



Epidemiological situation of mycobacterioses in Ukraine and the worldwide at the beginning of the 21st century: A literature review

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Abstract. The lack of a unified reporting system for clinical outbreaks of mycobacterioses makes it difficult to objectively assess the epidemiological situation and identify patterns in the epidemic process, despite the growing relevance of this issue in human and veterinary medicine. The aim of this review was to study the epidemiological and aetiopathogenetic aspects of mycobacterioses in Ukraine and other countries on different continents. A comparative-geographic method and epidemiological analysis method were used in the study. As a result, it was found that in Ukraine, mycobacterioses in humans are widespread, with 94% of cases manifesting as pulmonary forms, often forming mixed infections with tuberculosis, making them difficult to diagnose. The most common aetiological factor is *M. avium complex* and disseminated mycobacteriosis usually develops in HIV-infected patients. In most of the analysed countries (Japan, South Korea, Iran, Turkey, Pakistan, Saudi Arabia, Egypt, Oman, Kuwait, China, France, Great Britain, Italy, Greece, Czech Republic, Poland, USA, Canada, Brazil, Australia and several African countries) during the period 2000-2023, there was an observed increase in the incidence of lung diseases caused by non-tuberculous mycobacteria, including an 8-fold rise in South Korea; an annual growth of 8% in the USA; and a 2.3-fold increase in Queensland (Australia) from 11.1 pcm in 2001 to 25.88 pcm in 2016. It was established that the epidemiological features of mycobacterioses are the predominant infection of patients with rapidly growing mycobacteria; an increased risk of mycobacterial infection with increasing age; detection of *M. avium complex*, *M. abscessus complex*, *M. kansasii* and *M. fortuitum* as the most common cause of mycobacterioses

Keywords: human mycobacterioses; nontuberculous mycobacteria; epidemiology of mycobacterioses; *M. avium complex*

✦ INTRODUCTION

According to the World Health Organisation's 2022 tuberculosis report, the annual number of diagnosed cases worldwide is around 6.4 million [1]. Nontuberculous mycobacteria (NTM) are the second most common cause of mycobacterial infections. M. Lipman *et al.* [2] established that there are about 190 species and 14 subspecies, with their number continuously increasing. Data from J.E. Gross *et al.* [3] and J.W. Alffenaar *et al.* [4] show that mycobacterioses of the nontuberculosis complex are a growing problem

in human medicine that is becoming increasingly relevant each year. There are many uncertainties regarding the treatment of nontuberculous mycobacterial lung diseases (NTM-LD), the peculiarities of their epidemiology have not been studied, methods of a comprehensive diagnosis of mycobacterioses and laboratory diagnosis, in particular, have not been unified, treatment protocols have not been unified, and prevention measures are extrapolated from the Guidelines for the control of other infections [5, 6].

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The nation's health is, first and foremost, healthy food free of pathogens common to humans and animals. Healthy food can be obtained from healthy animals. Currently, about a dozen species of NTM are known to be causative agents of mycobacterioses in humans and animals [7, 8]. In this context, the prevention of mycobacterioses in animals caused by NTM is an urgent problem for veterinary medicine in Ukraine [9, 10]. I. Pavlik *et al.* [8] found that every year in Ukraine, during planned allergic tests for tuberculosis in cows in 250 or more dairy farms, animals are found that give pseudo-allergic reactions to tuberculin, which indicates sensitisation of their bodies to NTM.

Research by P. Boiko *et al.* [11] indicates that pathological changes were found in the bodies of animals that reacted positively to PPD-tuberculin, and NTM were isolated, including *M. scrofulaceum* and *M. fortuitum*. This led to the conclusion that an infectious mycobacterial process was present in the cows reacting to tuberculin and that an epizootological process of mycobacteriosis caused by NTM was occurring in the herd. The isolation and identification of these pathogens are evidence of their importance as etiological factors of human mycobacteriosis. Mycobacterioses of productive, domestic and wild animals are also widespread in other countries of the world [12].

The absence of data on the diagnosis of mycobacterioses caused by NTM in official reports from government institutions responsible for epidemiological surveillance and control of infectious diseases in Ukraine, as well as in the World Health Organisation's global registry, hinders the ability to recreate a complete picture of the spatial-temporal dynamics of the epidemiological situation concerning NTM-caused mycobacterioses. Therefore, the study aimed to systematise and analyse the epidemiological results of studies of human mycobacterioses conducted by scientists from different countries, including Ukraine.

Epidemiological analysis was conducted on 49 scientific studies on the role of NTM in the infectious process of human mycobacterioses, its forms and duration, the impact of environmental factors and its manifestation in various countries worldwide from 2000 to 2023. The criteria for the scientific search were indicators that, first of all, characterise the intensity of the manifestation of the epidemiological process of mycobacterioses, the analysis of the role of various aetiopathogenetic factors, the influence of contributing and predisposing factors on the intensity of the epidemiological situation regarding human mycobacterioses for the specified period. The study used comparative-geographical and statistical research methods, as well as the method of epidemiological analysis.

◆ ENVIRONMENTAL MYCOBACTERIA – POTENTIAL PATHOGENS OF HUMAN AND ANIMAL MYCOBACTERIOSES

Mycobacteriosis (Latin: *mycobacteriosis*) is an infectious disease of humans and animals caused by representatives of a large group of NTM, including *Mycobacterium avium*, *M. fortuitum*, *M. kansasii*, *M. scrofulaceum*, *M. xenopi* and others [13, 14]. They are also called atypical mycobacteria (ATM) or environmental mycobacteria. During 2010-2020, there was a significant increase in the prevalence of NTM and the incidence of infections caused by them [15]. Mycobacterioses has become a major public health problem

worldwide. Among the numerous species of NTM, the *Mycobacterium avium* Complex (MAC) is the predominant species, which has been recognised as a ubiquitous microorganism – it is isolated from polluted water and soil [16]. However, the main causes of the increase in MAC-associated disease are not yet fully understood. This is mainly because human infection with MAC is associated with various sources of the infectious agent [17].

Identifying the causal links between the source of the infectious agent and its epidemiology is a crucial step towards developing new prevention strategies and effective control of MAC infection. This issue pertains not only to *M. avium* but also to most NTM. As research by many scientists indicates, the majority of these microorganisms are saprozoites. Only some of them, such as the *M. avium-intracellulare* complex, *M. kansasii*, *M. abscessus*, *M. chelonae* and some others, have formed the features of facultative, or even completed pathogens. This fully applies to *M. ulcerans*, which causes Buruli ulcer and is found in regions with hot tropical climates – Africa, Australia, Mexico and others [18]. This is evidence that the evolution of pathogenicity in these microorganisms continues [19].

Due to the widespread distribution of NTM in various biotic and abiotic environments, confirming their aetiopathogenetic role requires repeated isolation of these microorganisms from the source of infection. Consequently, the American Thoracic Society has developed microbiological, clinical, and radiological criteria for determining the etiological role of NTM in HIV-infected and non-HIV-infected patients [20].

Although NTM were discovered after *M. tuberculosis*, their potential ability to cause human lung disease was not recognised until the 1950s. In 1954, the Runyon classification of NTM was proposed [14], which divides mycobacteria into four main groups based on their growth rate, colony morphology, and ability to produce pigments. The most common NTM in clinical practice includes the *M. avium-intracellulare* complex (MAIC-complex), *M. kansasii*, *M. fortuitum*, *M. abscessus*, *M. chelonae*, *M. marinum*, and several others. These bacteria are frequently isolated from water, soil, and other environmental sources [21, 22].

Monitoring the epidemiological characteristics and aetiology of mycobacterioses in different countries of the world usually concerns NTM isolated from patients with pulmonary pathology, while skin and soft tissue infections are analysed much less frequently. However, the results of microbiological studies of clinical samples indicate that NTM were isolated from extrapulmonary tissues (maxillary and frontal sinuses, wounds and skin) no less often than from pulmonary samples [23]. These data indicate the pleiotropic pathogenic action of mycobacteria on different tissues and organs of the infected organism, which in turn suggests that NTM possess a broad spectrum of aggressive factors with genotypic control and phenotypic expression. The epidemiological process of mycobacteriosis includes the interaction of three main components: the source of infection, the mechanisms of transmission of the pathogen, and organisms susceptible to the disease. This interaction takes place under the influence of various environmental factors. At the same time, the latter factor often plays a decisive role in the manifestation of the infectious process of mycobacteriosis [24].

The sources of mycobacterial infections in humans are individuals infected with NTM. However, given the relatively young age of the problem of mycobacterioses, the first link in the epidemiological chain has been insufficiently studied. However, it has been established that NTM is present in water, biofilms, soil, and aerosols, meaning these microbes are ubiquitous. They are natural inhabitants of the human environment, especially drinking water distribution systems. Thus, it is quite likely that everyone is exposed to them daily. This is one of the reasons for the increase in the incidence of mycobacterial infections caused by environmental mycobacteria [25]. It is obvious that the incidence of mycobacterioses caused by environmental NTM will continue to grow. This growth will be partly due to increased awareness of these microbes as human disease pathogens, and partly to improved methods of detection, cultivation and identification of the pathogens themselves [26].

Mycobacterioses, according to some scientists, mainly have a tuberculosis-like clinical pattern and therefore are difficult to identify using classical diagnostic methods. They often occur in the form of mixed infections with other mycobacterioses, including tuberculosis [27]. In addition, atypical mycobacteria are characterised by a wide range of resistance and are potentially pathogenic for humans and animals. Up to 80% of cases of human mycobacterioses are caused by *M. avium complex*. Mycobacterioses are most commonly found in people infected with the human immunodeficiency virus (HIV), and a CD4+ lymphocyte count below 50/μL can lead to the development of disseminated mycobacteriosis. The causative agent of this type of mycobacterial infection is usually MAC (90% of cases) [28]. Considering that the reservoir of *M. avium* is open water bodies, NTM aerosols formed over the water surface infect people by air. Sick poultry are also a powerful source of NTM and thus play an important role in the local functioning of the epidemiological process of mycobacteriosis.

It has been established that disinfection may, in part, contribute to the resistance of *M. avium* and *M. intracellulare* in drinking water distribution systems. Thus, *M. avium* and *M. intracellulare* are many times more resistant to chlorine, chloramine, chlorine dioxide, and ozone than other waterborne microorganisms. Therefore, disinfection of drinking water leads to the predominance of mycobacteria over other water microbiota. In the absence of competitors, even slowly growing mycobacteria can proliferate in the water distribution system [29]. Studies of the spatiotemporal characteristics of the spread of mycobacterioses in Ukraine and around the world can help to identify new patterns in the development of epidemic processes and determine their defining factors for mycobacterioses.

★ MYCOBACTERIOSES IN HUMANS: SPATIOTEMPORAL PATTERNS OF THE EPIDEMIC PROCESS IN UKRAINE AT THE BEGINNING OF THE 21ST CENTURY

The increasing incidence of mycobacterioses caused by NTM in different regions of the world is attracting increasing attention from scientists. It has been noted that the geographical location of a country affects the species prevalence of NTM [12, 16]. Studying the epidemiological situation of mycobacterioses in Ukraine, L. Todoriko & O. Shevchenko [14] found that the incidence of this

infectious disease is 2.3 per 100,000 population (2.3 pcm). It has been established that mycobacterioses in humans can manifest in various forms, including pulmonary (nodular bronchiectatic form usually occurs in older (70 years old) women; cavitary form (fibro-nodular) is typical for men 40-50 years old who smoke and abuse alcohol; hypersensitivity lung syndrome, which usually proceeds subacutely; patients are more often young people who do not smoke).

Pulmonary manifestation of the infection is the primary form and is observed in 94% of cases. In addition, disseminated mycobacterioses are often diagnosed, which develop in patients with stage IV AIDS, after kidney or heart transplantation, with prolonged use of GCs (glucocorticosteroids) and patients with leukaemia. The main causative agents are *M. avium* and *M. kansasii*. Another form of manifestation of mycobacterioses is lymph node damage, which occurs mainly in children under 5 years of age. The affected lymph nodes are typically tonsillar, preauricular, and/or submandibular on one side. The causative agent in most cases is MAC. Without treatment, the lymph node may spontaneously rupture, leading to the formation of a fistula [14].

O. Shevchenko *et al.* [27] demonstrated that in the clinic of internal infectious diseases, mycobacterioses of various types are increasingly being diagnosed, indicating a growing role of atypical mycobacteria in the development of respiratory system pathology. The clinical pattern resembles tuberculosis, they are difficult to diagnose, and often form mixed infections with tuberculosis. NTM are characterised by a wide range of resistance to disinfectants, antibacterial agents, and environmental factors and are potentially pathogenic for humans.

It has been established that risk factors for developing mycobacterioses include a history of respiratory diseases (COPD, bronchiectasis, pneumoconiosis, cystic fibrosis), previous tuberculosis (mycobacterial disease incidence increases tenfold compared to the population level), work with farm animals and poultry; increased joint stress, mitral valve prolapse, gastroesophageal reflux disease, rheumatoid arthritis, taking GCs in doses greater than 15 mg/day for more than 14 days, and immunosuppressants [14].

O. Zhurilo *et al.* [17] studied the species diversity of NTM on the territory of Ukraine during 2014-2018. Phenotypic identification of isolates was carried out using cultural and biochemical methods. The most common isolates were *M. avium-complex* – 45.5%, the number allocated *M. fortuitum* – 13.5%, less often – *M. xenopi* (7.1%), *M. kansasii* (5.8%) and *M. scrofulaceum* – 3.2%. At the same time, slowly growing mycobacteria were isolated 6 times more often than rapidly growing.

Based on the genotypic identification of mycobacterial cultures using GenoType Mycobacterium CM/AS, 11 NTM species were identified, 7 of which were assigned to slowly growing NTM groups (groups I–III according to Runyon), including *M. avium*, *M. intracellulare*, *M. gordonae*, *M. kansasii*, *M. xenopi*, *M. malmoence*, *M. scrofulaceum*, and 4 to the group of rapidly growing NTM (group IV according to Runyon), including *M. abscessus*, *M. chelonae*, *M. fortuitum*, *M. peregrinum*. The frequency of MAC among NTM in general was 53.24% (71/133). However, regional variations were observed, with MAC predominating among slowly growing NTMs in the Dnipropetrovsk, Zhytomyr, Chernihiv, Chernivtsi, and Cherkasy regions.

In contrast, in the Poltava and Kyiv regions, MAC was not the predominant group among slowly growing NTM. A notable feature of the Chernivtsi region was that within the MAC group, *M. intracellulare* was more common than *M. avium*, whereas, in all other regions, *M. avium* predominated within the MAC group. Among rapidly growing NTM, the predominant species in all regions of Ukraine was *M. fortuitum* (86.96% among rapidly growing NTM). Single isolates of *M. abscessus*, *M. chelonae* i *M. peregrinum* were identified [17].

The data show that significant attention is paid to the study of the aetiopathogenesis and epidemiological features of human mycobacterioses in Ukraine. However, the problem of mycobacterioses is multifaceted and requires a deeper study of other aspects of the infectious and epidemiological process of this infectious pathology.

★ EPIDEMIOLOGICAL ASPECTS OF HUMAN MYCOBACTERIOSES IN THE WORLD DURING 2000-2023

Aiming to predict the epidemiological situation and clinical manifestations of lung diseases caused by NTM, (NTM-LD) and tuberculosis, Japanese scientists conducted a multifactorial epidemiological analysis of all cases of mycobacterial isolation at Fukuji Hospital during the period 2006-2016. Identification of mycobacterial isolates was carried out according to the microbiological criteria of the American Thoracic Society and the Infectious Disease Society of America. It was found that the most common isolates were the *M. avium* complex (87.3%), the *M. abscessus* complex (5.5%), and *M. kansasii* (3.9%) [30].

In studying the characteristics of the epidemic process and the dynamics of the intensity of the epidemic situation regarding mycobacterioses of the population of South Korea from 2001 to 2015, Korean scientists found that the incidence of NTM-LD increased nearly 8-fold during this period – from 7.0 pcm (in 2001) to 55.6 pcm (in 2015). Just like in Japan, in South Korea, the most common causative agent of NTM-LD was the *M. avium* complex (n = 1,746; 75%), *M. abscessus* (n = 519; 22%) and *M. kansasii* (n = 64; 3%) [31].

In China, lung diseases caused by NTM are being diagnosed more and more often each year. This is causing growing concern in the healthcare sector. A study of the aetiology and epidemiological characteristics of mycobacterioses in the population of South China during the period (2013-2016) showed that the most common causative agents of this infectious pathology were the *M. avium* complex (44.5%), the *M. abscessus* complex (40.5%), and much less often *M. kansasii* (10.0%) and *M. fortuitum* (2.8%). The authors believe that the epidemiological characteristics of mycobacterioses are as follows: significantly higher infection rates with rapidly growing mycobacteria compared to slowly growing ones; a sharp increase in the risk of infection with rapidly growing mycobacteria with advancing age; and pulmonary diseases caused by rapidly growing mycobacteria being more common among migrants than among the resident population [32]. The data obtained by Chinese scientists confirm the conclusions drawn by Japanese and Korean researchers and indicate that the most commonly identified causative agents of mycobacterial infections are *M. avium* complex, *M. abscessus* complex, *M. kansasii* and *M. fortuitum*.

Scientific research by a team of authors is dedicated to highlighting individual aspects of the epidemiology of mycobacterioses caused by NTM in Middle East countries [33]. They found that out of 1,084 strains isolated from primary clinical samples, 434 (40.0%) were identified in Iran, 280 (25.8%) in Turkey, 137 (12.6%) in Saudi Arabia, 116 (10.7%) in Pakistan, 47 (4.3%) in Egypt, 43 (3.9%) in Lebanon, 14 (1.2%) in Kuwait, and 13 (1.1%) in Oman. At the same time, 637 (58.7%) isolates were identified as slowly growing mycobacterial species, and 447 (41.2%) as rapidly growing; *M. fortuitum* was the most common isolate (269 out of 447; 60.1%) [34]. The data obtained give reason to assert that in Middle Eastern countries, mycobacterioses is not an uncommon phenomenon in infectious pathology, but a fully formed nosological unit that should be under constant control of infectious disease specialists.

According to scientific publications, mycobacterioses of the population caused by NTM are registered annually in almost all countries of the American continent. Thus, during 2015-2017 in the USA, the incidence of mycobacterioses caused by NTM ranged from 2.3 to 3.9 pcm. The prevalence of NTM-LD in the United States in 2019 was significantly higher than the prevalence of tuberculosis. The results of epidemiological monitoring confirm an annual increase in the incidence of NTM-LD by 8% annually [35].

Analysis of the results of microbiological studies of clinical samples from 20,617 patients with lung diseases in the population of Ontario (Canada) for the period 2001-2013 showed that in 10,936 cases, which is 53%, NTM were isolated, including MAC and *M. abscessus* complex, which were more often isolated from clinical samples taken from female patients [36]. This fact requires prolonged and repeated validation to be considered an objective pattern, but it merits the attention of infectious disease specialists.

Monitoring the aetiology of mycobacterioses in the USA is primarily focused on NTM isolated from patients with pulmonary pathology, while skin and soft tissue infections are analysed much less frequently. The results of microbiological studies of clinical samples from 1,033 patients in North Carolina (USA) indicate that *M. chelonae* and *M. fortuitum* (both rapidly growing species) were most often isolated from extrapulmonary tissues (maxillary and frontal sinuses, wounds and skin), while *M. avium* was isolated from pulmonary samples [37].

The incidence of pulmonary diseases caused by nontuberculous mycobacteria is also growing in South America. For example, in Brazil (Rio Grande do Sul state) in Porto Alegre, data from 100 patients with NTM-LD were analysed during the period 2003-2013. It was found that the most common NTM species isolated from patients were *M. avium* complex (MAC) – in 35% of cases; *M. kansasii* – in 17%; and *M. abscessus* – in 12% [38].

The data obtained indicate, on the one hand, that the dominant NTM species in human infectious pathology in Asian countries are the same as in American countries, indicating that the main pathogenicity factors of Asian NTM species differ little in virulence from American ones. On the other hand, this may be evidence that the evolution of mycobacterial pathogenicity proceeded simultaneously on all continents, with the formation of the main mechanisms of the aetiopathogenesis of mycobacterioses occurring

against the backdrop of the interaction between microorganisms and macroorganisms. In this interaction, the key factor from the microorganism's side was the development and expression of pathogenic factors, while from the microorganism's side, it was the multifaceted mechanism of specific protection against these factors.

In the European Union countries during 2011-2016, there has been an increase in the tension of the epidemiological situation regarding NTM infections, in particular, the incidence of various population groups is growing annually, both in individual countries and on the continent as a whole [39]. Thus, in Greece, the epidemiological situation regarding pulmonary NTM infections is largely unknown. However, a multifactorial epidemiological analysis and the results of bacteriological studies of clinical samples for the period 2007-2013 showed that the incidence of pulmonary NTM infections of the aetiology of the population of Greece is 18.9 pcm among inpatients and 8.8 pcm among outpatients. Identification of isolates was carried out according to microbiological criteria established by the American Thoracic Society and the Infectious Disease Society of America. At the same time, the microbial spectrum of NTM species was quite wide and amounted to 13 species, but most often *M. avium* – 13%, *M. intracellulare* – 10%, *M. goodii* – 14%, *M. fortuitum* – 12% were identified [40].

NTM play a significant role in the aetiology of infectious lung diseases in France. Thus, among 1,582 patients with cystic fibrosis, the prevalence of NTM was between 3.7-9.6%. The most commonly identified were *M. abscessus* complex and *M. avium* complex. At the same time, isolates of the first species predominated in groups of persons aged 11-15 years, while isolates of the second species were in patients older than 25 years. Scientific observations of the prevalence of NTM-related diseases conducted at the Bordeaux University Hospital (France) for the period 2002-2013 showed that lung diseases were detected in 170 patients (54.1%), followed by skin and soft tissue infections (22.9%), disseminated cases (10.6%), lymphadenitis (7.7%), bone and joint infections (2.9%), and the remaining 1.8% were catheter-related infections. A total of 16 NTM species were identified. The most commonly isolated were *M. avium* (31.8%) and *M. intracellulare* (20%), *M. marinum* (13.5%), *M. kansasii* (10.6%), *M. xenopi* (9.4%); at the same time, rapidly growing mycobacteria accounted for 9.4%, and slowly growing mycobacteria – 5.3% [41].

Epidemiological aspects of pulmonary infections caused by NTM were studied in Poland by G. Przybylski *et al.* [42] during 2013-2022. Of the 395 patients with infectious lung pathology, 149 cases met the diagnostic criteria for NTM-LD. At the same time, *M. kansasii* (51.68%) and *M. avium* complex (46%) were most often identified.

In Italy during the period 2004-2014, 42,055 clinical samples collected from 15,000 patients with suspected mycobacterial infection were tested. At the same time, mycobacteria were isolated from 595 patients. In 448 (75.3%) patients, *M. tuberculosis* complex was isolated, and NTM was isolated from 147 (24.7%) patients. A total of 16 NTM species were identified, the most common of which was *M. avium* subsp. *hominissuis* (41.5%). This was followed by the number of identified cases: *M. intracellulare* – 14.3%, *M. goodii* – 11.6%, *M. xenopi* – 9.5%, *M. fortuitum* – 6.8% and *M. kansasii* – 4.8% [43].

The species profile and incidence of NTM-related diseases were significantly different in the historical territories of Moravia and Silesia (Czech Republic). A team of scientists conducted an epidemiological analysis of the incidence of NTM-related mycobacterioses for the period 2012-2018 and investigated the correlation with some socio-economic and environmental factors. It was found that the most commonly isolated NTM were *M. avium-intracellulare*, *M. kansasii* and *M. xenopi*. The incidence of NTM-LD in the population was 1.10 pcm, while among men it was 1.33 pcm and 0.88 pcm among women [44].

The conclusions made by the authors suggest that geographical living conditions influence the species composition of mycobacterioses pathogens, the intensity of the epidemic process as indicated by disease incidence, and the greater susceptibility of men compared to women. This may reflect the impact of provoking (such as hypodynamia, psychogenic stress) and/or contributing (such as smoking, alcohol abuse, etc.) factors on the male organism.

Regarding the United Kingdom, there is limited analytical data on the incidence of NTM-LD. At the same time, there is no consensus on the optimal treatment regimens for this infectious pathology. A team of scientists conducted a retrospective study of NTM-LD at a London teaching hospital for the period 2000-2007. The criteria for inclusion in the retrospective analysis were as follows: only cultures of slowly growing mycobacteria were considered, the age of patients was over 18 years, they were HIV-negative, and the NTM isolates met the criteria of the American Thoracic Society. As a result, it was found that *M. kansasii* was identified in 93% of patients, *M. avium intracellulare* in 63%, *M. malmoense* in 60%, and *M. xenopi* in 25% [45].

A study of the aetiopathogenesis and the intensity of the epidemiological situation regarding NTM infections in the Netherlands from 2013 to 2019 showed that the isolation of NTM increased from 1.0% to 3.6% during this period. Single isolation of NTM in adults was 53.7% and in children – 60.0%. *M. abscessus* and *M. avium* complex were most commonly identified – 47.1% and 30.9%, respectively. The authors conclude that the increase in the number of positive cases of NTM identification is a consequence of unsatisfactory treatment outcomes and the associated decline in lung function. The researchers emphasise that NTM-LD is a serious health problem among patients with cystic fibrosis in the Netherlands [46]. Analysing the data presented in this and the previous article, it can be noted that in the aetiology of mycobacterioses, the predominant influence on the manifestation of the infectious and epidemiological process comes from contributing and predisposing factors, rather than the pathogenic properties of NTM.

The overall prevalence of NTM in pulmonary samples in Sub-Saharan Africa (Nigeria, Mali, Ghana, Zambia, South Africa, Kenya, Uganda, Tanzania, and Ethiopia) was 7.5% (7.2-7.8%). *MAC* species constituted 28.0% of all isolated NTMs. The prevalence of *MAC* complex NTM in Tanzania ranged from 15.0% to 57.8% [47]. Regional variability in the distribution of NTMs was observed. Specifically, 76.4% (2,355 isolates out of 3,084) of *MAC* complex isolates from South Africa were *M. intracellulare*, while all *MAC* complex isolates from Mali were *M. avium*. Rapidly growing mycobacteria, such as *M. fortuitum*, *M. chelonae* and *M. abscessus*, accounted for only 1.2% [48, 49].

From 2001 to 2016, there were 12,219 registered cases of NTM in patients over the age of 18 in Queensland, Australia. The most common species were *M. intracellulare* (39.1%), *M. avium* (9.8%), *M. abscessus* (8.5%), *M. fortuitum* (8.3%), *M. chelonae* (3.3%), and *M. kansasii* (2.4%). Over 15 years (2001-2016), the incidence rate increased 2.3-fold, from 11.1 pcm in 2001 to 25.88 pcm in 2016 [16].

As can be seen from the data presented, the species composition of aetiopathogenetic NTM species on the Australian continent is similar to that in most countries of the world. At the same time, there is a steady increase in the incidence of mycobacterioses in the population of Oceania, which, first of all, indicates an increasing role of NTM in the infectious pathology of the respiratory system and other body systems of humans. Summarising the above, it can be stated that the problem of mycobacterioses requires comprehensive study in each individual country and the world as a whole.

◆ CONCLUSIONS

According to the results of the epidemiological analysis of the spatiotemporal features of the spread of mycobacterioses caused by NTM in Ukraine and on different continents of the world from 2000 to 2023, a significant increase in the incidence of these infections has been identified. In 94% of cases, mycobacterioses in Ukrainian patients manifest as pulmonary diseases, often forming mixed infections with tuberculosis. At the same time, *M. avium complex* is the isolated aetiological factor in almost 80% of cases. In most of the analysed countries, an increase in the incidence of NTM-LD was observed throughout observation, including an 8-fold increase in South Korea; an annual increase of 8% in the USA; and a 2.3-fold increase in Queensland (Australia) from 11.1 pcm in 2001 to 25.88 pcm in 2016.

Among the epidemiological characteristics of mycobacterioses, it is noteworthy that patients are predominantly infected by rapidly growing mycobacteria, the risk of infection increases with age, and there is a higher prevalence of mycobacterial lung infections among migrants compared to the local population. The most frequently isolated strains from biological samples were the *M. avium complex* (87.3%), *M. abscessus complex* (5.5%), and *M. kansasii* (3.9%). The data presented by various researchers

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indicate the pleiotropic of the pathogenic action of mycobacteria on tissues and organs, which, in turn, suggests a broad spectrum of aggressive factors.

Analysing the features of the infectious and epidemiological processes of mycobacterioses in different countries of the world, it can be assumed that the evolution of the pathogenicity of nontuberculous mycobacteria proceeded simultaneously on all continents, and the formation of the main mechanisms of the aetiopathogenesis of mycobacterioses was carried out against the background of the interaction of the microorganism and the macroorganism. At the same time, the determining factor from the side of the microorganism was the formation and implementation of pathogenicity factors, and from the side of the macroorganism – a multifactorial mechanism of specific protection against these factors. This, in turn, led to a special manifestation of the epidemiological process of this infection, a comprehensive study of which will reveal the details of its driving forces and will serve as the basis for the development of effective prevention measures for this infectious pathology.

The evolution of these relationships against the background of the constant or permanent influence of the stressful political-social and anthropo-ecological situation is developing towards an increase in the virulent properties of mycobacteria, which leads to a change in the way of existence of a number of mycobacteria species – from saprophytic to parasitic, thereby increasing the population of true pathogens. The study of the ecology of the most common causative agents of NTM infections, and their survival in animal products during technological processing will be the next stage of the author's scientific research, the results of which will make it possible to more effectively control the epidemiological process of mycobacterioses at the link of the mechanism, routes and factors of transmission of the causative agent of this infectious pathology of humans.

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◆ CONFLICT OF INTEREST

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Епідемічна ситуація щодо мікобактеріозів в Україні та світі на початку XXI століття: огляд літератури

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Анотація. Відсутність єдиної системи звітності про клінічні спалахи мікобактеріозів ускладнює об'єктивну оцінку епідемічної ситуації та виявлення закономірностей епідемічного процесу, незважаючи на зростаючу актуальність цієї проблеми в гуманній та ветеринарній медицині. Метою цього огляду було вивчення епідеміологічних та етіопатогенетичних аспектів мікобактеріозів як в Україні, так і в інших країнах різних континентів. В роботі використано порівняльно-географічний метод та метод епідеміологічного аналізу. Внаслідок проведеної роботи встановлено, що в Україні мікобактеріози людей мають значне поширення, у 94 % випадків перебігають у легеневої формі, часто формують мікст-інфекції з туберкульозом, а тому важко діагностуються. Найчастіше етіологічним чинником виступає *M. avium complex*, а у ВІЛ-інфікованих пацієнтів зазвичай розвивається дисемінований мікобактеріоз. У більшості аналізованих країн (Японія, Південна Корея, Іран, Туреччина, Пакистан, Саудівська Аравія, Єгипет, Оман, Кувейт, Китай, Франція, Великобританія, Італія, Греція, Чехія, Польща, США, Канада, Бразилія, Австралія та низка країн Африки) за період 2000-2023 рр. спостерігалось зростання захворюваності населення на хвороби легень, спричинені нетуберкульозними мікобактеріями, зокрема у Південній Кореї у 8 разів; у США щорічно на 8 %; у Квінсленді (Австралія) у 2,3 рази – з 11,1 рсм у 2001 році до 25,88 рсм у 2016 році. Встановлено, що епідеміологічними особливостями мікобактеріозів є переважне інфікування пацієнтів швидкоростучими мікобактеріями; зростання ризику інфікування мікобактеріями із збільшенням віку; виявлення *M. avium complex*, *M. abscessus complex*, *M. kansasii* і *M. fortuitum*, як найчастішої причини мікобактеріозів

Ключові слова: мікобактеріози людини; нетуберкульозні мікобактерії; епідеміологія мікобактеріозів; *M. avium complex*