Clinical and diagnostic features of respiratory diseases of combined etiology in children

Gulnoza Turakhodjaevna Makhkamova
Tashkent State Medical University

Abstract: *Respiratory diseases of combined etiology in children represent one of the most significant challenges in contemporary pediatrics. These conditions, which often involve the interaction of viral, bacterial, allergic, and environmental factors, contribute substantially to morbidity and mortality rates among pediatric populations worldwide. The complexity of these diseases stems from their multifactorial nature, overlapping clinical manifestations, and diagnostic difficulties due to mixed pathogen involvement. This study explores the clinical and diagnostic characteristics of respiratory diseases of combined etiology in children, emphasizing pathogenetic mechanisms, diagnostic approaches, and the importance of comprehensive clinical evaluation for effective treatment and prevention.*

Keywords: *respiratory infections; combined etiology; pediatric diagnostics; viral-bacterial co-infection; clinical features; children's respiratory diseases*

Introduction

Respiratory diseases remain a leading cause of illness and hospitalization among children globally. The pediatric respiratory system is anatomically and functionally distinct from that of adults, with narrower airways, immature immune responses, and greater susceptibility to environmental and infectious agents. In recent years, there has been a marked increase in the incidence of respiratory diseases of mixed or combined etiology. These conditions arise when multiple causative factors - most commonly viral and bacterial pathogens - act simultaneously or sequentially to provoke complex pathological processes within the respiratory tract. The synergistic effects of co-infections and environmental influences complicate both diagnosis and management.

Combined etiology respiratory diseases are characterized by their dynamic course, variable clinical presentation, and resistance to monotherapeutic interventions. The prevalence of viral-bacterial co-infection is particularly high among infants and preschool-aged children, where respiratory syncytial virus (RSV), influenza viruses, parainfluenza, adenoviruses, and rhinoviruses often coexist with Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis. Moreover, allergic sensitization, air pollution, and passive tobacco exposure serve as cofactors that exacerbate disease progression and severity. The identification of combined etiology in pediatric respiratory pathology has become increasingly possible through the use of advanced diagnostic tools, including polymerase chain reaction (PCR), serological assays, and high-resolution imaging. However, challenges persist due to overlapping symptoms and the polymicrobial nature of these infections.

Materials and Methods

This review is based on an analysis of clinical studies, diagnostic protocols, and epidemiological data related to pediatric respiratory diseases of mixed etiology. Particular attention was given to publications describing co-infections in the lower and upper respiratory tracts, as well as studies employing modern molecular diagnostic methods. A comparative evaluation of clinical manifestations, laboratory findings, and imaging results was conducted to identify characteristic features of mixed infections. Data on pathogen prevalence, immune response patterns, and therapeutic

outcomes were integrated to develop a comprehensive understanding of diagnostic and clinical patterns.

Results and Observations

The clinical course of respiratory diseases of combined etiology in children is influenced by the interplay between viral and bacterial agents, host immune status, and environmental exposure. The initial viral infection often disrupts the respiratory mucosal barrier, facilitating bacterial colonization and invasion. This sequence is particularly evident in acute bronchitis, bronchiolitis, and pneumonia, where a preceding viral infection predisposes the child to secondary bacterial involvement. Clinically, children present with a combination of symptoms including fever, cough, nasal congestion, wheezing, and dyspnea. In cases of combined etiology, the course tends to be more prolonged, and systemic manifestations such as lethargy, loss of appetite, and toxic syndrome are more pronounced than in monoinfectious cases.

Physical examination frequently reveals mixed signs of upper and lower respiratory involvement. Auscultatory findings may include both moist rales and wheezes, suggesting concurrent bronchial obstruction and parenchymal inflammation. The presence of tachypnea and chest indrawing indicates lower respiratory tract involvement. A distinguishing feature of combined etiology diseases is the fluctuating nature of clinical symptoms, where viral features such as catarrhal inflammation are followed or overlapped by bacterial purulent changes.

From a laboratory perspective, the diagnosis of mixed respiratory infections requires careful interpretation of results. Peripheral blood analysis often shows moderate leukocytosis with a shift toward neutrophilia, elevated erythrocyte sedimentation rate (ESR), and increased C-reactive protein (CRP), which reflect bacterial involvement. At the same time, lymphocytosis or normal leukocyte counts may persist due to the underlying viral process. The concurrent detection of viral antigens and bacterial cultures in respiratory samples confirms the combined etiology.

Molecular diagnostic techniques, particularly PCR, have revolutionized the identification of co-infecting agents. Studies indicate that up to 40-60% of children with severe respiratory illness harbor two or more pathogens. For instance, RSV and Streptococcus pneumoniae co-infection is associated with more severe hypoxemia and longer hospital stays. Similarly, influenza virus combined with Staphylococcus aureus or Haemophilus influenzae leads to increased risk of complications such as bacterial pneumonia and respiratory failure.

Radiological findings in combined respiratory infections are diverse. Chest X-rays may show peribronchial thickening, patchy infiltrates, or segmental consolidations, often bilateral. Computed tomography (CT) provides more detailed visualization, revealing ground-glass opacities and areas of atelectasis, reflecting the complex pathophysiology of mixed infections. These imaging patterns are essential in differentiating viral-bacterial pneumonia from purely viral or bacterial types.

Discussion

The clinical and diagnostic complexity of respiratory diseases of combined etiology in children lies in their multifactorial pathogenesis. The initial viral infection plays a primary role in altering mucociliary clearance, damaging epithelial cells, and modulating immune responses. This immunomodulation reduces macrophage and neutrophil activity, paving the way for bacterial superinfection. In turn, bacterial toxins and inflammatory mediators amplify tissue damage, perpetuating the disease process. The combination of viral replication and bacterial colonization results in enhanced inflammatory responses, increased airway obstruction, and impaired gas exchange.

The immune response in children with combined respiratory infections is characterized by dysregulation between innate and adaptive mechanisms. Cytokine profiles show elevated levels of

interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ), reflecting intense inflammatory activity. However, the immature immune system of young children often fails to localize the infection, resulting in systemic manifestations and complications. Recurrent or prolonged episodes of mixed respiratory infections may contribute to chronic airway remodeling and predispose to asthma or bronchiectasis in later life.

The diagnostic process must therefore integrate clinical, laboratory, and instrumental data. Clinical symptoms alone are insufficient to establish combined etiology, as they often overlap with single-pathogen infections. Laboratory tests, particularly inflammatory markers, provide indirect evidence but must be interpreted alongside pathogen detection techniques. The combination of PCR for viral agents, culture or antigen testing for bacteria, and serological assays for immune response offers the highest diagnostic accuracy. Radiological examination, although non-specific, provides crucial information on the extent and localization of pulmonary involvement.

Treatment strategies for respiratory diseases of combined etiology should be individualized based on the predominant pathogens and the clinical severity. Since viral-bacterial interactions can influence antibiotic efficacy, indiscriminate antibiotic use should be avoided unless bacterial involvement is confirmed or strongly suspected. Supportive therapy, including adequate hydration, antipyretics, bronchodilators, and oxygen supplementation, remains essential. The use of antiviral medications is indicated for specific viral infections such as influenza, whereas bacterial infections require targeted antibiotics. Immunomodulatory and anti-inflammatory therapies are increasingly recognized as beneficial in reducing prolonged inflammation and tissue injury.

Preventive measures play a vital role in reducing the incidence and severity of combined respiratory diseases. Vaccination against influenza, pneumococcus, and Haemophilus influenzae type b (Hib) has been shown to significantly decrease the frequency of co-infections. Environmental control, including reduction of passive smoke exposure and improvement of indoor air quality, contributes to better respiratory health. Strengthening immune function through balanced nutrition, vitamin D supplementation, and timely management of allergic conditions also supports prevention.

Conclusion

Respiratory diseases of combined etiology in children represent a multifaceted clinical problem that requires an integrated diagnostic and therapeutic approach. The interaction between viral, bacterial, and environmental factors leads to complex disease manifestations, prolonged course, and increased risk of complications. Early recognition and precise diagnosis are crucial to optimize treatment and improve outcomes. Advances in molecular diagnostics have enhanced the ability to identify co-infections and understand their pathophysiology, yet clinical assessment remains indispensable. Pediatricians must remain vigilant to the possibility of combined etiology when managing respiratory diseases, particularly in young children with severe or recurrent symptoms. A multidisciplinary approach involving clinicians, microbiologists, and public health specialists is essential to reduce the burden of these diseases and to promote child health. Continued research into host-pathogen interactions, immune responses, and preventive strategies will further improve the management of respiratory infections of combined etiology in the pediatric population.

References

1. Hemming, V. G. (1994). Viral respiratory diseases in children: classification, etiology, epidemiology, and risk factors. The Journal of pediatrics, 124(5), S13-S16.

2. Sutmöller, F., Ferro, Z. A., Asensi, M. D., Ferreira, V., Mazzei, I. S., & Cunha, B. L. (1995). Etiology of acute respiratory tract infections among children in a combined community and hospital study in Rio de Janeiro. Clinical Infectious Diseases, 20(4), 854-860.

3. Wenner, H. A., Christodoulopoulou, G., Weston, J., Tucker, V., & Liu, C. (1963). The etiology of respiratory illnesses occurring in infancy and childhood. Pediatrics, 31(1), 4-17.
4. Ouédraogo, S., Traoré, B., Nene Bi, Z. A. B., Yonli, F. T., Kima, D., Bonané, P., ... & Gueudin, M. (2014). Viral etiology of respiratory tract infections in children at the pediatric hospital in Ouagadougou (Burkina Faso). PloS one, 9(10), e110435.
5. Kleszyk, M., Mizgała-Izworska, E., Góra, A., Przybył, M., & Machura, E. (2021). Multifactorial aetiology of recurrent respiratory tract infections in children. Paediatrics and Family Medicine, 17(3), 227.
6. Yen, C. Y., Wu, W. T., Chang, C. Y., Wong, Y. C., Lai, C. C., Chan, Y. J., ... & Hung, M. C. (2019). Viral etiologies of acute respiratory tract infections among hospitalized children–A comparison between single and multiple viral infections. Journal of Microbiology, Immunology and Infection, 52(6), 902-910.
7. Suryadevara, M., Cummings, E., Bonville, C. A., Bartholoma, N., Riddell, S., Kiska, D., ... & Domachowske, J. B. (2011). Viral etiology of acute febrile respiratory illnesses in hospitalized children younger than 24 months. Clinical pediatrics, 50(6), 513-517.