LUMEN ET VIRTUS
ISSN: 2177-2789

DIAGNOSIS AND TREATMENT OF MYCOPLASMA PNEUMONIAE INFECTION: A SYSTEMATIC REVIEW

https://doi.org/10.56238/levv15n42-050

Submitted on: 20/10/2024 **Publication date:** 20/11/2024

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ABSTRACT

Objective: The general objective of the present study is to analyze the scientific production on Mycoplasma pneumoniae and its relationship with atypical bacterial pneumonia, seeking to identify the main complications and diagnostic and therapeutic methods associated with this infection. Methodology: This is a systematic review focused on understanding infections caused by Mycoplasma pneumoniae. The research was guided by the question: "What are the complications and treatment methods of Mycoplasma pneumoniae infection based on the evidence available in the scientific literature?". To find answers, searches were performed in the PubMed database using three descriptors combined with the Boolean term "AND". This resulted in 123 articles. 20 articles were selected for analysis and 14 articles were used to compose the collection. Results: Mycoplasma pneumoniae is a common cause of community-acquired pneumonia (CAP) and presents with a range of clinical manifestations ranging from mild respiratory infections to severe complications, including extrapulmonary manifestations. The most frequent extrapulmonary complications include neurological, dermatological, and hematological complications. This review highlighted the importance of modern diagnostic methods, such as nucleic acid

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amplification (PCR), which allows for rapid and accurate detection of infection. In treatment, macrolides, especially azithromycin, are preferred because of their safety profile, especially in children. In addition, the use of corticosteroids and immunoglobulins has been explored in severe cases with extrapulmonary complications, although further studies are needed to validate these treatments. Conclusion: Mycoplasma pneumoniae infection represents a significant clinical challenge due to its wide range of manifestations and the need for effective diagnostic and therapeutic methods. The review emphasizes the importance of rapid and accurate diagnostic approaches, as well as the need for therapeutic strategies that can address both respiratory infections and extrapulmonary complications. More research is needed to improve the understanding of associated complications and develop innovative therapeutic interventions.

Keywords: Mycoplasma pneumoniae. Atypical bacterial pneumonia. Complications. Treatment. Diagnosis.

INTRODUCTION

Community-acquired pneumonia (CAP) is associated with high morbidity and mortality, and the disease is also a major threat to public health worldwide. About 8–40% of CAP in children admitted to hospitals were caused by Mycoplasma pneumoniae. Based on cases reported in China, M. pneumoniae infections accounted for 19.2% of all cases of CAP in adults, and the prevalence of CAP in children and adolescents ranged from 10% to 30%. In the US, a recent study of 2,254 children hospitalized with CAP showed that 8% of children with a mean age of 7 years were positive for M. pneumoniae by polymerase chain reaction (PCR) (JIANG et al., 2021).

Mycoplasma pneumoniae (M. pneumoniae) is a small microorganism (2-5 μm) that is Gram-negative, without a cell wall, and can replicate autonomously (JIANG et al., 2021). As a common pathogen, M. pneumoniae can cause pneumonia, especially in children between the ages of 5 and 15 and older adults over the age of 50. For children aged 5-15 years, M. pneumoniae infection accounts for 10-20% of hospitalizations for community-acquired pneumonia and for 30-40% during cyclical epidemics every 3-5 years (SHEN et al., 2024).

Airborne droplets containing M. pneumoniae can be transmitted and spread between people through coughing and sneezing. M. pneumoniae causes upper and lower respiratory tract infections, and in most cases, clinical symptoms are nonspecific. Tracheobronchitis is the most common type of lower respiratory infection, the incidence of which is about 20 times higher than that of pneumonia, and 10–40% of respiratory tract infections caused by M. pneumoniae will eventually develop into pneumonia. Although most cases of pneumonia caused by M. pneumoniae (MPP) are benign, some cases may progress to severe pneumonia and refractory pneumonia with pleural effusion, multi-organ dysfunction, and severe long-term sequelae, including bronchiolitis obliterans and bronchiectasis (JIANG et al., 2021).

Respiratory infections with M. pneumoniae are associated with asthma exacerbation, during which patients will suffer from a combination of symptoms, including sudden or progressive cough, difficulty breathing, wheezing, or chest pain. The onset of asthma is due to mycoplasma-mediated cytokine release in infected patients. Respiratory infections caused by M. pneumoniae are also associated with a wide range of extrapulmonary manifestations, such as meningoencephalitis, myocarditis, nephritis, atherosclerosis, and mucocutaneous eruptions, etc. More importantly, M. pneumoniae induces mucocutaneous diseases, including Stevens-Johnson syndrome and M. pneum-associated mucositis These mucocutaneous diseases are often associated with systemic inflammation and a higher risk of long-term sequelae (JIANG et al., 2021).

Due to the atypical symptoms produced during M. pneumoniae infection, pneumonia may be underestimated during the initial stage of infection. There are no distinctive clinical or radiographic features in patients with M. pneumoniae infections, so laboratory diagnosis is mainly based on rapid culture of throat swab specimens, PCR, and serological assays in addition, enzyme-linked immunosorbent assays (ELISA) that detect the N-terminal fragment of the P116 protein and the C-terminal region of the P1 protein are promising for serodiagnosis. IgM ELISA assays based on short recombinant P116 and P1 proteins have been shown to improve the specificity of the immunodiagnostic assay. Although M. pneumoniae infection is usually self-limiting and does not require antibiotic treatment, patients of all age groups can develop severe, fatal, or extrapulmonary illness. Antibiotics such as tetracycline and fluoroquinolone have been reported to be effective in eliminating M. pneumoniae infections, but tetracyclines cause discoloration of bones and teeth in young children. Fluoroquinolones can also affect muscles, joints, and tendons. Instead, macrolides, which have fewer side effects, have been the drug of choice to treat M. pneumoniae infection in recent years (JIANG et al., 2021).

This systematic review article aims to compile and analyze the scientific evidence on the diagnosis and management of Mycoplasma pneumoniae infection. The objective is to provide a comprehensive and up-to-date view, which synthesizes existing knowledge and identifies gaps in research, guiding future investigations and clinical practices. In-depth analysis of the evidence is intended to be a useful resource for healthcare professionals, researchers, and academics, contributing to the improvement of diagnostic and therapeutic approaches.

METHODOLOGY

This study consists of a systematic review that seeks to understand the main aspects related to *Mycoplasma pneumoniae* infection and atypical bacterial pneumonia, as well as to demonstrate the main associated complications. For the development of this research, a guiding question was elaborated based on the PVO (Population, Variable and Objective) strategy: "What are the complications and treatment methods of *Mycoplasma pneumoniae* infection based on the evidence available in the scientific literature?". The searches were performed using the PubMed database, applying three descriptors in combination with the Boolean term "AND": *Mycoplasma pneumoniae*, *Atypical bacterial pneumonia*, and *Prognosis of Mycoplasma*. The search strategy included combinations such as *Mycoplasma pneumoniae* AND *Atypical bacterial pneumonia* and *Mycoplasma pneumoniae* AND *Prognosis of Mycoplasma*, resulting in a total of 123 articles identified.

The inclusion criteria adopted were: articles published in English, Portuguese, or Spanish, from 2019 to 2024, that addressed the proposed themes; in addition to review, observational and experimental studies, which were available in full. On the other hand, the exclusion criteria included: duplicate articles, articles available only in abstract form, articles that did not directly address the study proposal or that did not meet the other inclusion criteria.

After applying the inclusion and exclusion criteria, 20 relevant articles were selected for the analysis, of which 14 studies were used to compose the final collection. These studies provided a comprehensive view of the complications and treatment methods of *Mycoplasma pneumoniae* infection, standing out for the use of modern diagnostic techniques, such as nucleic acid amplification (PCR), and for the preference for the use of macrolides, especially azithromycin, for treatment, due to their safety profile, especially in children. In addition, the use of corticosteroids and immunoglobulins has been explored in severe cases with extrapulmonary complications, although further studies are needed to validate these treatments.

RESULTS

Table 1 – created by the author

Authors	Main Collaborations
Al et al. (2023)	They described the discovery of *Mycoplasma pneumoniae* and its importance as one of the most common causes of community-acquired pneumonia (CAP) in children. They detailed the variable clinical presentation of the infection, including self-limited cases and those with serious complications, in addition to providing data on the epidemiology and mortality associated with *Mycoplasma pneumoniae*.
Kim et al. (2022)	They examined the species of mycoplasmas that can cause respiratory and reproductive diseases in humans, highlighting the challenges in diagnosis due to the absence of a cell wall. They provided insights into the limited efficacy of beta-lactam antibiotics and the importance of macrolides in the treatment of *Mycoplasma pneumoniae infections*.
Yang et al. (2024)	They discussed the variability of the clinical manifestations of *Mycoplasma pneumoniae infection*, emphasizing the prevalence of extrapulmonary manifestations, such as neurological and hematological complications. They stressed the importance of modern molecular diagnostic techniques, such as nucleic acid amplification (PCR), for the accurate detection of the pathogen.
Xue, Wang and Han (2023)	They explored the immune response to *Mycoplasma pneumoniae*, detailing how the bacterium induces the production of pro-inflammatory cytokines, such as IL-8 and TNF-α, and described the role of alveolar epithelial cells and alveolar macrophages in the immune response and maintenance of lung homeostasis.
Kant et al. (2024)	They analyzed the risk factors and modes of transmission of *Mycoplasma pneumoniae*, highlighting the importance of direct contact and respiratory droplets. They described the impact of environmental factors and hygiene practices on the spread of the pathogen, as well as the influence of age and immune status on susceptibility to infection.
Mirijello et al. (2020)	They contributed with a detailed analysis of the direct and indirect pathogenic mechanisms of *Mycoplasma pneumoniae*, including cytoadherence and direct cytotoxicity, in addition to exploring the immune-mediated disease due to autoimmunity. They emphasized the importance of cross-reactions between human

	cells and bacterial cell components in the development of extrapulmonary complications.
Liu and Li (2021)	They investigated the extrapulmonary manifestations of *Mycoplasma pneumoniae infection*, focusing on neurological, dermatological, and hematological complications. They discussed the diagnostic and therapeutic challenges associated with these manifestations and highlighted the importance of early treatment to reduce severe complications.
Georgakopoulou et al. (2024)	They provided a comprehensive analysis of traditional and modern diagnostic techniques for *Mycoplasma pneumoniae*, with an emphasis on the transition from culture and serology to molecular methods such as PCR. They discussed the benefits and limitations of different diagnostic methods and highlighted the importance of rapid and accurate diagnoses for effective infection management.
Hu et al. (2023)	They analyzed the extrapulmonary pathogenic mechanisms of *Mycoplasma pneumoniae*, dividing them into three parts: direct damage, indirect damage, and vascular occlusion. They discussed how blood transmission can lead to extrapulmonary complications, including damage caused by autoimmunity and drug reactions.
Oishi and Ouchi (2022)	They discussed the treatment guidelines for *Mycoplasma pneumoniae infection*, highlighting the efficacy of macrolides, such as azithromycin, in reducing the duration of the disease. They also addressed the challenges in treating children with tetracyclines and fluoroquinolones due to adverse effects.

DISCUSSION

Mycoplasma pneumoniae is an intracellular bacterium that was discovered in 1944 by Eaton, when an expectation of a patient with primary pneumonia with atypical characteristics was cultivated. In 1963, its taxonomic denomination was proposed (AI et al., 2023). Mycoplasma pneumoniae infection is one of the most common causes of community-acquired pneumonia (CAP) in children, accounting for approximately 30% to 40% of cases. Some cases of M pneumoniae infection have been considered a self-limiting disease, while other cases of M pneumoniae infection have led to poor clinical outcomes with serious complications. There are 200 known mycoplasma species, including six major species, that can cause diseases of the human respiratory and reproductive tract, among other diseases (KIM et al., 2022) (YANG et al., 2024).

It has been reported that the mortality rate of elderly patients with MP is as high as 30%. MP, a gram-negative microorganism, is the smallest self-replicating bacterium with an extremely small genome. As a prokaryotic pathogen, it has three membranes without a cell wall, and its survival depends on the exchange of nutrients with the host. The pathogen is spread through direct contact between infected and susceptible people, as well as through droplets emitted by infected people when they sneeze, cough, or talk. After the MP enters the respiratory tract with air, due to the lack of cell wall, the MP membrane may be in direct contact with epithelial cells, transferring or exchanging membrane components. PM can produce various pathogen-associated molecular patterns (PAMPs), such as membrane lipoprotein, polysaccharide, and invasive ribozyme, which can cause a number of pathophysiological changes of the host. PM induces host cells to produce interleukin (IL)-8,

tumor necrosis factor (TNF)-a, and other proinflammatory cytokines. The IL-8 and TNF-a content in the patient's serum increased with the worsening of the PM infection (XUE; WANG; HAN, 2023).

The lung epithelium is the site for gas exchange between the lung and the blood, and is the first line of mucus barrier for defense against foreign invasion and pathogenic factors. Mature alveolar epithelial cells (AECs) are composed of type I (AECIs) and type II (AECIIs) alveolar epithelial cells (AECIIs), accounting for 95% and 5%, respectively. The AECIs are flat cells that cover capillaries that provide the thin surface of the alveoli and are the most important site for gas exchange. In addition to serving as a physical barrier against pathogens and various environmental particles that enter, AECIIs are also involved in the immune system (XUE; WANG; HAN, 2023).

After entering the respiratory tract, MP adheres to AECIIs via surface adhesion molecules to induce host cells to produce TGF-b and extracellular vesicles carrying miRNA, which activate alveolar macrophages to clear MP. Alveolar macrophages (AMs), free in the alveolar cavity, are primary immune cells in the lung and are the main cellular sensors for pathogens with the characteristics of phagocytosis and cytokine secretion. Membrane lipoprotein from binding PM to Toll-like receptors (TLRs) on AMs activates signaling pathways such as nuclear factor (NF)-kB and causes the secretion of pro-inflammatory cytokines, promoting neutrophil aggregation and pathogen phagocytosis. More and more evidence demonstrates that the interaction of structural cells and immune cells with each other is essential to resist external pathogens In the lung, AMs and AECs communicate with each other to coordinate their actions to maintain lung homeostasis and gas exchange (XUE; WANG; HAN, 2023).

Infections are as endemic as they are epidemic around the world. Generally, epidemic waves occur every 4-7 years. Assuming that these fluctuations are related to antigenic changes in Mycoplasma strains, decreased herd immunity in populations, or a combination of both. During outbreak epidemics, M. pneumoniae may account for up to 25% of community-associated pneumonia cases, this proportion drops to 1-8% in interdepidemic periods. M. pneumoniae infections can affect both children and adults. Most infections are self-limiting, especially in adults. They are exceptional in children under one year of age and are more frequent between 5 and 15 years of age. It can occur at any time of the year without important seasonal variations. It is transmitted from person to person by respiratory droplets infected in close contact. The incubation period is 2 to 3 weeks. (AI et al., 2023)

The pathogen spreads primarily through respiratory droplets, thriving in crowded environments such as schools and households. Factors such as close contact with infected individuals, poor hygiene practices, and environmental conditions contribute to transmission. The primary mode of transmission for M. pneumoniae is through the inhalation of respiratory secretions expelled during coughing or sneezing by an infected person. Although less common, transmission can also occur by touching surfaces contaminated with respiratory secretions from an infected person. Several risk factors contribute to the efficient transmission of this pathogen, including age (particularly children and young adults), crowded environments (schools, hospitals, military barracks, and daycare homes), weakened (compromised) immune systems due to certain medical conditions or medications, and seasonal variations such as temperate weather conditions, late summer, fall, and early winter. Prior exposure to the bacteria can reduce the likelihood of reinfection through the development of immunity. Although these factors increase the risk of transmission, not everyone exposed to the bacterium necessarily develops symptoms or an infection (KANT et al., 2024).

Very often, M. pneumoniae infection is asymptomatic, especially in adults. When the infection manifests clinically, it usually affects the upper respiratory tract and it is difficult to distinguish other respiratory infections caused by viruses or other atypical bacteria. The most typical syndrome, especially in children, is tracheobronchitis accompanied by a wide variety of upper respiratory manifestations, such as pharyngitis or rhinitis. Manifestations may also occur in areas close to the airways, such as conjunctivitis or myringitis. The most frequent manifestation of the lower respiratory tract is pneumonia, included in the so-called "atypical pneumonias", which develops slowly and can last for weeks or months. The most frequent symptoms are chills, fever, cough, headache, myalgias, arthralgia and general malaise. Diffuse and wheezing crackles may be detected on auscultation. Pleural effusion is scarce, occurs in 15-20% of patients with pneumonia, and empyema is rare (AI et al., 2023).

In addition to the typical respiratory symptoms, M. pneumoniae can produce other extrarespiratory manifestations, which can appear before, during, or after pulmonary manifestations, but also in the absence of these. These manifestations can appear up to 25% of those infected. There is a range of extrapulmonary manifestations of M. pneumoniae infection that can potentially involve all systems and organs. The concomitant occurrence of mycoplasmemia was obtained in the involvement of the mycoplasmic central nervous system, which proved that M. pneumoniae could transfer to distant organs by blood transmission to cause disease. The extrapulmonary pathogenic mechanisms of M.

pneumoniae can be divided into three parts: direct damage, indirect damage, and vascular occlusion. Early-onset extrapulmonary complications may be related to direct damage caused by blood transmission of M. pneumoniae, while late-onset disease may be associated with indirect damage caused by autoimmunity, vascular damage, and drug reaction (HU et al., 2023).

MP represents an intracellular pathogen with peculiar virulence characteristics, such as cytoadherence, motility, and direct cytotoxicity. Although the pathogenesis has not been completely defined, the main mechanisms of the disease are: Direct: cytoadhesion to membrane cells, such as those of the respiratory tract (responsible for pulmonary manifestations), erythrocytes (direct hemolysis) and probably other organs (liver and central nervous system) induces direct cytotoxicity with consequent activation of the local inflammatory cascade due to the presence of the microorganism at the site of inflammation and Indirect: immune-mediated disease due to autoimmunity through cross-reactivity between human cells and bacterial cell components and vascular occlusion due to vasculitis with obstruction of blood flow. The indirect mechanism has been suggested to account for most of the extrapulmonary manifestations of PM infection through an autoimmune reaction and molecular mimicry. This triggers the production of antibodies against phospholipids, glycolipids, and proteins with associated vasculitic/thrombotic disorders, both in the presence and absence of a systemic hypercoagulable state (MIRIJELLO et al., 2020).

Previous studies have reported that Mycoplasma pneumoniae is involved in extra-respiratory skin, musculoskeletal, cardiovascular, hematological, gastrointestinal, neurological, and renal diseases. These conditions may have variable clinical characteristics and may appear in immunologically predisposed children with recurrent or persistent Mycoplasma pneumoniae infection; a retrospective study of children with Mycoplasma pneumoniae infection demonstrated that delayed effective treatment was associated with extrapulmonary manifestations. A prospective study found that serum immunoglobulin E level in children with Mycoplasma pneumoniae-related extrapulmonary diseases was significantly higher compared to children with Mycoplasma pneumoniae-related respiratory diseases alone (LIU; LI, 2021).

One of the most important manifestations, although not frequent, are neurological, including encephalitis that are produced in all children. Of the dermatological manifestations, Stevens-Johnson syndrome is the most severe, and urticaria, and erythema multiforme are the most frequent, probably mediated by immune complexes (AI et al., 2023). Thrombosis is one of the extrarespiratory manifestations associated with

Mycoplasma pneumoniae infection. With a better understanding of Mycoplasma pneumoniae, reports of thrombosis cases associated with Mycoplasma pneumoniae infection are increasing. Thrombosis is one of the leading causes of mortality and disability worldwide. Arterial thrombosis is usually associated with plaque rupture, which causes platelets to develop platelet-rich clots; However, venous thromboembolism is associated with endothelial dysfunction and blood stasis, leading to fibrin- and erythrocytes-rich thrombus. After Mycoplasma pneumoniae infection, thrombosis may occur in a different part of the body, sometimes affecting the prognosis of the disease (LIU; LI, 2021).

The imaging features of Mycoplasma pneumoniae infections reflect their elusive nature. Chest X-rays commonly reveal diffuse interstitial patterns, occasionally disproportionate to the physical symptoms of patients. On chest CT scans, the interstitial changes apparent on radiographs manifest as tree-in-bud formations. In a prospective study involving 1,280 pediatric cases of pneumonia caused by Mycoplasma pneumoniae between 2010 and 2014, a substantial proportion of patients had extensive and irregular infiltrates, both unilateral and overall bilateral, suggesting that the diagnosis of pneumonia could not be determined solely on the basis of imaging characteristics (GEORGAKOPOULOU et al., 2024).

Traditionally, the diagnosis of Mycoplasma pneumoniae depended on cultures and serology, with culture isolation already considered the gold standard. However, due to the slow and inconsistent growth of Mycoplasma pneumoniae, routine culture is no longer common and offers limited clinical utility. Other diagnostic avenues include serological studies using ELISA to quantify bacterial antibody expression, microparticle agglutination, and complement fixation assays. Definitive diagnosis in serologic studies required paired sera demonstrating a significant 4-fold increase in IgG or subsequent frequent seroconversion 3-4 weeks later. However, due to delayed antibody production and seroconversion, these tests have limited utility for the diagnosis of acute Mycoplasma pneumoniae infections in clinical settings and are more retroactive (GEORGAKOPOULOU et al., 2024).

Because culture and serology have deficiencies in diagnosing Mycoplasma pneumoniae, diagnostic methods are shifting to faster molecular techniques such as nucleic acid amplification. fication. Molecular diagnosis allows for the timely detection of Mycoplasma pneumoniae infections and is increasingly essential in clinical diagnosis. A number of laboratory techniques, such as nucleic acid amplification, multilocus variable-number tandem repeat analysis, and multilocus sequence typing, are becoming prominent. These tests provide fast, highly specific, and sensitive results. Several tests employ real-

time PCR to target specific genetic regions of Mycoplasma pneumoniae, including those encoding the P1 gene, nibonucleotide 165 RNA soma, the ATPase operon, and community-acquired respiratory distress syndrome toxin (GEORGAKOPOULOU et al., 2024).

Infection caused by Mycoplasma pneumoniae often goes unnoticed, as patients tend to fail to seek treatment due to the gradual onset of symptoms. The bacterium has an extended incubation period of 3 weeks, and symptomatic elimination may persist for up to 4 months; however, most cases resolve naturally within 2 to 4 weeks without treatment. When patients seek clinical care, their treatment is usually directed by the IDSA guidelines for CAP, considering assessing the patient's symptoms and imaging outcomes. Mycoplasma pneumoniae is a bacterium without a cell wall, so beta-lactam antibiotics that target bacterial cell walls are not effective. Because antibiotics that target cell walls are not an option to treat M pneumoniae infection, antibiotic treatment options for M pneumoniae infections include those that play a role in disrupting protein synthesis (e.g., macrolides and tetracyclines) and inhibiting DNA replication (e.g., fluoroquinolones). However, tetracyclines and fluoroquinolones have limited use for children due to a lack of information on safety in this population, although effective, they are associated with unfavorable side effects that are more problematic in younger patients such as discoloration of the dentition with tetracyclines and tendinitis with fluoroquinolones. Therefore, macrolides have been the first choice for treating M pneumoniae infection in children and adults. Despite this, it is usually treated in treatment of empirical CAP with macrolide, often in the absence of a confirmatory laboratory diagnosis. This antimicrobial treatment has the potential to reduce the duration of illness by requiring a course of antibiotics ranging from 5 days to 2 weeks, depending on the antibiotic selected for individuals affected by the infection (KIM et al., 2022) (OISHI; OUCHI, 2022) (GEORGAKOPOULOU et al., 2024).

Within macrolides, azithromycin, roxithromycin, or clari-thromycin are preferred over erythromycin because of their better tolerance, better administration, and shorter duration of treatment. According to the Antimicrobial Therapeutic Guide of the National Health System (PRAN), in childhood the most used treatment for atypical pneumonia of choice is oral azithromycin, a dose of 10 mg/kg/day, one dose per day on the first day (maximum dose 500 mg) followed by 5 mg/kg/day (maximum dose 250 mg/day) on days 2 to 5. Alternatively, oral clarithromycin is used: 15 mg/kg/day as a single dose (maximum 1 gram/day) for 7 days (AI et al., 2023).

Managing extrapulmonary symptoms or complex cases of Mycop infection/asthma pneumoniae beyond antibiotic treatment Treatment remains uncertain in terms of specific

treatment protocols. For patients with extra-association to Mycoplasma pneumoniae lung conditions, understanding the inflammatory nature of the bacteria is crucial. Through pathways linked to the Toll-like receptor 2, the bacterium can stimulate the production of pro-inflammatory cytokines and the activity of the inflammasome. This may shed light on why symptoms are more common among young adults, as they often have a stronger immune response compared to infants or elderly patients who may not generate the same level of response. In patients with central nervous system complications or severe pneumonia caused by Mycoplasma pneumoniae, there have been reports suggesting the potential benefits of steroids and immunoglobulin therapy, although these findings have not been validated in clinical trials (GEORGAKOPOULOU et al., 2024).

CONCLUSION

Mycoplasma pneumoniae infection is a relevant public health problem, especially because of its potential to cause both self-limiting infections and severe clinical manifestations, including extrapulmonary complications. This atypical bacterium has complex virulence mechanisms, such as cytoadherence and direct cytotoxicity, which favor its persistence in the body and the induction of significant inflammatory responses. The variability of clinical manifestations, ranging from mild respiratory infections to severe extrapulmonary complications, requires special diagnostic attention, since M. pneumoniae is often not identified in routine clinical investigations.

The diagnosis of infection is evolving, with molecular methods becoming more and more prominent to the detriment of culture and serology, which, although effective, have limitations in acute diagnoses. The introduction of PCR-based techniques and other genetic analyses have contributed to a more accurate and rapid detection of the pathogen. With regard to treatment, macrolides, especially azithromycin, are preferred in the management of respiratory infections caused by M. pneumoniae, especially in children, because of their safety profile. However, extrapulmonary complications represent an additional challenge, and the use of corticosteroids and immunoglobulins has shown some benefit in severe cases, although more studies are needed to validate these treatments.

This review highlights the need for an integrated and up-to-date approach to the diagnosis and treatment of Mycoplasma pneumoniae infection, considering its complex interactions with the immune system and its potential impact on multiple organ systems. Future studies should focus on rapid diagnosis strategies and specific therapies for extrapulmonary complications, contributing to a more effective and safe management of this infection in different age groups and epidemiological contexts.

REFERENCES

1. AI, Á. V., et al. (2023). Macrolide-resistant Mycoplasma pneumoniae: Do we know the situation in Europe? Revista Española de Quimioterapia: Publicación Oficial de la Sociedad Española de Quimioterapia, 36(3), 259–266. https://doi.org/10.37201/revesp.2023.36.03.005

2. Georgakopoulou, V. E., et al. (2024). Atypical pneumonia. Experimental and Therapeutic Medicine, 28(5), 424. https://doi.org/10.3892/etm.2024.12357

3. Hu, J., et al. (2023). Insight into the pathogenic mechanism of Mycoplasma pneumoniae. Current Microbiology, 80(1), 14. https://doi.org/10.1007/s00284-023-02888-6

4. Jiang, Z., et al. (2021). Mycoplasma pneumoniae infections: Pathogenesis and vaccine development. Pathogens, 10(2), 119. https://doi.org/10.3390/pathogens10020119

5. Kant, R., et al. (2024). Critical insights from recent outbreaks of Mycoplasma pneumoniae: Decoding the challenges and effective intervention strategies. International Journal of Infectious Diseases, 107, 200. https://doi.org/10.1016/j.ijid.2024.01.013

6. Kim, K., et al. (2022). Global trends in the proportion of macrolide-resistant Mycoplasma pneumoniae infections: A systematic review and meta-analysis. JAMA Network Open, 5(7), e2220949. https://doi.org/10.1001/jamanetworkopen.2022.20949

7. Liu, J., & Li, Y. (2021). Thrombosis associated with Mycoplasma pneumoniae infection. Experimental and Therapeutic Medicine, 22(3), 1–9. https://doi.org/10.3892/etm.2021.10473

8. Mirijello, A., et al. (2020). Venous thromboembolism during Mycoplasma pneumoniae infection: Case report and review of the literature. European Review for Medical and Pharmacological Sciences, 24(19), 10061–10068. https://doi.org/10.26355/eurrev_202010_22859

9. Oishi, T., & Ouchi, K. (2022). Recent trends in the epidemiology, diagnosis, and treatment of macrolide-resistant Mycoplasma pneumoniae. Journal of Clinical Medicine, 11(7), 1782. https://doi.org/10.3390/jcm11071782

10. Shen, T., et al. (2024). Association between Mycoplasma pneumoniae infection, high-density lipoprotein metabolism, and cardiovascular health. Biomedical Reports, 20(3), 1–10. https://doi.org/10.3892/br.2024.1441

11. Xue, Y., Wang, M., & Han, H. (2023). Interaction between alveolar macrophages and epithelial cells during Mycoplasma pneumoniae infection. Frontiers in Cellular and Infection Microbiology, 13, 1052020. https://doi.org/10.3389/fcimb.2023.1052020

12. Yang, Z., et al. (2024). Insights into the defensive roles of lncRNAs during Mycoplasma pneumoniae infection. Frontiers in Microbiology, 15, 1330660. https://doi.org/10.3389/fmicb.2024.1330660