. abscessus subsp. *abscessus*	126 (24.8)	49 (9.6)	175 (34.4)
M. abscessus subsp. *massilense*	23 (4.5)	21 (4.1)	44 (8.6)
M. abscessus subsp. *bolletii*	3 (0.6)	3 (0.6)	6 (1.2)
Not subspeciated	3 (0.6)	2 (0.4)	5 (1.0)
M. fortuitum complex (total)	**19 (3.7)**	**16 (3.1)**	**35 (6.9)**
M. fortuitum	17 (3.3)	15 (2.9)	32 (6.3)
M. peregrinum	3 (0.6)	1 (0.2)	4 (0.8)
M. porcinum	0	0	0
M. chelonae	**9 (1.8)**	**4 (0.8)**	**13 (2.6)**
M. mucogenicum	**8 (1.6)**	**0**	**8 (1.6)**
M. smegmatis	0	0	0
Slow-Growers			
M. avium complex (total)	**41 (8.1)**	**1** (0.2)	**42 (8.3)**
M. chimaera	24 (4.7)	1 (0.2)	25 (4.9)
M. intracellulare	9 (1.8)	0	9 (1.8)
M. avium	8 (1.6)	0	8 (1.6)
M. gordonae	95 (18.7)	6 (1.2)	101 (19.8)
M. kansasii	24 (4.7)	1 (0.2)	25 (4.9)
M. szulgai	20 (3.9)	0	20 (3.9)
M. marinum	0	6 (1.2)	6 (1.2)
M. interjectum	0	5 (1.0)	5 (1.0)
M. simiae	3 (0.6)	0	3 (0.6)
M. asiaticum	2 (0.4)	0	2 (0.4)
M. ulcerans	0	1 (0.2)	1 (0.2)
M. triplex	0	2 (0.4)	2 (0.4)
M. parascrofulaceum	0	1 (0.2)	1 (0.2)
M. arupense	1 (0.2)	1 (0.2)	2 (0.4)
M. lentiflavum	0	3 (0.6)	3 (0.6)
M. yongonense	1 (0.2)	1 (0.2)	2 (0.4)
M. gastri	0	1 (0.2)	1 (0.2)
M. phocaicum	1 (0.2)	1 (0.2)	2 (0.4)
M. stomatepiae	0	1 (0.2)	1 (0.2)
M septicum	1 (0.2)	0	1 (0.2)
M. xenopi	0	0	0
M. terrae complex	0	0	0
M. malmoense	0	0	0
M. haemophilum	0	0	0
M. scrofulaceum	0	0	0
***Mycobacterium tuberculosis* complex**			
Not subspeciated	2 (0.4)	0	2 (0.4)

administration of macrolide and fluoroquinolones for treatment of NTM disease could be playing a role in developing *erm* genes in *M. fortuitum* complex isolates. Future micro-ecologic and antibiotic stewardship studies investigating this matter can perhaps provide an answer.

Slow growing NTM pathogens were found to be mostly susceptible to macrolides, however with developing intermediate range susceptibilities for rifampin/rifabutin. This rising resistance to rifampin/rifabutin likely reflects an increasing use of rifamycins as a backbone for treating slow-growing NTM. More studies are needed to elucidate further the mechanism of this developing resistance to rifamycins.

Our study found that most of *M. gordonae* isolates where found among patients living with HIV and lung transplant recipients.

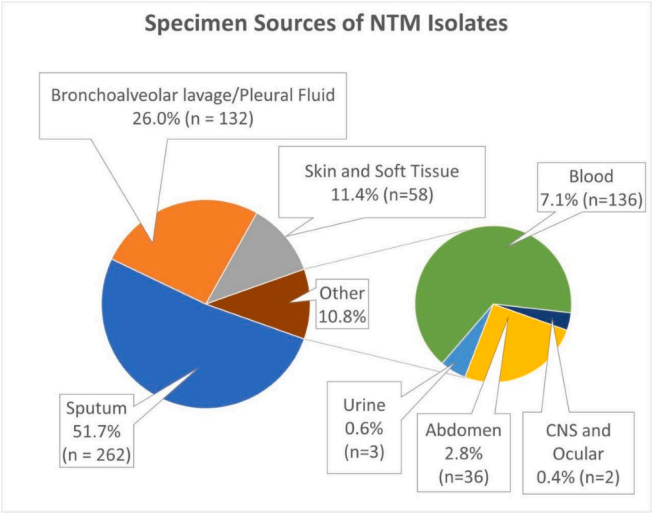

Fig. 2. Anatomical Source of confirmed pulmonary, integumental and sites of dissemination/bloodstream infection sites with non-tuberculous mycobacteria Isolated from inpatients at Tampa General Hospital (January 1, 2011 to December 31, 2017).

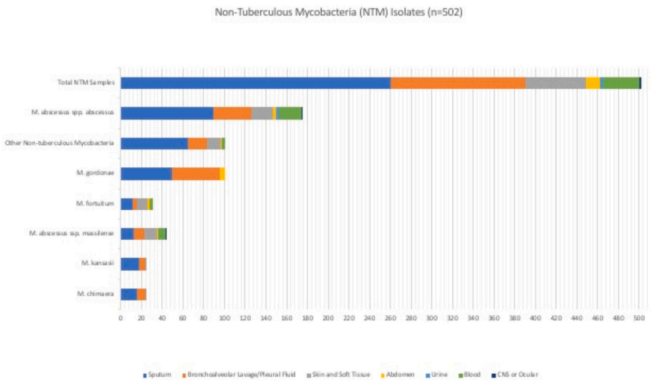

Fig. 3. Graphical representation of confirmed pulmonary, integumental and sites of dissemination/bloodstream infection sites non-tuberculous mycobacteria Isolated from inpatients at Tampa General Hospital (January 1, 2011 to December 31, 2017).

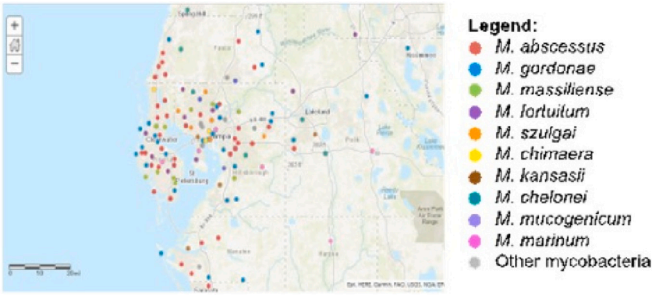

Fig. 4. Geospatial distribution of confirmed pulmonary, integumental and sites of dissemination/bloodstream infection sites non-tuberculous mycobacteria Isolated from inpatients at Tampa General Hospital (January 1, 2011 to December 31, 2017), overlapped onto a detailed mapping for Tampa-St. Petersburg metropolitan area.

M. gordonae is widely considered in the majority of cases to be a contaminant, and thus it is not unusual for it to be seen in the two populations in which we have documented here (Fig. 3).

There were a few limitations to our study. NTM pulmonary or extrapulmonary disease is not a reportable disease in the state of Florida. Due to the lack of a formal surveillance network, specimens are sent to different reference laboratories for speciation and susceptibility testing, which further compounds the challenges in data collection. Data of this study was collected only from one large tertiary referral acute care center (Tampa General Hospital) in Florida, which further limits generalizability of the results of this study to the state level. Also, the microbiologic data collected from our center are from inpatients and thus reflects the gravity of the NTM disease that presented to the medical center as well as noting that there was a male predominance of the patients reviewed. Thus, our data was also limited to only patients who were hospitalized and does not reflect the actual prevalence of NTM in the population of central Florida and thus cannot be correlated to geographical zip code of origin. However, this study can serve as a baseline for designing NTM disease surveillance system in the state of Florida as well as provide valuable data from the antibiogram established by the data. Inclusion of Veterans Affairs Centers and other health care facilities in the state can improve generalizability and accuracy of this study [22].

This study highlighted the logistical challenge of organizing, collecting, and accurately reporting NTM culture data to and from a remote reference lab into an accessible medical record. Of the 831 isolates reported through the TheraDoc® program, only 507 isolates were confirmed by the send out reference lab with only 259 isolates having susceptibility reports. First, multiple culture reports of the same isolate from the same individual were counted as only one isolate in the final analysis. Second, reports from the reference laboratory containing speciation and susceptibilities for the majority of excluded isolates could not be found, due to a lack of a standard protocol reporting system for results from the reference laboratory during 2011–2013, due in part to the launch of the hospital's electronic medical record (EMR) at the time. Third, the reference laboratory did not begin sub speciating isolates until 2013 when PCR methods became available, and standard for the identification of NTM and resistant gene mutations. Fourth, the time interval to speciate the isolate and determine susceptibilities prohibited timely follow up, as the majority of patients had already transitioned to an outpatient setting with a different EMR, leading to disruptions in care, or the loss of patient to follow up altogether. A standard reporting protocol for NTM cultures and susceptibilities from the reference laboratory was implemented in 2016, which should improve the quality of this study's data in succeeding years. From a data analysis perspective, challenges arose in that individual patients had an evolution in both species and resistance patterns found over time and often in multiple admissions to the facility.

5. Conclusions

This study identified a diversity of NTM species across a wide geographical and demographic distribution seen at our large Central Florida medical center. *M. abscessus* group had the highest prevalence. Furthermore, this demonstrates that clinicians must be aware that these pathogens are important causes of disease in certain populations, especially those with pulmonary disease (especially COPD and cystic fibrosis), immunocompromised status and those with severe HIV/AIDS. It is worth noting, that antimicrobial resistance patterns are different depending on the specific organism. Larger studies incorporating data from across diverse civilian and veteran hospital settings, would give an additional understanding into which populations are at risk for which species of NTM infection as well as insight into the optimal treatment options.

This statement of ethics by us the authors is to declare that the research methods were approved by the University of South Florida Institutional Review Board which governs research for Tampa General Hospital as well as the University of South Florida Morsani College of medicine.

6. Contributions

CVG: author, data collection; GET: author, data collection; KZ: author, data collection; RJ: author, data collection; JM: author, study design; BC: author, study design; SA: author, study design; APC: author, study design, data analysis; JPM: author, study design, data analysis, statistics, graphing, geomapping.

7. Grant Support

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8. Disclaimers

The viewpoints and conclusions made in this manuscript do not represent the communicate a specific position of the University of South Florida, Tampa General Hospital or the U.S. Department of Veterans' Administration.

9. Ethics statement

This statement of ethics by us the authors is to declare that the research methods were approved by the University of South Florida Institutional Review Board which governs research for Tampa General Hospital as well as the University of South Florida Morsani College of medicine.

CRediT authorship contribution statement

Cristina V. Garcia: Data curation, Investigation, Resources, Writing – original draft. **Greg E. Teo:** Data curation, Investigation, Resources, Writing – original draft. **Kristen Zeitler:** Data curation, Investigation, Resources, Writing – original draft. **Ripal Jariwala:** Data curation, Investigation, Resources, Writing – original draft. **Jose Montero:** Formal analysis, Investigation, Resources, Writing – original draft. **Beata Casanas:** Formal analysis, Investigation, Resources, Writing – original draft. **Sadaf Aslam:** Formal analysis, Investigation, Resources, Writing – original draft. **Anthony P. Cannella:** Conceptualization, Methodology, Supervision, Validation, Formal analysis, Investigation, Resources, Writing – original draft. **Jamie P. Morano:** Funding acquisition, Conceptualization, Methodology, Supervision, Conceptualization, Methodology, Supervision, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jctube.2021.100289.

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