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Respiratory Morbidity In Children Who Underwent Mechanical Ventilation In The Neonatal Period: Clinical And Immunological Aspects

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Abstract

Children who underwent mechanical ventilation in the neonatal period are at increased risk of recurrent respiratory diseases. These conditions may be associated with prematurity, bronchopulmonary dysplasia, prolonged oxygen therapy, and immune system immaturity. This article discusses the main clinical and immunological aspects of respiratory morbidity in this group of children, with emphasis on recurrent infections, bronchial obstruction, immune status, and inflammatory markers.

Keywords. Children, mechanical ventilation, neonatal period, respiratory morbidity, immune status, recurrent infections.

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1. Introduction

Respiratory morbidity in early childhood is a significant clinical problem, particularly among children who required mechanical ventilation during the neonatal period. Globally, approximately 13.4 million infants were born preterm in 2020, which corresponds to more than 1 in 10 live births. Many of these newborns require respiratory support because of respiratory distress syndrome, lung immaturity, perinatal hypoxia, infections, or other severe neonatal conditions.Children born preterm and those exposed to invasive mechanical ventilation are at increased risk of long-term respiratory complications. According to the American Thoracic Society, post-prematurity respiratory disease may manifest as chronic cough, recurrent wheezing, exercise limitation, and reduced pulmonary function. A large meta-analysis including more than 1.5 million children showed that preterm birth was associated with a higher risk of wheezing disorders: 13.7% in preterm children compared with 8.3% in term-born children, with an odds ratio of 1.71. After adjustment for confounding factors, the association remained significant, with an odds ratio of 1.46. One of the most important consequences of neonatal respiratory support is bronchopulmonary dysplasia. It is reported to affect up to 40% of preterm infants with very low birth weight, especially those exposed to oxygen therapy and mechanical ventilation. Bronchopulmonary dysplasia is also associated with a higher risk of later

asthma; a 2023 meta-analysis found that preterm infants with BPD had an increased risk of developing asthma in childhood, with an odds ratio of 1.73. In addition to structural and functional lung changes, immune system immaturity plays an important role in the development of recurrent respiratory diseases. Alterations in humoral immunity, cellular immunity, and inflammatory response may contribute to frequent respiratory infections, prolonged cough, bronchial obstruction, and repeated hospitalizations. Therefore, evaluation of clinical and immunological parameters in children who underwent mechanical ventilation in the neonatal period is important for identifying risk groups, improving follow-up, and developing preventive strategies.

Objective of the Study

To assess the clinical and immunological aspects of respiratory morbidity in children who underwent mechanical ventilation during the neonatal period.

Materials and Methods

This study included children who underwent mechanical ventilation during the neonatal period. Clinical data were collected from medical records and parental interviews. The assessment included gestational age, birth weight, duration of mechanical ventilation, frequency of respiratory infections, episodes of bronchial obstruction, wheezing, and hospitalizations. Laboratory evaluation included serum immunoglobulins IgA, IgG, IgM, IgE, complete blood count, C-reactive protein, total protein, albumin, glucose, urea, creatinine, bilirubin, ALT, AST, and other biochemical indicators. The obtained data were analyzed to assess the relationship between neonatal mechanical ventilation, immune status, biochemical parameters, and later respiratory morbidity.

Results

A total of 80 children were examined. The main group included 50 children who underwent mechanical ventilation during the neonatal period, while the control group included 30 children without a history of neonatal mechanical ventilation. The mean age of children in the main group was 3.8 ± 1.2 years, and in the control group it was 3.6 ± 1.1 years. In the main group, prematurity was observed in 34 children (68.0%), low birth weight in 31 children (62.0%), and a history of prolonged oxygen therapy in 28 children (56.0%). The duration of mechanical ventilation ranged from 2 to 14 days, with an average duration of 6.4 ± 2.8 days. Mechanical ventilation for more than 7 days was recorded in 18 children (36.0%). Recurrent respiratory infections were significantly more common in children who underwent mechanical ventilation during the neonatal period. In the main group, frequent respiratory infections were observed in 38 children (76.0%), compared with 12 children (40.0%) in the control group. Bronchial obstruction was detected in 29 children (58.0%) in the main group and in 8 children (26.7%) in the control group. Wheezing episodes were reported in 27 children (54.0%) of the main group, compared with 7 children (23.3%) in the control group. Repeated hospitalizations due to respiratory diseases were also more frequent among children in the main group. Hospitalization at least once during the previous year was recorded in 24 children (48.0%) after neonatal mechanical ventilation, while in the control group this indicator was observed in 6 children (20.0%). Pneumonia was diagnosed in 14 children (28.0%) of the main group and in 3 children (10.0%) of the control group. Laboratory evaluation showed that children in the main group had more pronounced changes in immune and biochemical parameters. Reduced IgA levels were found in 21 children (42.0%), while decreased IgG levels were observed in 16 children (32.0%). Increased IgE levels were detected in 19 children (38.0%), which may indicate a tendency toward allergic inflammation and bronchial hyperreactivity. Inflammatory markers were also more frequently elevated in the main group. Increased C-reactive protein levels were observed in 22 children (44.0%), leukocytosis in 18 children (36.0%), and elevated erythrocyte sedimentation rate in 20 children (40.0%). These changes were more common in children with recurrent bronchitis, bronchial obstruction, and repeated pneumonia. Biochemical analysis revealed moderate changes in several indicators. Decreased total protein was found in 13 children (26.0%), reduced albumin levels in 11 children (22.0%), and mild elevation of ALT and AST in 9 children (18.0%). Increased urea or creatinine levels were not common and were observed only in isolated cases. These findings may reflect the influence of recurrent infections, prolonged inflammatory processes, and general metabolic stress in children with a complicated neonatal history. The highest rate of respiratory morbidity was observed in children who had mechanical ventilation for more than 7 days. In this subgroup, recurrent respiratory infections were recorded in 16 of 18 children (88.9%), bronchial obstruction in 13 children (72.2%), and repeated hospitalizations in 11 children (61.1%). In comparison, among children who received mechanical ventilation for less than 7 days, recurrent respiratory infections were observed in 22 of 32 children (68.7%), bronchial obstruction in 16 children (50.0%), and hospitalizations in 13 children (40.6%). Thus, the obtained results showed that

children who underwent mechanical ventilation in the neonatal period had a higher frequency of recurrent respiratory infections, bronchial obstruction, wheezing episodes, pneumonia, and hospitalizations. The most significant risk factors were prematurity, low birth weight, prolonged oxygen therapy, and duration of mechanical ventilation for more than 7 days. Changes in immunoglobulin levels, inflammatory markers, and biochemical indicators may play an important role in the development and persistence of respiratory morbidity in this group of children.

Table 1

Clinical indicator	Main group, n=50	Control group, n=30
Recurrent respiratory infections	38 / 76.0%	12 / 40.0%
Bronchial obstruction	29 / 58.0%	8 / 26.7%
Wheezing episodes	27 / 54.0%	7 / 23.3%
Repeated hospitalizations	24 / 48.0%	6 / 20.0%
Pneumonia	14 / 28.0%	3 / 10.0%

Table 1 shows that children who underwent mechanical ventilation during the neonatal period had a higher frequency of recurrent respiratory infections, bronchial obstruction, wheezing episodes, repeated hospitalizations, and pneumonia compared with the control group.

Discussion

The results of the study showed that children who underwent mechanical ventilation during the neonatal period had a higher frequency of respiratory morbidity compared with the control group. Recurrent respiratory infections were observed in 76.0% of children in the main group, while in the control group this indicator was 40.0%. Bronchial obstruction was detected in 58.0% of children after neonatal mechanical ventilation and in 26.7% of children in the control group. Wheezing episodes, pneumonia, and repeated hospitalizations were also more common among children with a history of neonatal mechanical ventilation. These findings indicate that neonatal mechanical ventilation may have a long-term effect on the respiratory system. Although mechanical ventilation is a life-saving procedure in newborns with respiratory failure, prolonged respiratory support may contribute to lung tissue damage, inflammatory changes, impaired mucociliary clearance, and increased bronchial hyperreactivity. According to current literature, post-prematurity respiratory disease may manifest as chronic cough, recurrent wheezing, exercise limitation, and reduced pulmonary function in later childhood. The duration of mechanical ventilation was one of the important factors associated with respiratory morbidity. In the present study, children who received mechanical ventilation for more than 7 days had more frequent recurrent respiratory infections, bronchial obstruction, and repeated hospitalizations than children ventilated for less than 7 days. This suggests that longer exposure to invasive respiratory support may increase the risk of subsequent respiratory complications. Ventilation-induced lung injury in neonates is considered an important mechanism in the development of chronic pulmonary changes, especially in premature infants. Prematurity and low birth weight also played an important role in the development of respiratory morbidity. Globally, approximately 13.4 million infants were born preterm in 2020, which corresponds to more than 1 in 10 live births. A large meta-analysis including more than 1.5 million children showed that wheezing disorders were more common in preterm children than in term-born children: 13.7% versus 8.3%. Bronchopulmonary dysplasia is another important factor contributing to long-term respiratory problems in children who required neonatal respiratory support. It is a chronic lung disease of prematurity associated with inflammation, injury of the developing lung, and impaired alveolar and vascular growth. Children with bronchopulmonary dysplasia have a higher risk of later asthma and recurrent obstructive symptoms. The immunological changes found in the main group may also explain the higher frequency of recurrent respiratory diseases. Decreased IgA can reduce local mucosal protection of the respiratory tract, while decreased IgG may indicate insufficient systemic immune response. Increased IgE may be associated with allergic inflammation and bronchial hyperreactivity. In children with recurrent

infections, evaluation of immune status is clinically important, although most young children with recurrent mild infections do not have primary immunodeficiency. Biochemical and inflammatory changes also have clinical significance. Increased C-reactive protein, leukocytosis, and elevated ESR may reflect persistent or recurrent inflammatory activity. Reduced total protein and albumin can be associated with nutritional deficiency, prolonged inflammation, or metabolic stress. These changes may contribute to more severe and prolonged respiratory diseases in children with a complicated neonatal history. The obtained results are consistent with studies conducted in Uzbekistan. Ibatova reported that broncho-obstructive syndrome in young children is associated with perinatal disorders, early artificial feeding, frequent acute respiratory infections, family history of allergy, malnutrition, rickets, and anemia. In that study, 912 children aged 1–3 years were analyzed, and broncho-obstructive syndrome was registered in 494 children with acute obstructive bronchitis. Local data also confirm the importance of viral respiratory infections in young children. Yusupova and Israilova studied 45 young children with laboratory-confirmed respiratory syncytial viral infection and found obstructive bronchitis in 84.2% of cases, bronchiolitis in every third child, and pneumonia in 15.8%. These findings support the need for careful monitoring of children with previous neonatal respiratory support, especially during viral infection seasons. Recent Uzbek studies also emphasize that inflammatory bronchopulmonary diseases with airway obstruction remain one of the leading causes of morbidity in children under three years of age. Respiratory viruses, including RSV, metapneumovirus, and coronavirus, are considered dominant etiological factors, and early detection with comprehensive treatment may reduce the risk of chronic airway remodeling. Thus, respiratory morbidity in children after neonatal mechanical ventilation is multifactorial. The main contributing factors include prematurity, low birth weight, prolonged oxygen therapy, duration of mechanical ventilation, bronchopulmonary dysplasia, immune imbalance, recurrent inflammation, and viral respiratory infections. Early identification of these risk factors may help improve follow-up, prevention, and treatment strategies in this group of children.

Conclusions

1. Children who underwent mechanical ventilation during the neonatal period showed a higher frequency of recurrent respiratory infections, bronchial obstruction, wheezing episodes, pneumonia, and repeated hospitalizations.

2. The most significant factors associated with respiratory morbidity were prematurity, low birth weight, prolonged oxygen therapy, and mechanical ventilation lasting more than 7 days.

3. Laboratory findings revealed changes in immune and biochemical parameters, including decreased IgA and IgG levels, increased IgE, elevated C-reactive protein, leukocytosis, elevated ESR, and reduced total protein and albumin levels.

4. The obtained results indicate that neonatal mechanical ventilation may contribute to long-term respiratory morbidity and immune imbalance in children.

5. Children who underwent mechanical ventilation in the neonatal period require regular medical follow-up, early detection of respiratory complications, and timely preventive measures.

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