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Clinical and immunological aspects of metapneumovirus infection in children

Vera F. Sukhovetskaya[1], Tatyana A. Kaplina[1], Vladimir N. Timchenko[1], Tatyana M. Chernova[1], Elena V. Barakina[1], Oksana V. Bulina[1], Ekaterina G. Golovacheva[2], Veronika S. Timonina[2], Olga P. Gurina [1], Alexander E. Blinov[1], Olga N. Varlamova[1]

[1] Saint Petersburg State Pediatric Medical University, 2 Litovskaya str., Saint Petersburg, 194100, Russian Federation

[2] A.A. Smorodintsev Research Institute of Influenza, 15/17 Professora Popova str., Saint Petersburg, 197022, Russian Federation

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ABSTRACT. ***Introduction.*** Metapneumovirus infection is one of the leading causes of lower respiratory tract infection in children. ***The aim of the study*** – to identify the features of immunopathogenesis and clinical course of metapneumovirus infection in children to predict the severity of the disease and optimize therapeutic approaches. ***Materials and methods.*** A retrospective analysis of the medical records of 210 children aged 1 month to 14 years hospitalized in infectious disease hospitals in St. Petersburg from 2019 to 2025 was conducted. Etiological identification was performed using PCR in nasopharyngeal swabs. Cytokine status (IL-1β, -6, -8, -10, -17, IFN-α and -γ levels) was determined using ELISA in serum. ***Results.*** Metapneumovirus infection in children was detected in 6.6% of acute respiratory viral infections. Patients with mono-metapneumovirus infection under 3 years of age accounted for 72%, of which 53% had lower respiratory tract lesions. Acute obstructive laryngitis was most often observed in children aged 1–3 years (23.4%). Children with grade I laryngeal stenosis accounted for 64.3%. Acute bronchitis/BOS was more often recorded in children under 1 year (48.8%) and 1-3 years (46.7%). Grade I–II respiratory failure was observed mainly in young patients (85.7%). Pneumonia was diagnosed in 21.5% of children under 1 year of age. Activation of cellular immunity was accompanied by an increase in proinflammatory cytokines (IL-1β, -6, -8, -17) and an anti-inflammatory cytokine (IL-10), which plays a role in limiting excessive inflammation. A simultaneous decrease in interferon levels (IFN-α and -γ) was observed. ***Conclusions.*** Metapneumovirus infection in young children primarily affects the lower respiratory tract and is associated with a high rate of complications. The immunopathogenesis of this infection is characterized by increased production of proinflammatory and anti-inflammatory cytokines, coupled with decreased interferon levels, reflecting an imbalance in the immune response that contributes to the severity of clinical manifestations.

KEYWORDS: *metapneumovirus infection, children, interferons, interleukins*

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✉ *Vera F. Sukhovetskaya*. E-mail: verafedotovna@mail.ru

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Клинико-иммунологические аспекты метапневмовирусной инфекции у детей

Вера Федотовна Суховецкая[1], Татьяна Анатольевна Каплина[1], Владимир Николаевич Тимченко[1], Татьяна Маратовна Чернова[1], Елена Владимировна Баракина[1], Оксана Владимировна Булина[1], Екатерина Георгиевна Головачева[2], Вероника Сергеевна Тимонина[2], Ольга Петровна Гурина[1], Александр Евгеньевич Блинов[1], Ольга Николаевна Варламова[1]

[1] Санкт-Петербургский государственный педиатрический медицинский университет, 194100, г. Санкт-Петербург, ул. Литовская, д. 2, Российская Федерация

[2] Научно-исследовательский институт гриппа имени А.А. Смородинцева, 197022, г. Санкт-Петербург, ул. Профессора Попова, д. 15/17, Российская Федерация

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РЕЗЮМЕ. ***Введение.*** Метапневмовирусная инфекция – одна из лидирующих в поражении нижних отделов респираторного тракта у детей. ***Цель исследования*** – выявить особенности клинического течения и иммунопатогенеза метапневмовирусной инфекции у детей для прогнозирования тяжести болезни и оптимизации терапевтических подходов. ***Материалы и методы.*** Проведен ретроспективный анализ медицинских карт 210 детей в возрасте от 1 месяца до 14 лет, госпитализированных в инфекционные стационары Санкт-Петербурга в 2019–2025 гг. Этиологическая расшифровка проводилась методом полимеразной цепной реакции в носоглоточных смывах. Цитокиновый статус (содержание ИЛ-1β, -6, -8, -10, -17, ИФН-α и -γ) определяли методом иммуноферментного анализа в сыворотке крови. ***Результаты.*** Метапневмовирусная инфекция у детей выявлена в 6,6% случаев острой респираторной вирусной инфекции. Пациенты с монометапневмовирусной инфекцией в возрасте до 3 лет составили 72%, из которых 53% имели поражение нижних отделов респираторного тракта. Острый обструктивный ларингит чаще наблюдался у детей в возрасте 1–3 лет (23,4%). Дети со стенозом гортани I степени составили 64,3%. Острый бронхит/бронхообструктивный синдром чаще регистрировался у детей в возрасте до 1 года (48,8%) и 1–3 лет (46,7%). Дыхательная недостаточность I–II степени отмечалась преимущественно у пациентов раннего возраста (85,7%). Пневмония диагностирована у 21,5% детей до 1 года. Активация клеточного иммунитета сопровождалась повышением провоспалительных цитокинов (ИЛ-1β, -6, -8, -17) и противовоспалительного цитокина (ИЛ-10), играющего роль в ограничении чрезмерного воспаления. Одновременно отмечалось снижение уровня интерферонов (ИФН-α и -γ). ***Выводы.*** Метапневмовирусная инфекция у детей преимущественно поражает нижние дыхательные пути и сопровождается высокой частотой осложнений. Иммунопатогенез данной инфекции характеризуется усиленной продукцией провоспалительных и противовоспалительных цитокинов на фоне снижения уровня интерферонов, что отражает дисбаланс иммунного ответа, способствующего тяжести клинических проявлений.

КЛЮЧЕВЫЕ СЛОВА: *метапневмовирусная инфекция, дети, интерфероны, интерлейкины*

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

✉ *Вера Федотовна Суховецкая.* E-mail: verafedotovna@mail.ru

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INTRODUCTION

Acute respiratory viral infections (ARVI) continue to be the leading cause of infectious diseases in children. The incidence of ARVI remains consistently high, primarily due to the lack of specific immunoprophylaxis, the instability of the immune response, the ability of some viruses to persist latently, and chronic sensitization of the body. Young children, particularly those under three years of age, remain particularly vulnerable, with ARVI being one of the leading causes of hospitalization in this age group [1, 2]. More than 200 viruses are known to cause respiratory tract infections. The most common pathogens are: influenza viruses, parainfluenza viruses, respiratory syncytial (RS) virus, and adenoviruses, rhinoviruses, bocaviruses, metapneumoviruses, coronaviruses, and enteroviruses. The listed agents do not exhaust the etiological spectrum of ARVI in children, since currently, even with the help of modern laboratory diagnostic methods, it is possible to identify no more than 70% of all acute respiratory tract infections recorded in childhood [3, 4].

In recent years, there has been an increase in the prevalence of metapneumovirus infection, which is a cause for particular concern in pediatrics and virology. The role of metapneumovirus as a trigger for the development of chronic diseases and complications requires a more in-depth study of pathogenetic and immunological mechanisms. Metapneumovirus is capable of persisting in the respiratory tract for long periods with possible reactivation upon a decline in immunity, which contributes to the chronicity of the infection. Clinical manifestations range from mild respiratory symptoms to severe conditions: bronchiolitis, bronchial obstructive syndrome, and pneumonia, particularly in immunocompromised children [5, 6].

Metapneumovirus belongs to the family *Pneumoviridae* (formerly *Paramyxoviridae*) and is a single-stranded RNA virus. It was first identified in 2001 in the Netherlands. Analysis of serum samples from patients showed that it had been circulating in the human population since the mid-20th century. Metapneumovirus has two main genotypes — A and B — each of which includes several subtypes that determine the severity of the disease and the spread of the infection. There is evidence of a new variant of metapneumovirus unrelated to genotypes A and B, suggesting its potentially broader heterogeneity [7, 8].

The immaturity of the immune system in young children and the ability of respiratory pathogens to suppress interferon production reduce the body's antiviral defense, leading to the development of the disease. Interferons (IF) block the synthesis of viral proteins, preventing further viral replication and the spread of infection. Suppression of IF production leads to an imbalance between pro-inflammatory and anti-inflammatory cytokines, particularly interleukins (ILs), which exacerbates inflammation, triggers the development of allergic reactions, and causes airway obstruction syndrome [9, 10].

In young patients with acute respiratory infections, including metapneumovirus infection, reduced functional activity of immunocompetent cells and inadequate regulation of Th-1 interferons in the cellular immune response are observed, leading to a more severe course of the disease with predominant involvement of the lower respiratory tract [11, 12].

A comprehensive analysis of the clinical and immunological characteristics of metapneumovirus infection in children is a key prerequisite for elucidating pathogenetic mechanisms, improving methods of early diagnosis, predicting disease severity, and optimizing therapeutic strategies.

AIM

To identify the characteristics of the clinical course and immunopathogenesis of metapneumovirus infection in children in order to predict disease severity and optimize treatment.

MATERIALS AND METHODS

A retrospective analysis was conducted of the medical records of 210 children aged 1 month to 14 years with metapneumovirus infection who were treated at pediatric infectious disease hospitals in St. Petersburg (N.F. Filatov Children's City Clinical Hospital No. 5, St. Olga Children's City Clinical Hospital No. 4) between 2019 and 2025. Monoinfection was observed in 164 patients (78.1%), and co-infections with other respiratory viruses were observed in 46 children (21.9%).

This study presents an analysis of the clinical and immunological characteristics of patients with monometapneumovirus infection, whose age distribution is as follows: 1 month to 1 year — 41 (25.0%), 1 to 3 years — 77 (47.0%), 3 to 7 years — 34 (20.7%), 7 to 14 years — 12 (7.3%).

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Inclusion criteria for the study: seeking medical care within the first three days of symptom onset, no use of antiviral or topical antiseptic therapy prior to laboratory testing, and no comorbidities that could interfere with an objective assessment of the results (diabetes mellitus, tuberculosis, chronic liver and kidney diseases, cancer at any stage, HIV infection).

The diagnosis of metapneumovirus infection was based on clinical signs, including fever, redness of the oropharyngeal mucosa, nasal congestion, rhinitis, cough, shortness of breath, as well as percussion and auscultatory changes in the lungs. The patients' condition was monitored daily. Chest X-rays were performed when there were clinical and laboratory indications to detect pneumonia and other complications.

During the first day of the patient's hospitalization, a nasopharyngeal specimen was tested for respiratory viral antigens using real-time reverse transcription polymerase chain reaction (RT-PCR) with the "AmpliPrime® ARVI-Complex" and "AmpliPrime® SARS-CoV-2 / Flu (A/B/H1pdm09)" (NextBio LLC, Moscow). Cytokine status (levels of IFN-α and IFN-γ, IL-1β, -6, -8, -10, and IL-17) was assessed in blood serum by enzyme-linked immunosorbent assay (ELISA) during the acute phase of the disease. The assays were performed using commercial kits (Cytokine LLC, St. Petersburg) in the laboratory of the State Scientific Research Institute of Ultra-Pure Biopreparations.

Statistical analysis was performed using the STATISTICA 13.0 software package. Quantitative results are presented as absolute values with the percentage (%) and a confidence interval (CI) calculated using the Klopper–Pearson method. The Pearson's χ^2 test was used to assess differences between groups. Differences were considered statistically significant at a p-value <0.05. To identify cytokine markers, we used the binary logistic regression method with stepwise inclusion of variables (p <0.05).

RESULTS

An analysis of laboratory test results for patients with acute respiratory infections observed between 2019 and 2025 showed that a viral cause was identified in 84.9% (n=3,181) of cases, while in 15.1% (n=565) of cases, test results for the respiratory virus group were negative. Metapneumovirus infection was confirmed in 210 patients, accounting for 6.6% of all confirmed cases of ARVI. Monoinfection was observed in 164 patients (5.2%), and mixed infection in 46 (1.4%).

Mixed infection included various combinations, predominantly of two viral genomes (Fig. 1). An association between metapneumovirus and RSV was detected in the overwhelming majority of cases (26.1%), which is explained by the coincidence of the peaks in the circulation of these viruses [1]. Co-infection of metapneumovirus with coronaviruses was recorded in 21.7% of cases, which is associated with the high prevalence of SARS-CoV-2 during the pandemic [3]. Co-infection of metapneumovirus with rhinovirus (17.4%) and influenza virus (13.0%) was detected less frequently. According to the literature, influenza viruses and rhinoviruses are among the leading causative agents of ARVI and remain relevant pathogens to this day [4]. Less frequently, cases of viral-viral coinfections involving metapneumovirus with adenovirus (10.9%), bocavirus (6.5%), and parainfluenza virus (4.4%) were recorded.

An analysis of gender characteristics reveals a higher prevalence among boys compared to girls [2]. A similar trend was observed among patients with monometapneumovirus infection: among the 164 patients examined, boys accounted for 73.2% (n=120) and girls for 26.8% (n=44) (p <0.05). Among those hospitalized, the majority of patients were under

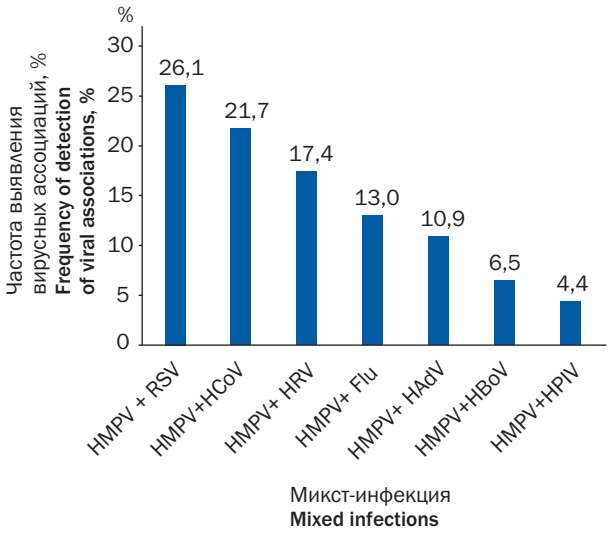

Fig. 1. Structure of viral associations in children examined in 2019–2025 (n=46): HAdV — adenovirus; HBoV — bocavirus; HCoV — coronavirus; HMPV — metapneumovirus; HPIV — parainfluenza; HRV — rhinovirus; Flu — influenza; RSV — respiratory syncytial virus (the figure is prepared by the authors)

Рис. 1. Структура вирусных ассоциаций у обследованных детей в 2019–2025 гг. (n=46): HAdV — аденовирус; HBoV — бокавирус; HCoV — коронавирус; HMPV — метапневмовирус; HPIV — парагрипп; HRV — риновирус; Flu — вирусы гриппа; RSV — респираторно-синцитиальный вирус (рисунок подготовлен авторами)

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three years of age (n=118/72.0%), which is explained by the immaturity of the immune system and the high susceptibility of children in this age group to viral infections [7].

The rate of hospitalization of children with monometapneumovirus infection was significantly higher when the lower respiratory tract was involved (n=112/68.3%) compared to the upper respiratory tract (n=52/31.7%) (p <0.05). A high incidence of lower respiratory tract involvement was observed across various age groups: 1 month to 1 year — 87.8%, 1–3 years — 66.2%, and 3–7 years — 61.8%. In children aged 7–14 years, upper respiratory tract involvement was recorded in the majority of cases (66.7%) (Table 1). Young children with lower respiratory tract involvement (n=87/53.0%) accounted for more than half of those hospitalized with monometapneumovirus infection.

Upper respiratory tract involvement in the form of rhinopharyngitis was detected in 24 children (14.6%) (Table 2). The course of metapneumovirus infection involving exclusively the upper respiratory tract was characterized by an acute onset. Hospitalization of patients was due to hyperthermia reaching 38.5–39.0 °C, which was difficult to control in an outpatient setting and persisted in the hospital for 3–5 days from the onset of symptoms. The intoxication syndrome manifested as a deterioration in general condition, lethargy, headache, and loss of appetite. The catarrhal syndrome was moderately pronounced from the first days of the illness, manifesting as serous rhinorrhea, nasal congestion, oropharyngeal hyperemia, and a persistent, non-productive cough.

Acute obstructive laryngitis was observed in 28 patients, predominantly in children aged 1–3 years (n=18/23.4%). With increasing age, the frequency of clinical manifestations of laryngeal stenosis decreased: in the 3–7-year-old group — 6 children; in the 7–14-year-old group — 2 patients. Croup more often complicated the course of the underlying disease on the second (n=15/53.6%) and third day (n=9/32.1%) from the onset of respiratory symptoms; it was less common on the first day of the illness (n=4/14.3%). At the same time, grade I laryngeal stenosis was diagnosed significantly more often (n=18/64.3%) than grade II (n=10/35.7%) (p <0.05). No cases of grade III laryngeal stenosis were observed. In 60.7% (n=17) of patients, the symptoms of stenosis were completely resolved within the first day of hospitalization; in

Table 1. Levels of respiratory tract damage in hospitalized children of different ages with mono-metapneumovirus infection in 2019–2025 (n=164)

Таблица 1. Уровни поражения респираторного тракта при монометапневмовирусной инфекции у госпитализированных детей различного возраста в 2019–2025 гг. (n=164)

Возраст Age	Уровень поражения респираторного тракта Respiratory tract lesion level	
	верхние дыхательные пути upper respiratory tract n/%	нижние дыхательные пути lower respiratory tract n/%
1 месяц — 1 год 1 month — 1 year (n=41)	5/12,2	36/87,8*
1–3 года 1–3 years (n=77)	26/33,8	51/66,2*
3–7 лет 3–7 years (n=34)	13/38,2	21/61,8*
7–14 лет 7–14 years (n=12)	8/66,7*	4/33,3
Всего детей Total children (n=164)	52/31,7	112/68,3*

The table is prepared by the authors using their own data

Таблица составлена авторами по собственным данным

Note: n — the number of patients; * — p <0.05 in relation to the corresponding indicator between the levels of respiratory tract damage.

Примечание: n — число пациентов; * — p <0,05 по отношению к соответствующему показателю между уровнями поражения респираторного тракта.

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Table 2. The nature of respiratory tract damage in hospitalized children of various ages with confirmed monometapneumovirus infection in 2019–2025 (n=164)

Таблица 2. Характер поражения респираторного тракта у госпитализированных детей различного возраста с подтвержденной монометапневмовирусной инфекцией в 2019–2025 гг. (n=164)

Возраст Age	Характер поражения респираторного тракта The nature of the respiratory tract lesion				
	острый ринофарингит acute rhinopharyngitis (n/%)	острый обструктивный ларингит acute obstructive laryngitis (n/%)	острый трахеит acute tracheitis (n/%)	острый бронхит/БОС acute bronchitis/BOS (n/%)	вирусная пневмония viral pneumonia (n/%)
1 месяц — 1 год 1 month — 1 year (n=41)	3/7,7	2/4,9	7/17,1	20/48,8*	9/21,5
1–3 года 1–3 years (n=77)	8/10,4	18/23,4	9/11,7	36/46,7*	6/7,8
3–7 лет 3–7 years (n=34)	7/20,6	6/17,6	3/8,8	14/41,2*	4/11,8
7–14 лет 7–14 year (n=12)	6/50,0	2/16,7	1/8,3	2/16,7	1/8,3
Всего детей Total children (n=164)	24/14,6	28/17,1	20/12,2	72/43,9*	20/12,2

The table is prepared by the authors using their own data

Таблица составлена авторами по собственным данным

Note: BOS — bronchial obstruction syndrome; n — number of patients, * — p <0.05 in relation to the corresponding indicator for acute rhinopharyngitis.

Примечание: БОС — бронхообструктивный синдром; n — число пациентов; * — p <0,05 по отношению к соответствующему показателю при остром ринофарингите.

28.6% (n=8) of patients, they resolved on the second day; and in only 10.7% (n=3) did croup symptoms persist for three days. Twenty patients (12.2%) were diagnosed with acute tracheitis, which manifested as a dry cough that progressed to a productive wet cough as the disease advanced.

In 72 children (43.9%), monometapneumovirus infection presented with symptoms of acute bronchitis, and 72.2% (n=52) of them exhibited bronchial obstructive syndrome (BOS) of varying severity. The age distribution of acute bronchitis/BOS was characterized by a predominance of young children: 1 month to 1 year — 48.8%, 1 to 3 years — 46.7%, with a tendency toward a decrease in frequency in older age groups: 3–7 years — 41.2%, 7–14 years — 16.7%. The complication developed in the majority of patients within the first three days — in 64.4%, and from the 4th to the 5th day — in 35.6% of children (p <0.05). The leading components of the clinical symptom complex were signs of respiratory failure (RF) against a background of obstructive syndrome, severe intoxication, and fever persisting for several days. Clinical signs of grade I–II RI were observed in 35 (21.3%) patients, with infants accounting for 85.7% (n=30) compared to children in older age groups — 14.3% (n=5) of cases (p <0.05).

In 20 (12.2%) patients with monometapneumovirus infection, pneumonia developed, more frequently in children aged 1 month to 1 year (21.5%). In other age groups, pneumonia was recorded with varying frequency: from 1 to 3 years of age — 7.8%, from 3 to 7 years of age — 11.8%, and from 7 to 14 years of age — 8.3%. In 75.0% of cases, pneumonia was detected within the first three days of the illness; in 25.0% of patients, it was diagnosed on the 4th–5th day of the illness. Radiographic examination revealed infiltrative changes predominantly in the VIII and IX segments of the right and/or left lung. In all children, the disease was accompanied by an elevated body temperature, with half of the children experiencing febrile temperatures (38.1–38.9 °C) for 3–7 days, and was accompanied by a pronounced intoxication syndrome.

We analyzed the results of a study examining serum levels of IFN-α and -γ and cytokines (IL-1β, -8,

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Table 3. Serum cytokine levels in healthy children and patients with mono-metapneumovirus infection, depending on the severity of respiratory tract damage

Таблица 3. Содержание цитокинов в сыворотке крови у пациентов с монометапневмовирусной инфекцией в зависимости от уровня поражения респираторного тракта

Цитокины Cytokines	Норма, пг/мл Standard, pg/ml (M±m)	Характер поражения респираторного тракта The nature of the respiratory tract lesion			
		острый ринофарингит, пг/мл acute rhinopharyngitis, pg/ml (M±m) (n=28)	острый обструктивный ларингит, пг/мл acute obstructive laryngitis, pg/ml (M±m) (n=20)	острый бронхит/БОС, пг/мл acute bronchitis / BOS pg/ml (M±m) (n=26)	вирусная пневмония, пг/мл viral pneumonia, pg/ml (M±m) (n=20)
ИЛ-1β	15,6±2,4	28,2±4,1	31,0±5,4	41,2±4,2*	44,7±5,1*
ИЛ-8	25,1±3,5	68,4±23,4	72,3±24,7	239,3±26,8*	326,4±27,9*
ИЛ-10	15,6±2,4	26,0±3,5	32,4±4,3	63,6±5,9*	81,0±4,6*
ИЛ-17	21,0±3,1	41,3±11,4	175,6±47,6*	267,6±39,5*	245,2±41,3*
ИФН-α	23,3±3,8	48,5±1,6	26,4±1,3	20,1±1,2*	15,4±1,1*
ИФН-γ	25,6±2,7	52,2±3,2	45,4±3,6	16,4±1,3*	10,4±1,2*

The table is prepared by the authors using their own data

Таблица составлена авторами по собственным данным

Note: BOS — bronchial obstruction syndrome; * — p<0,05 in relation to the corresponding indicator for acute rhinopharyngitis.

Примечание: БОС — бронхообструктивный синдром; * — p <0,05 по отношению к соответствующему показателю при остром ринофарингите.

-10, and -17) in patients with varying degrees of respiratory tract involvement due to mono-metapneumovirus infection (Table 3).

The study found that in children with viral pneumonia, the level of the pro-inflammatory cytokine IL-1β increases significantly, reaching 44.7±5.1 pg/mL, which is 1.6 times higher than the levels observed in acute rhinopharyngitis (28.2±4.1 pg/mL) (p <0.05). The increase in IL-8 is particularly pronounced, with its concentration rising more than fourfold, from 68.4±23.4 to 326.4±27.9 pg/mL, reflecting the intensity of the inflammatory response in the airways. The increase in IL-10 levels from 26.0±3.5 to 81.0±4.6 pg/mL indicates the activation of compensatory anti-inflammatory mechanisms aimed at limiting inflammation and protecting tissues from damage. The more than sixfold increase in IL-17, from 41.3±11.4 to 267.6±39.5 pg/ml, indicates the key role of this cytokine in the pathogenesis of obstructive inflammatory processes in the lower respiratory tract, which contributes to the recruitment and activation of neutrophils and other inflammatory cells [12]. Concurrently, a significant decrease in interferon levels is observed: IFN-α decreases from 48.5±1.6 pg/mL in acute rhinopharyngitis to 15.4±1.1 pg/mL in viral pneumonia, and IFN-γ from 52.2±3.2 to 10.4±1.2 pg/mL, respectively, indicating a substantial suppression of the antiviral interferon response [10], particularly in cases of lower respiratory tract involvement.

DISCUSSION

The analysis showed that, between 2019 and 2025, metapneumovirus infection accounted for 6.6% of confirmed cases of ARVI in children, of which 5.2% were monoinfections and 1.4% were mixed infections. The demographic profile of patients with monometapneumovirus infection was characterized by a predominance of young children (under 3 years of age) (72%), of whom 53% had inflammatory changes in the lower respiratory tract. Boys predominated among those examined (73.2%).

Acute obstructive laryngitis was most common in children aged 1–3 years (23.4%), and first-degree laryngeal stenosis was diagnosed in 64.3% of cases. Croup developed predominantly on the 2nd–3rd day of the illness (53.6% and 32.1%, respectively).

Acute bronchitis/bronchopneumonia was more frequently recorded in children aged 1 month to 1 year (48.8%) and 1–3 years (46.7%), with this complication occurring within the first three days of the illness in 64.4% of cases. Clinical signs of grade I–II respiratory distress syndrome were observed in 85.7% of young children.

Viral pneumonia was diagnosed predominantly in infants under 1 year of age (21.5%), with 75% of cases occurring within the first three days, indicating rapid progression of the inflammatory process in the lower respiratory tract. Consequently,

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acute bronchitis/BRD and pneumonia developed predominantly in the early stages of the illness.

The cytokine profile of patients was characterized by a significant increase in pro-inflammatory cytokines IL-1β (up to 44.7±5.1 pg/mL), IL-8 (up to 326.4±27.9 pg/mL), IL-17 (up to 267.6±39.5 pg/mL), as well as the anti-inflammatory cytokine IL-10 (up to 81.0±4.6 pg/mL), particularly in cases of lower respiratory tract involvement. At the same time, a decrease in IFN-α and -γ levels (to 15.4 and 10.4 pg/mL, respectively) was observed, reflecting a weakened antiviral immune response.

CONCLUSION

Metapneumovirus infection in children is characterized by predominant involvement of the lower respiratory tract and a high incidence of complications, such as acute obstructive laryngitis, bronchial obstruction syndrome, and pneumonia, which leads to a severe course of the disease and necessitates a comprehensive approach to diagnosis and treatment. Immune dysregulation in the form of an imbalance between pro- and anti-inflammatory cytokines, as well as a reduced interferon response, can serve as markers for monitoring the course of the disease and form the basis for optimizing therapy aimed at restoring antiviral immunity.

ADDITIONAL INFORMATION

Authors' contribution. Concept of the article — V.F. Sukhovetskaya, T.A. Kaplina, V.N. Timchenko, T.M. Chernova, E.V. Barakina, O.V. Bulina, E.G. Golovacheva, V.S. Timonina, O.P. Gurina, A.E. Blinov, O.N. Varlamova; text development — V.F. Sukhovetskaya, T.A. Kaplina, V.N. Timchenko, T.M. Chernova, E.V. Barakina, O.V. Bulina, E.G. Golovacheva, V.S. Timonina, O.P. Gurina, A.E. Blinov, O.N. Varlamova; editing — V.F. Sukhovetskaya, T.A. Kaplina, V.N. Timchenko; approval of the final version of the article — V.F. Sukhovetskaya, V.N. Timchenko.

All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Концепция статьи — В.Ф. Суховецкая, Т.А. Каплина, В.Н. Тимченко, Т.М. Чернова, Е.В. Баракина, О.В. Булина, Е.Г. Головачева, В.С. Тимонина, О.П. Гурина, А.Е. Блинов, О.Н. Варламова; написание текста — В.Ф. Суховецкая, Т.А. Каплина, В.Н. Тимченко, Т.М. Чернова, Е.В. Баракина, О.В. Булина, Е.Г. Головачева, В.С. Тимонина, О.П. Гурина, А.Е. Блинов, О.Н. Варламова; редактирование — В.Ф. Суховецкая, Т.А. Каплина, В.Н. Тимченко; утверждение окончательного варианта статьи — В.Ф. Суховецкая, В.Н. Тимченко.

Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

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Authors' info

✉ **Vera F. Sukhovetskaya** — Cand. Sci. (Med.), Associate Professor, Department of Infectious Diseases in Children named after Professor M.G. Danilevich.
E-mail: verafedotovna@mail.ru;
https://orcid.org/0000-0002-1566-7137; SPIN: 3633-2952
Tatyana A. Kaplina — Cand. Sci. (Med.), Associate Professor, Department of Infectious Diseases in Children named after Professor M.G. Danilevich. E-mail: k.kta@yandex.ru;
https://orcid.org/0000-0003-1659-2058; SPIN: 1381-9580
Vladimir N. Timchenko — Dr. Sci. (Med.), Professor, Head of the Department of Infectious Diseases in Children named after Professor M.G. Danilevich.
E-mail: timchenko220853@yandex.ru;
https://orsid.org/0000-0002-4068-1731; SPIN: 8594-0751
Tatyana M. Chernova — Cand. Sci. (Med.), Associate Professor, Department of Infectious Diseases in Children named after Professor M.G. Danilevich. E-mail: t-chernova@mail.ru;
https://orcid.org/0000-0003-4845-3757; SPIN: 3146-3629
Elena V. Barakina — Cand. Sci. (Med.), Associate Professor, Department of Infectious Diseases in Children named after Professor M.G. Danilevich. E-mail: elenabarakina@mail.ru;
https://orcid.org/0000-0002-2128-6883; SPIN: 9313-2879
Oksana V. Bulina — Cand. Sci. (Med.), Associate Professor, Department of Rehabilitation, Postgraduate and Additional Professional Education. E-mail: oksanabulina@yandex.ru;
https://orcid.org/0000-0002-2997-7777; SPIN: 7960-2040
Ekaterina G. Golovacheva — Dr. Sci. (Med.), Leading Researcher, Department of Respiratory Viral Infections in Children. E-mail: okdixi@mail.ru;
https://orcid.org/0000-0002-1934-7288; SPIN: 4129-3846
Veronika S. Timonina — Researcher, Department of Respiratory Viral Infections in Children.
E-mail: karina88888888@list.ru;
https://orcid.org/0000-0002-2887-0126; SPIN: 5848-0774
Olga P. Gurina — Cand. Sci. (Med.), Senior Researcher at the Laboratory Medical and Social Problems in Pediatrics, Scientific and Research Center.
E-mail: ol.gurina@yandex.ru;
https://orcid.org/0000-0002-1066-5423; SPIN: 4251-0563
Alexander E. Blinov — Senior Researcher at the Laboratory of Medical and Social Problems in Pediatrics, Scientific and Research Center.
E-mail: aleks.blinov@mail.ru;
https://orcid.org/0009-0003-9852-256X; SPIN: 1378-8191
Olga N. Varlamova — Researcher at the Laboratory of Medical and Social Problems in Pediatrics, Scientific and Research Center.
E-mail: on.varlamova@mail.ru;
https://orcid.org 0000-0002-2195-0756; SPIN: 7101-5829

Об авторах

✉ **Вера Федотовна Суховецкая** — к.м.н., доцент, кафедра инфекционных заболеваний у детей им. профессора М.Г. Данилевича. E-mail: verafedotovna@mail.ru;
https://orcid.org/0000-0002-1566-7137; SPIN: 3633-2952

Татьяна Анатольевна Каплина — к.м.н., доцент, кафедра инфекционных заболеваний у детей им. профессора М.Г. Данилевича. E-mail: k.kta@yandex.ru;
https://orcid.org/0000-0003-1659-2058; SPIN: 1381-9580
Владимир Николаевич Тимченко — д.м.н., профессор, заведующий кафедрой инфекционных заболеваний у детей им. профессора М.Г. Данилевича.
E-mail: timchenko220853@yandex.ru;
https://orsid.org/0000-0002-4068-1731; SPIN: 8594-0751
Татьяна Маратовна Чернова — к.м.н., доцент, кафедра инфекционных заболеваний у детей им. профессора М.Г. Данилевича. E-mail: t-chernova@mail.ru;
https://orcid.org/0000-0003-4845-3757; SPIN: 3146-3629
Елена Владимировна Баракина — к.м.н., доцент, кафедра инфекционных заболеваний у детей имени профессора М.Г. Данилевича. E-mail: elenabarakina@mail.ru;
https://orcid.org/0000-0002-2128-6883; SPIN: 9313-2879
Оксана Владимировна Булина — к.м.н., доцент, кафедра реабилитологии ФП и ДПО. E-mail: oksanabulina@yandex.ru;
https://orcid.org/0000-0002-2997-7777; SPIN: 7960-2040

Екатерина Георгиевна Головачева — д.м.н., ведущий научный сотрудник отделения респираторных вирусных инфекций у детей. E-mail: okdixi@mail.ru;
https://orcid.org/0000-0002-1934-7288; SPIN: 4129-3846
Вероника Сергеевна Тимонина — научный сотрудник отделения респираторных вирусных инфекций у детей.
E-mail: karina88888888@list.ru;
https://orcid.org/0000-0002-2887-0126; SPIN: 5848-0774
Ольга Петровна Гурина — к.м.н., старший научный сотрудник лаборатории медико-социальных проблем в педиатрии, Научно-исследовательский центр.
E-mail: ol.gurina@yandex.ru;
https://orcid.org/0000-0002-1066-5423; SPIN: 4251-0563
Александр Евгеньевич Блинов — старший научный сотрудник лаборатории медико-социальных проблем в педиатрии, Научно-исследовательский центр.
E-mail: aleks.blinov@mail.ru;
https://orcid.org/0009-0003-9852-256X; SPIN: 1378-8191
Ольга Николаевна Варламова — научный сотрудник лаборатории медико-социальных проблем в педиатрии, Научно-исследовательский центр.
E-mail: on.varlamova@mail.ru;
https://orcid.org 0000-0002-2195-0756; SPIN: 7101-5829

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