Doctoral school of medical Sciences

As a manuscript,
UDC: 616.23/.24-007.17-02-07-053.32(043.2)

COTOMAN Aliona

BRONCHOPULMONARY DYSPLASIA IN CHILDREN: ETIOLOGICAL FACTORS AND CLINICAL-PARACLINICAL DIAGNOSIS

322.01– PEDIATRICS AND NEONATOLOGY

Summary of the Ph.D. Thesis in Medical Sciences

Chișinău, 2025

The present Ph.D. thesis was developed within the Department of Pediatrics at the *Nicolae Testemițanu State University of Medicine and Pharmacy PI, the Republic of Moldova.*

Scientific advisor:
Șciuca Svetlana, Dr.Habil., Professor, corresponding member of the ASM

Members of the Advisory Committee:
Gudumac Eva, Dr.Habil., Professor, academician of the ASM

Curteanu Ala, Dr.Habil., research assoc., MPHI Institute of Mother and Child

Selevestru Rodica, MD, assoc. Prof., Nicolae Testemițanu SUMPH

The defense will take place on May 28, 2025, at 2:00 p.m., in the premises of the "*Nicolae Testemitanu" University of Medicine and Pharmacy*, 165 Stefan cel Mare si Sfânt Blvd., office 205, in the meeting of the Commission for the public defense of the doctoral thesis, approved by the decision of the Scientific Council of the Consortium in 23.12.2024 (minutes nr.50).

Doctoral Thesis Public Defense Committee:
Chairperson:
Corlăteanu Alexandru, Dr. Habil., Professor,
Head of the Department of Pulmonology and Allergology,
Nicolae Testemițanu State University of Medicine and Pharmacy

Members:
Șciuca Svetlana, Dr.Habil., Professor
corresponding member of the ASM

Țurea Valentin, Dr.Habil., Professor

Official Referees:
Gudumac Eva, Dr.Habil., Professor, academician of the ASM

Iavorschii Constantin, Dr.Habil., Professor

Nalivaico Nicolai, MD, assoc. prof.

Author: Cotoman Aliona

CONTENTS

CONCEPTUAL FRAMEWORK OF THE RESEARCH

Relevance and significance of the topic

Bronchopulmonary Dysplasia (BPD) is a chronic lung disease of prematurity. It is defined by the need for supplemental oxygen and/or respiratory support at 28 days of life or at 36 weeks postmenstrual age (PMA), along with characteristic radiological changes. A simplified definition based only on oxygen or ventilation requirement is commonly used in clinical studies and practice due to its ease of application. However, it does not reflect disease severity or predict long-term pulmonary outcomes [1,2,3,4,6,7,8,13]. The 2001 definition does not account for newer respiratory technologies, such as high-flow nasal cannula, which provides positive pressure without added oxygen. Therefore, the NICHD proposed updated diagnostic criteria in 2016 [10,12,13]. BPD severity classification applies to infants born before 32 weeks of gestation who still require oxygen or ventilatory support at 36 weeks PMA and present with radiographic evidence of lung damage [4,6,12]. BPD has a multifactorial etiology, with prematurity as the central factor. Prenatal (e.g., intrauterine growth restriction) and postnatal (mechanical ventilation, oxygen toxicity, infections) exposures contribute to pulmonary inflammation and injury [5,11]. Premature lungs are structurally immature, lack surfactant, have poor antioxidant defenses, and exhibit impaired mucus clearance. Risk increases as birth weight decreases, being highest in infants born before 28 weeks gestation [16]. Intrauterine growth restriction independently increases susceptibility to lung injury and impairs pulmonary vascular development [11,14]. Aggressive mechanical ventilation, particularly due to volutrauma, plays a key role in BPD pathogenesis, while barotrauma has a lesser impact [14]. To reduce BPD risk, modern strategies favor non-invasive ventilation methods like nCPAP, aiming to avoid intubation and limit invasive mechanical ventilation. Variations in neonatal center practices influence BPD incidence. Among extremely low birth weight infants, prolonged oxygen exposure in the first two weeks of life increases the risk [13].

Research Aim: To evaluate etiological factors and clinical-paraclinical diagnosis of BPD in preterm infants to develop prognostic criteria for disease progression.

Objectives: 1) Investigate causal and risk factors of BPD in children. 2) Assess clinical manifestations of BPD. 3) Examine pulmonary imaging findings in BPD cases.4) Establish prognostic criteria for BPD progression and severity in preterm infants.

Scientific Novelty: The study provided original national data on BPD risk factors and highlighted the evolution and sequelae of the disease. Clinical and imaging findings were correlated with gestational age, birth weight, and prematurity level, offering insights into severity-related patterns.

Theoretical Significance: BPD is influenced by multiple etiologic factors, including prematurity, mechanical ventilation, and oxygen exposure. A distinct early clinico-paraclinical profile was identified, potentially guiding targeted therapies and preventive strategies.

Practical Value: Findings were implemented in clinical practice at the IMSP IMC Pulmonology Clinic and integrated into the educational process at the USMF "Nicolae Testemițanu" Department of Pediatrics. The study contributed to the update of National Clinical Protocol PCN-393 on BPD, supporting improved care and continuous medical education.

Keywords: Bronchopulmonary dysplasia, prematurity, risk factors, mechanical ventilation, CPAP, chest X-ray, pulmonary CT.

RESEARCH METHODOLOGY

An analytical observational cohort study was designed to fulfil the study's objectives. Children were selected from the Pneumonology Department of the MPHI Mother and Child Institute, based on their admission file records.

Inclusion criteria comprised premature infants admitted to the Pneumonology Department of the Mother and Child Institute whose medical histories suggested BPD. This included a history of premature birth, neonatal respiratory distress syndrome, and oxygen therapy during the neonatal period.

Exclusion criteria included parental refusal of study participation, children with hereditary diseases, congenital bronchopulmonary anomalies, foreign bodies in the bronchial tree, and specific infections such as HIV/AIDS or tuberculosis.

The required number of observation units (children both with and without BPD) was calculated using the following formula:

$$n = \frac{1}{(1-f)} \times \frac{2(Z_\alpha + Z_\beta)^2 xP(1-P)}{(P_o - P_1)^2}$$

whereas:

Po – based on references, the rate of children with dysplasia ranges from 15% to 37% (P0 = 0.37);

P_1 –it is assumed that the value in the research group will be 74% (P1 = 0.74);

P = (P0 + P1)/2=0,555;

Zα – the table value for a statistical significance of 95% is Zα = 1.96;

Z_β –the table value for a statistical power of 80.0% is Zβ = 0.84;

f = the rate of subjects expected to leave the study for reasons other than the investigated effect; q=1/(1-f), f=10.0% (0.1).

Entering the data into the formula, the following was obtained:

$$n = \frac{1}{(1-0.1)} \times \frac{2(1.96+0.84)^2 x0.555x0.445}{(0.37-0.74)^2} = 31$$

The study's research group was expanded to include a minimum of 31 children diagnosed with BPD. Recognizing observed demographic and clissnical variations, the decision was made to include 53 children with BPD and 52 children without BPD to design an appropriate control group.

The research protocol was meticulously planned to use a variety of methods, each carefully selected and adapted to suit the specific stages of the study. Initially, epidemiological observation techniques were implemented to gather the necessary informative data. This data collection was completed through both direct and indirect means. Direct methods (clinical observation, surveys, and parental interviews) contributed to the appropriate and detailed data collection concerning the children's health. A comprehensive questionnaire, divided into rubrics covering general information, diagnosis, medical history, clinical assessment, and imaging results, was developed for the child assessment. This questionnaire proved fundamental for systematically organizing information and ensuring a rigorous analysis.

The study received a positive approval from the Research Ethics Committee of Nicolae Testemițanu SUMPh as per the minutes No. 73 from May 31, 2017. This approval confirms that the research adhered to ethical standards and safeguarded the rights of the patients involved. These measures provided a strong foundation for the study, ensuring that the collected data were both relevant and aligned with ethical principles, which ultimately led to significant findings in the assessment of BPD in children.

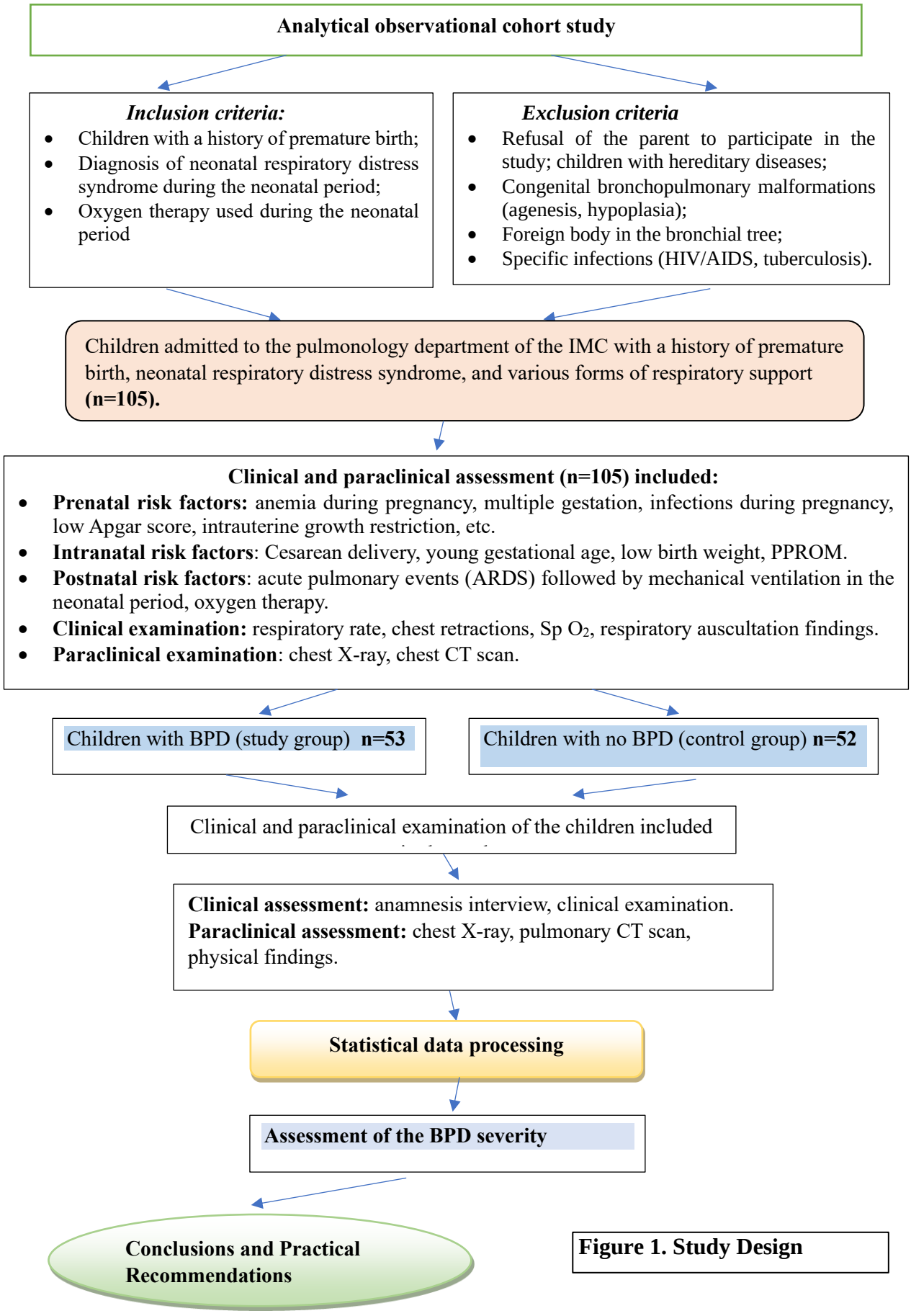

Figure 1. Study Design

CHAPTER SUMMARY

Chapter 1, "Literature Review," addresses the current state of childhood morbidity, with a particular focus on respiratory illness, especially among premature infants. Prematurity is a significant risk factor for respiratory problems, and an analysis of immature lung development reveals the vulnerability of this population. The chapter highlights the elevated incidence of respiratory conditions in premature infants, particularly bronchopulmonary dysplasia (BPD), a common ailment contributing to long-term complications. An examination was undertaken of both endogenous factors—genetic predispositions and pre-existing conditions—and exogenous factors, such as secondhand smoke exposure and viral infections, known to worsen respiratory illnesses. This chapter establishes the rationale for the present study, emphasizing the critical need for a comprehensive understanding of these factors to inform the development of effective prevention and treatment approaches. Relevant specialized literature has been reviewed to support the conclusions presented. Overall, this section provides a solid data framework for subsequent research, drawing attention to the necessity of early interventions and careful monitoring, which are essential for improving the prognosis and quality of life for premature infants.

Chapter 2, "Materials and Methods," details the methodology employed in this analytical observational cohort study, conducted between 2017 and 2021. The study investigated respiratory morbidity in 105 children, aged 3 months to 3 years, suspected of having BPD. Participants were divided into two groups: a study group (children with BPD) and a control group (children without BPD). Inclusion and exclusion criteria were established to ensure the validity and comparability of the groups. Data collection involved a detailed medical inquiry, including prenatal and postnatal history, clinical evaluation, and imaging examinations (chest X-rays and computed tomography scans), which provided relevant information regarding respiratory status.

The research proceeded through four stages: planning, data acquisition, data analysis, and interpretation of findings. The *study design* is presented schematically in Figure 1, highlighting the research type, participant selection process, and data collection methods.

State-of-the-art statistical techniques were applied to analyse the data, allowing for an accurate and detailed interpretation of results, showing clinical significance. The chapter concludes with a presentation of the derived conclusions and practical recommendations, highlighting the importance of early BPD detection in pediatric patients. This chapter provides a solid methodological framework, demonstrating the requisite scientific consistency to validate the study's findings and their implications for clinical practice.

Modern statistical techniques were used for data analysis, enabling a thorough and detailed interpretation of the results, showing clinical relevance. The chapter ends up with conclusions and practical recommendations, emphasizing the importance of early BPD diagnosis in children. The chapter provides a solid methodological foundation, displaying the scientific accuracy necessary for validating the results and their significance to clinical practice.

Chapter 3, entitled **" The Study of Clinical and Imaging Parameters in Children with BPD,"** provides a detailed analysis of a cohort of children diagnosed with BPD, aiming to highlight the condition's unique developmental characteristics. The primary objective is to gain a deeper understanding of the clinical and imaging features associated with BPD. The study allowed for the identification of relevant demographic and clinical traits of the patients. Subgrouping the children according to inclusion criteria facilitated an effective comparison between different patient categories. Modern statistical analyses were employed to evaluate the relationships between clinical parameters (weight, height, respiratory parameters) and demographic variables (age, sex). Beyond the clinical analysis, imaging evaluation included X-rays and CT scans, which provided significant data on structural changes in the lungs and the extent of BPD-related damage. These investigations contributed to a deeper understanding of the disease's severity.

In conclusion, the chapter emphasizes the major role of clinical and imaging monitoring in the management of BPD and offers valuable support for the development of customized interventions for diseased children.

3.1 Prenatal risk factor evaluation in children with bronchopulmonary dysplasia

Multivariate analysis of maternal comorbidities identified the key predictive factors impacting gestational age at delivery. Existing specialized literature strongly suggests that maternal health conditions are major contributors to the increased rate of premature births. Premature rupture of membranes (PROM) is a frequent cause of preterm birth. PROM promotes amniotic fluid contamination, consequently increasing the risk of intrauterine infection [12,10]. As a recognized cause of preterm labour, PROM can potentially trigger BPD.

Figure 2 illustrates maternal and intrauterine factors associated to a high risk of BPD. Notably, gestational anaemia was identified as a perinatal factor with a negative impact on neonatal outcomes. The study showed a significantly higher incidence (χ^2=16.271; p<0.001) of maternal anaemia among children who later developed BPD–64.2 %, compared to 24.5% in the control group. This indicates a strong relation between maternal anaemia and BPD risk. These findings support the hypothesis that anaemia during pregnancy, often correlated with chronic intrauterine hypoxia, can impair foetal lung development, thereby increasing susceptibility to BPD after birth.

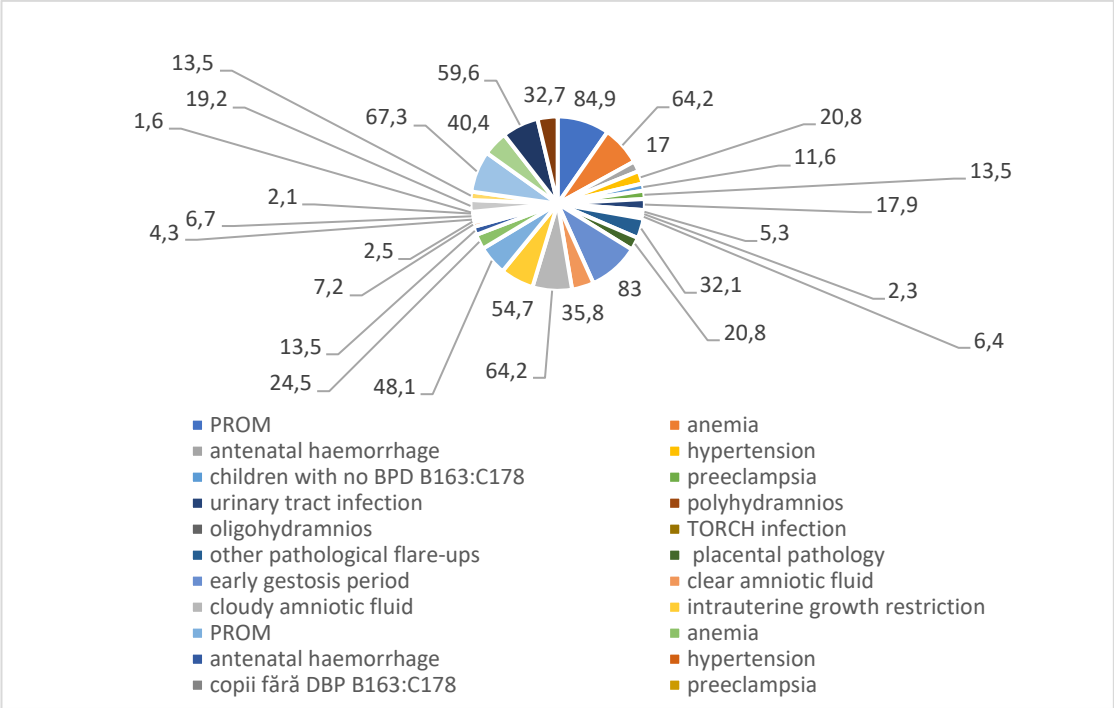

Figure 2. **Maternal risk factors in children with bronchopulmonary dysplasia**

Antenatal haemorrhage is among the causes of anaemia during pregnancy. It was identified in 17.0% of pregnant women in the group of children who developed BPD, compared to 13.5% in the control group (χ^2=0.252; p=0.616). The course of pregnancy is influenced by numerous factors, and the presence of early pre-eclampsia is an important indicator of fetal risk. In this study, signs of early pre-eclampsia were identified in a majority (83.0%) of pregnant women in the group of children with BPD, compared to approximately two-thirds of cases in the control group (χ^2=3.478; p=0.062) (Figure 2).

Gestational diabetes is one of the most frequent maternal comorbidities and is associated with a doubling of the risk of neonatal morbidity, compared to newborns from non-diabetic mothers. The condition is recognized for its contribution to extreme prematurity, respiratory distress syndrome, and congenital malformations. In the study, gestational diabetes was reported in 11.6% of premature infants with BPD, compared to 2.5% in the group of premature infants without BPD (χ^2=3.726; p=0.054), suggesting a noteworthy risk tendency.

Preeclampsia is another common complication associated with pregestational diabetes, occurring 2–3 times more frequently in pregnant individuals with this condition. In 87% of cases, it correlates with the duration of diabetes. This condition often leads to premature birth. In the study, preeclampsia-induced premature birth was reported in 13.5% of cases involving infants with BPD, compared to 4.3% in the control group. This difference approached statistical significance (χ^2=2.935; p=0.087). The composition of the amniotic fluid can indirectly reflect the foetus's intrauterine hypoxic condition. Clear amniotic fluid was reported in 35.8% of BPD cases (40.4% in the control group). The presence of turbid amniotic fluid was observed in 64.2% of infants with BPD and in 59.6% of the control group (χ^2=0.229; p=0.632) (Figure 2).

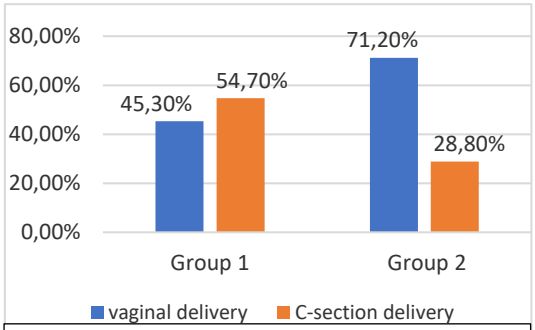

Figure 3. **Type of delivery in children with BPD**

Prenatal risk factors can negatively influence a foetus's intrauterine development, a finding supported by this study. Intrauterine growth restriction was observed in 54.7% of infants who developed BPD, compared to only 32.7% in the control group (χ^2=5.846; p=0.023).

While existing literature presents varying results, clinical practice strongly supports Caesarean sections in high-risk pregnancies [7], an issue that remains debated. Among premature infants who developed BPD, vaginal delivery occurred in only 45.3% of cases, compared to 71.2% in premature infants without BPD. This study revealed a significantly higher proportion of Caesarean births among children with BPD – 54.7%, versus 28.8% in the control group. The difference between the two groups was statistically significant (χ2=7.216; p<0.007), suggesting an association between non-physiological delivery and the risk of developing BPD in premature infants (Figure 3).

The research confirmed the presence of respiratory distress syndrome in most children, who later developed BPD – this was found in 90.6% of cases, with a very high validity compared to the group of children without BPD, where the rate was 34.6%, x2 = 35.19, p < 0.0001.

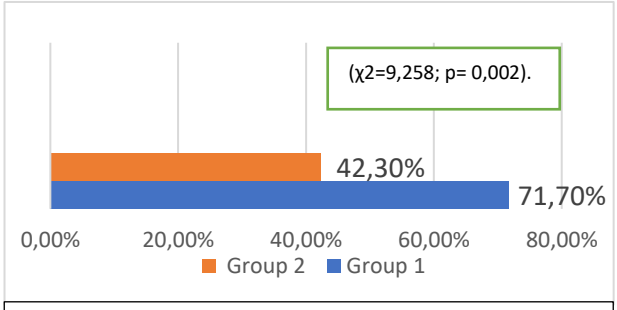

Figure 4. **Dexamethasone treatment in pregnant women from the study groups**

Prenatal corticosteroid administration, in combination with postnatal surfactant therapy, works synergistically to enhance pulmonary compliance. Research indicates that antenatal corticosteroid treatment significantly reduces the morbidity associated with neonatal respiratory distress syndrome (by 34%) and intracranial haemorrhages. A retrospective analysis of the children in the study revealed that 71.7% of those with BPD received prophylactic dexamethasone during pregnancy, compared to 42.3% in the control group (χ2 = 9.258; p = 0.002; Figure 4).

3.2 Etiopathogenic factors in the development of bronchopulmonary dysplasia in the neonatal period

Children with BPD were examined at an average age of 0.74 ± 0.44 years (*minimum* of 0.1 years, *median* of 0.7 years, *maximum* of 2.5 years, and *mode* of 0.17 years). This contrasts with an average age of 1.22 ± 0.58 years (minimum 0.17 years, median 1.1 years, maximum 3.0 years, and mode 0.17 years) for children without BPD (F statistic = 4.8, p > 0.03). The study groups' newborn distribution was analyzed according to the premature infant's sex (Figure 5). Males represented 62.3% of the BPD group, while females represented 37.7%. In the non-BPD group, the distribution was 51.9% for males and 48.1% for females (χ2 = 1.146; p = 0.284). These figures suggest a tendency for males to be more prevalent in the

BPD group. Existing literature, however, does not offer compelling evidence of sex-specific differences in premature infants in relation to BPD [11, 12].

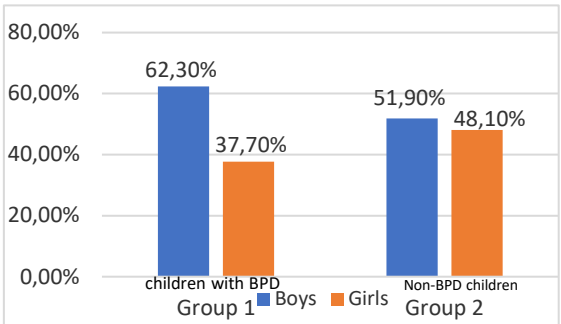

Figure 5. **Distribution of children with BPD by sex**

The correlation between average gestational age and the risk of BPD in premature infants has led to more in-depth studies to understand the severity of this relationship [9,10]. When gestational age at birth was assessed in premature infants with BPD, it averaged 27.28 ± 2.24 weeks (95% CI [26.67-27.90]), ranging from 23 to 31 weeks. This contrasted sharply with infants born without BPD, where gestational age at birth was significantly greater, averaging 29.78 ± 2.71 weeks (95% CI [28.76-30.27]) and ranging from 24 to 35 weeks. A comparative analysis confirmed a statistically significant difference between these two groups, demonstrating a high level of significance (F=25.21; p<0.0001), as detailed in Figure 6.

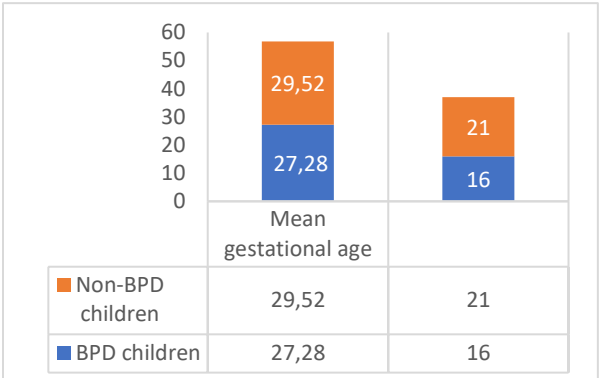

Figure 6. **Distribution of children with BPD by gestational age at birth**

Gestational age is a prognostic indicator of viability in premature infants. Of all premature births, 93% occur at a gestational age greater than 28 weeks, and only 6% occur at a gestational age between 22 and 27 weeks. The existing literature suggests that the minimum gestational age for viability is considered to be 23 weeks. Notably, mortality among these infants is four times higher compared to infants born after 28 weeks of gestation [9], and BPD is a significant complication that interacts with the degree of prematurity [7, 5, 16].

The mean birth weight in the group of preterm infants who developed BPD was very low—1006.46±239.51 g (95%CI [940.47–1072.51]), with a minimum value of 457 g and a maximum of 1650 g; the median was 1006.49 g. In comparison, the mean birth weight in the group of preterm infants without BPD was 1424±401.42 g (95%CI [1312.74–1536.26]), with values ranging from 640 g to 2100 g; the median was 1424.50 g. Statistical analysis based on birth weight revealed a significant difference between the two groups (F=42.173; p<0.0001), showing considerably lower birth weights among preterm infants who later developed BPD (Figure 7).

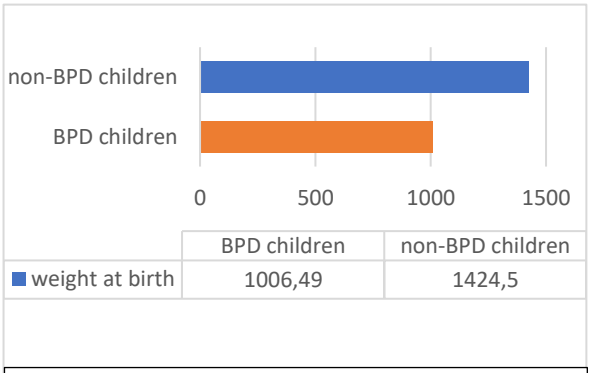

Figure 7. **Mean birth weight of children with BPD**

The distribution of children with BPD in relation to ***birth weight*** revealed that a considerable ratio were preterm infants weighing under 1000 g (45.3%) and between 1000–1449 g (50.9%). Only one child in the group had a birth weight between 1500–1999 g, and one between 2000–2500 g. Among the group of preterm infants who did not develop BPD, there was a significant predominance of those with a birth weight over 1500 g (82.7%), while only 17.3% were born weighing less than 1000 g. The results of this comparative study provide strong evidence for the significant influence of birth weight in preterm infants who developed BPD – $\chi^2 = 28.59$; $p < 0.0001$ (Figure 8).

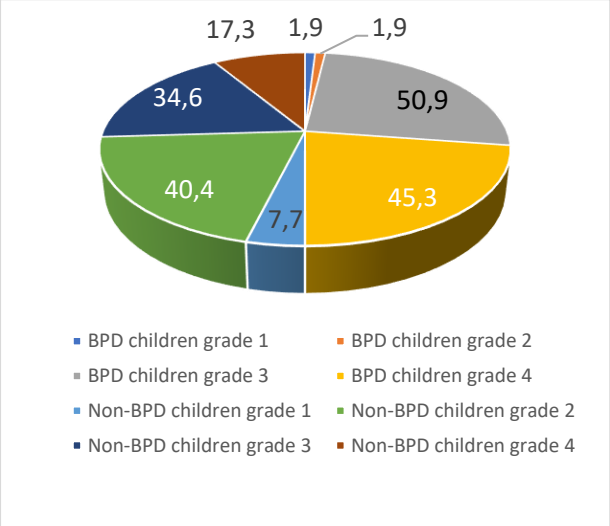

Figure 8. **Birth weight of children with BPD by severity grading**

Infants with BPD had a mean head circumference of 26.41±2.66 cm (range: 21-35 cm). The control group showed a significantly larger mean head circumference (F=10.703; p<0.001) of 28.15±2.78 cm, ranging from 23 cm to 38 cm**.**

The ***chest circumference*** at birth for infants in the study group was 23.49 ± 1.90 cm (minimum – 19 cm, maximum – 28 cm). In contrast, the chest circumference at birth for infants in the control group was significantly larger (F=15.388, p<0.0001), measuring 25.28 ± 2.72 cm (minimum – 18 cm, maximum – 36 cm (figure 9)).

The ***Apgar score***, particularly valuable in premature births, holds pathogenic significance for the newborn. The Apgar score subjectively reflects the infant's condition in the first minutes after birth and is relevant for implementing resuscitation methods and stabilizing the infant's condition. Low

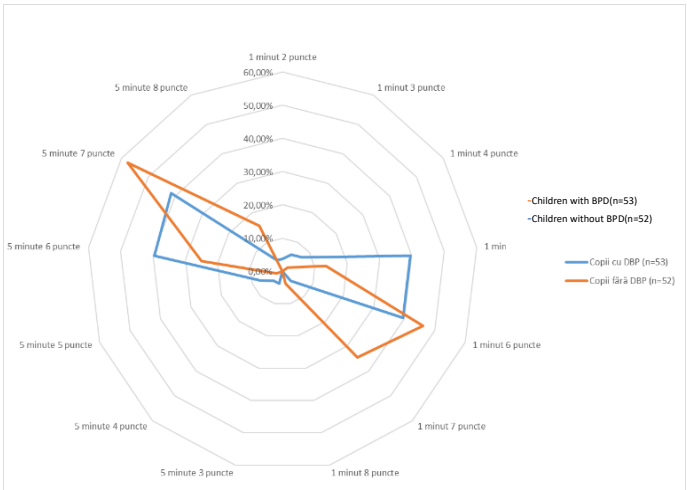

Figure 10. **Apgar score at birth in preterm newborns**

Comparing the study's findings with existing literature suggests a strong correlation: lower birth weight and gestational age increase the likelihood of developing BPD. Notably, all newborns in the study weighing less than 1000 grams at birth developed BPD.

Waist circumference analysis at birth in the premature infant study group yielded a mean of 35.75±3.02 cm, ranging from 29 cm to 42 cm. This was significantly smaller (F=23.86; p<0.0001) compared to the control group, where the mean waist circumference was 39.42±4.53 cm, ranging from 30 cm to 49 cm (Figure 9). Within the premature infant study group, an examination of ***head circumference at birth*** in infants with and without BPD revealed notable differences between the two subgroups.

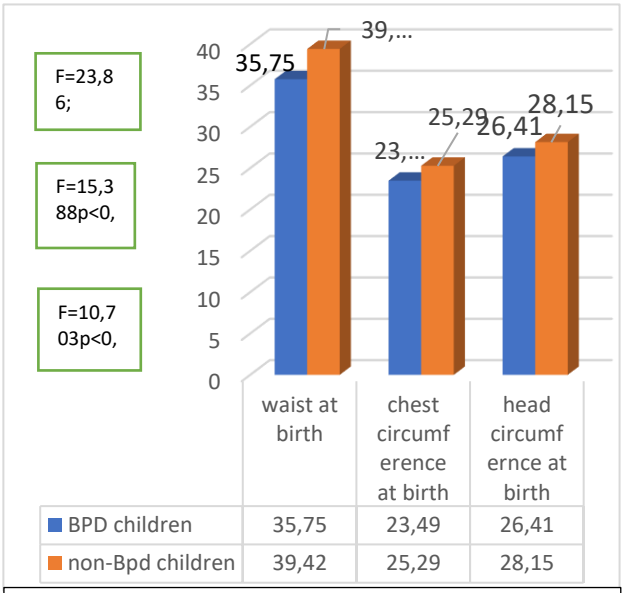

Figure 9. **Birth anthropometric indicators of children with BPD**

scores (<3 points at 1 minute of life) indicate severe intrauterine foetal distress. A low Apgar score at 5 minutes after birth suggests a poor short-term prognosis. In this study, an Apgar score of 2 at 1 minute after birth was observed in 3.8% of infants with BPD, and a score of 3 in 5.7%, indicating severe asphyxia. These scores were not found in premature infants in the control group. An Apgar score of 4 was given to 7.5% of infants with BPD, compared to 1.9% in the group without BPD; a score of 5 in 39.6% of the study group, versus 13.5% in the control group; and a score of 6 in 39.6% of the study group and 46.2% of the control group. A score of 7 was observed

in 3.8% of infants with BPD and 34.6% in the group without BPD. An Apgar score of 8 was given only to infants without BPD (3.8%).

To assess the infants' condition after birth, the 5-minute Apgar score was analysed. The study group showed a score of 3 in 3.8% of cases, while the control group showed a score of 4 in 3.8% of cases. Among infants with BPD, 7.5% had a score of 5, compared to 1.9% in those without BPD. A score of 6 was recorded for 39.6% of the study group and 25.0% of the control group. A score of 7 was achieved by 41.5% of the study group and 57.7% of the control group. A score of 8 was found in 3.8% of infants with BPD and 15.4% of those without BPD. These data are presented in Figure 10. The difference in Apgar scores between the two groups at 1 minute and 5 minutes was statistically significant ($\chi2=28.79$, $p<0.0001$ at 1 minute; $\chi2=12.50$, $p=0.028$ at 5 minutes). This strongly suggests that severe neonatal asphyxia plays a significant role in the subsequent development of the pathogenic mechanisms underlying BPD.

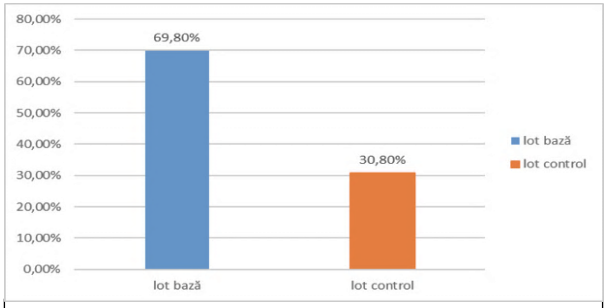

Figure 11. **Neonatal surfactant therapy for premature infants**

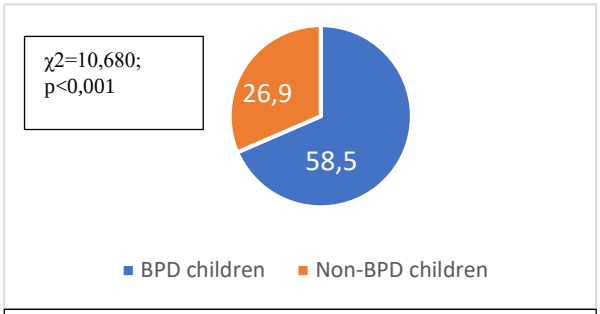

Figure 12. **Retinopathy assessment in children with bronchopulmonary dysplasia**

Surfactant therapy was initially developed to treat RDS arising from surfactant deficiency, the condition's defining characteristic. The study found that surfactant was administered to 69.8% of infants in the BPD group, a significantly higher percentage than the 30.8% in the group without BPD ($\chi2=16.005$; $p<0.0001$) (Figure 11).

The development of ***retinopathy of prematurity*** (ROP) [17,18] is complex and influenced by several factors, including retinal immaturity and arterial blood oxygen levels in the retina. The study showed that ROP occurred in 58.5% of premature infants with BPD, a considerably larger proportion than the 26.9% was observed in infants without BPD ($\chi2=10.680$; $p<0.001$) (Figure 12).

3.3 Assessment of respiratory support techniques in the neonatal period

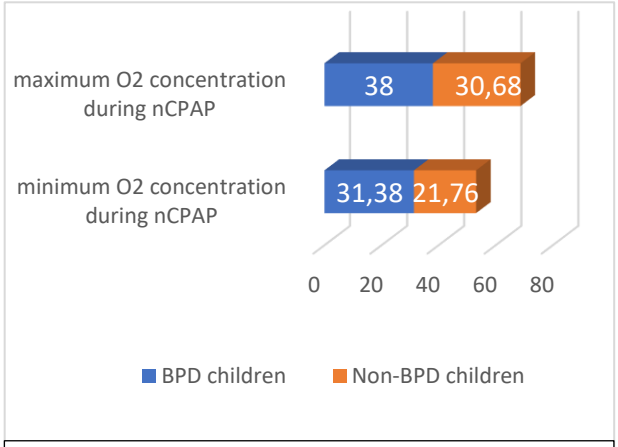

Figure 13. **Maximum and minimum O_2 amount in nCPAP during the neonatal period.**

Children with BPD required nasal continuous positive airway pressure (nCPAP) in 79.2% of cases, compared to 76.9% in those without BPD ($\chi2=0.083$; $p=0.77$).

The minimum O_2 concentration during nCPAP for children with BPD averaged 31.38±1.79%, ranging from 20% to 31%. In comparison, the control group's average minimum O_2 concentration was 21.76±2.35%, ranging from 20% to 30% ($F=0.699$; $p=0.406$). This difference was not statistically significant (Figure 13).

The maximum O_2 concentration during nCPAP in the BPD group averaged 38.00±4.90%, ranging from 30% to 45%. This compared to an average maximum of 30.68±3.72% in children without BPD, ranging from 21% to 45% ($F=2.346$; $p=0.130$), as shown (Figure 13).

This research analyzed positive airway pressure respiratory support, assessing both oxygen concentration and duration (in days). Infants diagnosed with BPD required significantly more prolonged ventilator-assisted pneumonia (VAP) support (90.6%) than those without BPD (51.9%), a statistically significant difference (χ^2=19.206; df=1; p<0.0001).

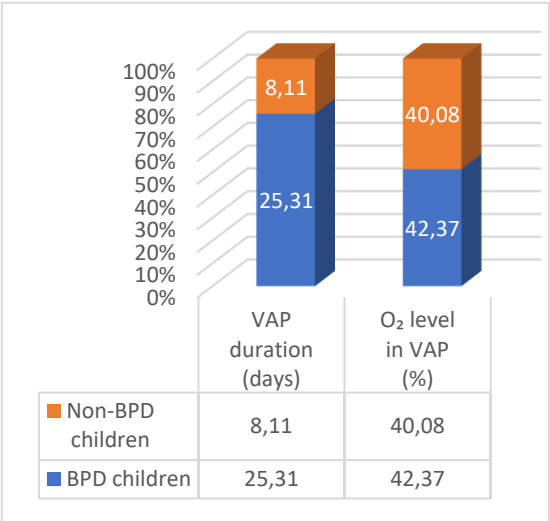

Figure 14. **VAP duration and oxygen levels in the neonatal period**

Oxygen therapy duration in the BPD group averaged 25.31±29.15 days (range: 1 to 130 days). The control group's duration was significantly shorter, averaging 8.11±7.25 days (range: 1 to 31 days), a significant difference (F=9.034; p=0.004) (Figure 14). Oxygen concentration during VAP averaged 42.37±12.92% in the BPD group, compared to 40.08±18.50% in the non-BPD group (F=0.323; p=0.572) (Figure 14).

Table 1. **Neonatal HFOV in infants with bronchopulmonary dysplasia**

HFOV	**BPD children (n=53)**		**Non-Bpd children (n=52)**	
	n	**%**	**n**	**%**
Yes	44	81,5	3	5,9
No	10	18,5	48	94,1
	χ2=60,626; **p<0,0001**			

High-frequency oscillatory ventilation (HFOV) is another respiratory support method, used in 81.5% of premature infants who developed BPD in contrast to the 5.9% of infants without BPD who didn't require HFOV support. Statistical analysis confirms a significant difference between these groups (χ2=60.626; p<0.0001), as detailed in table 1.

3.4 Assessing the respiratory symptoms in infants with bronchopulmonary dysplasia

Studies have shown that clinical characteristics influence the risk of developing morphostructural lung changes in infants with BPD [13]. These results emphasize the need for accurate monitoring and prompt intervention to manage respiratory issues in premature infants. This approach aims to avoid bronchopulmonary complications and enhance long-term outcomes.

Table 2. **Respiratory rate in children with bronchopulmonary dysplasia (breaths per minute)**

Study group	**M**	**Std Dev.**	**Minimum**	**Median**	**Maximum**	**p**
BPD children (n=53)	64,5	8,80	51	65	81	**p<0,001**
Non-BPD children (n=52)	42,2	6,21	37	41	47	

Analysis of respiratory rate indicators during clinical examination of premature infants with BPD revealed a mean of 64.5±8.80 breaths per minute, with a *minimum* of 51, a *median* of 65, and a *maximum* of 81 breaths per minute. This is in contrast to the respiratory rate observed in premature infants without BPD, which is significantly lower (F=55.63; p<0.001), averaging 42.2±6.21 breaths per minute (*minimum* of 37, *median* of 41, *maximum* of 47 breaths per minute (table 2). Therefore, an increased respiratory rate characterizes the severity of pulmonary involvement in bronchopulmonary dysplasia in premature infants and the onset of respiratory failure signs during diagnostic confirmation.

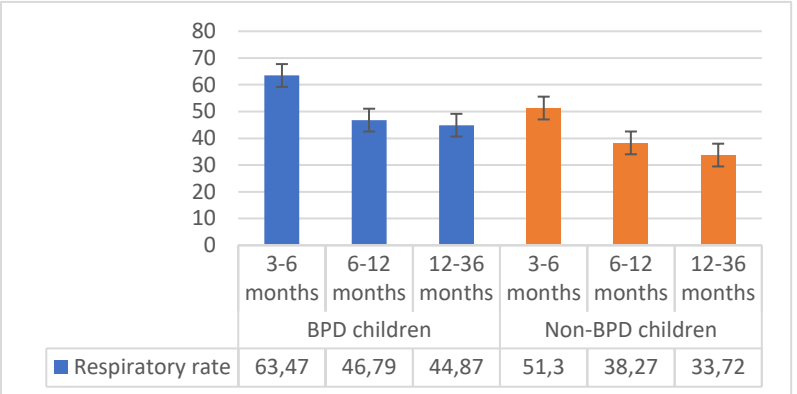

Figure 15. **Respiratory rate by age in children with BPD**

Respiratory rate, when assessed in relation to age in children with BPD, was found to be 63.47±9.30 b/min. in the 3-6 month age group, 46.79±7.69 b/min. in the 6-12 month age group, and 44.87±9.3 b/min. in the 12-36 month age group. In children without BPD, respiratory rates were 51.30±8.79 b/min. (3-6 months), 38.27±7.48 b/min. (6-12 months), and 33.72±6.09 b/min. (12-36 months) (F=11.506; p<0.0001) (figure 15).

Pulse oximetry is considered an informative indicator when assessing the effectiveness of respiration. Consequently, statistical analyses of oxygen saturation values, as determined by pulse oximetry, have been performed on children with BPD [14, 15]. To objectify respiratory insufficiency, oxygen saturation (SaO_2) was assessed in children with BPD, revealing significantly reduced average values. In the BPD group, SaO_2 reductions were more pronounced at 93.02±1.45% [CI 92.62–93.42%], compared to the control group's 97.4±0.83 [CI 97.17–95.37%], demonstrating a significant difference between the study groups (F=26.305; p<0.0001) (Table 3).

Table 3. **SaO_2 levels by pulse oximetry in children with DBP (%)**

Lotul de studiu	**N**	**Media**	**DS**	**95% ÎÎ**	**Minimum**	**Maximum**
BPD children	53	93,02	1,45	92,62-93,42	0	6
Non-BPD children	52	97,40	0,83	97,17-97,63	5	9
Total	105	94,81	2,83	94,25-95,37	0	9
	F=26,305; **p<0,0001**					

In premature infants with BPD, SaO_2 levels were assessed in relation to gestational age. Results showed that children with BPD had SaO_2 levels of 93.00±1.13%, ranging from 90-94%, at 3-6 months of age. From 6-12 months, levels were 93.0±1.49%, with a range of 90% to 95%. Between 12-36 months, SaO_2 levels increased slightly to 94.0±1.76%, ranging from 90-96%. By contrast, the group of children without BPD displayed significantly higher SaO_2 values: 97.80±1.44% (peak of 98%) in the 3–6-month age group; 96.25±5.1,35% (peak of 97%) in the 6–12-month age group; and 97.98±1.35% (peak of 98%) in the 12-36 month age group. Statistical comparison revealed a highly significant difference in SaO_2 levels between the two groups (F=6.82; p<0.0001), indicating compromised oxygenation in all age groups among children with BPD (Figure 16). These findings emphasize the need for careful oxygen saturation monitoring

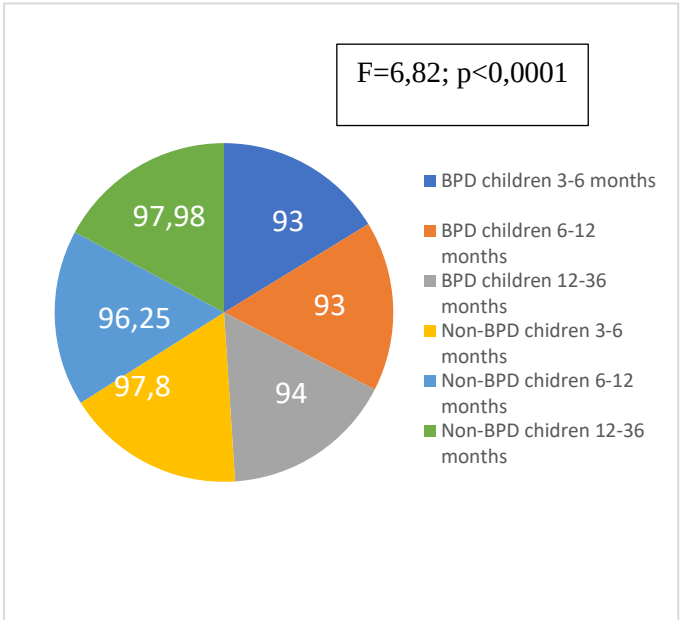

Figure 16. **SaO_2 levels in children with BPD by gestational age.**

in premature infants, particularly those with BPD, to enable prompt detection of hypoxemia and timely intervention with supplemental oxygen.

The study assessed clinical respiratory and stethoacoustic signs in children. Infants with BPD showed retractions in 83.0% of cases, a significantly higher rate than the 44.2% observed in premature infants without BPD ($\chi2$=17.10; p<0.0001). An analysis of the retractions revealed that intercostal retractions were present in 94.3% of children with BPD, compared to 42.3% of premature infants without BPD. Similarly, subcostal retractions were seen in 96.2% of children with BPD, contrasting sharply with the 7.7% observed in the group without BPD ($\chi2$=82.48; df=1; p<0.0001).

Table 4. **Characteristics of respiratory clinical signs in children with BPD (%)**

Clinical signs	**BPD children (n=53)**	**Non-BPD children (n=52)**	**$\chi2$; P**
Subcostal retractions	96,2	7,7	$\chi2$=82,48;gl=1;**p<0,0001**
Intercostal retractions	94,3	42,3	$\chi2$=32,97;gl=1;**p<0,0001**
Coarse rales	49,1	48,1	$\chi2$=0,010; gl=1; p=0,920
Weezing rales	71,7	11,5	$\chi2$=39,021;gl=1;**p<0,0001**
Mixed rales	28,3	13,5	$\chi2$=3,49; gl=1; p=0,062

On auscultation, there were detected coarse rales occurring at a comparable frequency in both the children with BPD (49.1%) and those without BPD (50.9%) ($\chi2$=0.010; df=1; p=0.920). However, wheezes were much more frequently identified during auscultation in children with BPD (71.7%) than in premature infants without BPD (28.3%), a statistically significant difference suggesting it as a characteristic sign of BPD (χ^2=39.021; df=1; p<0.0001). Furthermore, mixed rales were recorded in 28.3% of children with BPD, while they occurred half as often (13.5%) in the group without BPD, as detailed in Table 4.

Therefore, the clinical examination results suggest that tachypnea, SaO_2, and both subcostal and intercostal retractions are important indicators for evaluating respiratory failure in children with BPD and potentially other respiratory conditions [13].

3.5 Severity grades in children with bronchopulmonary dysplasia

Children with BPD were grouped by severity as follows: 45.3% had mild BPD, 24.5% moderate, and 30.2% severe. As a result, the study group predominantly included children with mild BPD ($\chi2$=32.637; p<0.001) (Figure 17). The correlation between mean gestational age and BPD severity was also assessed (Table 5). This evaluation revealed a mean gestational age of 28.17 ± 2.20 weeks (min. of 23 weeks, max.31 of weeks) for children with mild BPD. Premature infants with moderate BPD had a mean gestational age at birth of 27.15 ± 2.20 weeks (min. of 23 weeks, max. of 30 weeks). Those with severe BPD had the lowest average gestational age – 26.06 ± 1.94 weeks (min. of 24 weeks, max. of 30 weeks). A comparative analysis with a control group of children without BPD showed a statistically significant difference between the groups (F=9.88; p<0.0001); the control group's gestational age was 29.52 ± 2.71 weeks (min. of 24 weeks, max.of 35 weeks).

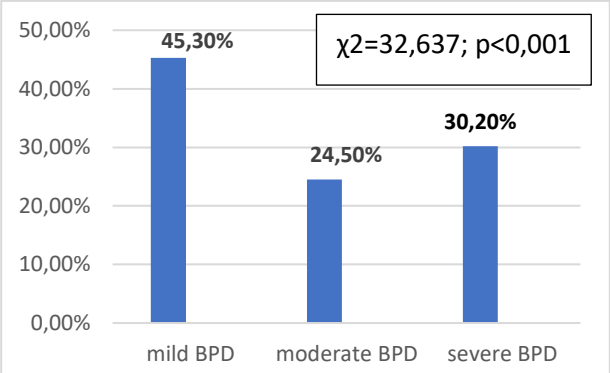

Figure 17. **BPD severity in preterm infants.**

Table 5. **Interactions between gestational age at birth and BPD severity grades**

Mild BPD (n=24)			**Moderate BPD (n=13)**			**Severe BPD (n=16)**			**Control**			
M	SD	95% CI	M	SD	95% CI	M	SD	95% CI	M	SD	95% CI	**P**
28,17	2,20	27,24-29,10	27,15	2,03	5,92-28,38	26,06	1,94	25,02-27.10	29,52	2,71	28,76-30,62	**p<0,0001**

The relationship between birth weight and the severity of BPD was also analysed. The correlation between anthropometric parameters and the degree of BPD revealed that among children with a birth weight of 2000–2500 g, mild BPD was diagnosed in 4.2% of cases, while no cases of moderate or severe BPD were recorded. In children weighing 1500–1900 g, only the severe form of BPD was observed (6.3%). Among preterm infants with a birth weight of 1000–1499 g, mild BPD was confirmed in 58.3% of cases, moderate in 69.2%, and severe in 25%. In preterm infants with very low birth weight (999 g or less), mild BPD was diagnosed in 37.5% of cases, moderate in 30.8%, and severe in 68.8%. A statistically significant difference was found between anthropometric parameters and the degrees of BPD severity ($\chi^2 = 37.25$; df = 4; $p < 0.0001$), as shown in Table 6.

Table 6. **Interactions between birth weight and BPD severity levels**

Study groups, weight	**BPD children with the following severity levels:**						**Non-BPD children**		X^2, gl=1, P
	mild		**moderate**		**severe**				**P**
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	
2000-2500 g	1	4,2	0	0	0	0,0	4	7,7	
1500-1999 g	0	0,0	0	0,0	1	6,3	21	40,4	
1000-1499 g	14	58,3	9	69,2	4	25,0	18	34,6	
≤999 g	9	37,5	4	30,8	11	68,8	9	17,3	**χ2=37,25; p<0,0001**
Total	24	100,0	13	100,0	16	100,0	52	100,0	

The analysed groups were characterised by the parameter values shown in Table 7, according to the BPD severity levels. Birth waist parameteres in the group with mild BPD was 36.12 ± 3.39 cm, showing a significant difference compared to the control group (F=8.4; p<0.0001); in the moderate BPD group it was 36.30 ± 2.71 cm, and in the severe group – 34.75 ± 2.56 cm.

Table 7. **Anthropometric parameters in children with different BPD levels**

Parameters	**Mild BPD (n=21)**		**95% CI**	**Moderate BPD (n=11)**		**95% CI**	**Severe BPD (n=10)**		**95% CI**	**Control (n=52)**		**P**
	M	**SD**		**M**	**SD**		**M**	**SD**		**M**	**SD**	
Waist at birth	36,12	3,39	34,69-37,55	36,30	2,71	34,66-37,95	34,75	2,56	33,38-36,11	39,42	4,53	**F=8,44; p<0,0001**
Head circumference	26,75	2,05	25,69-27,80	26.15	1,86	25,02-27,28	26,15	3,44	24,29-27,95	28,15	2,78	F=3,74; p =0,014
Chest circumference	21,67	2,30	20,62-22,72	22,09	2,91	21,98-23,8	23,75	2,26	24,29-27,95	25,28	2,72	**F=5,42; p =0,002**

Infants with mild BPD exhibited a mean head circumference of 26.75 ± 2.05 cm, compared to 26.15 ± 1.86 cm in those with moderate BPD, and 26.15 ± 3.44 cm in those with severe BPD. Thoracic circumference was also analyzed based on BPD severity, viz, in infants with mild BPD, it measured 21.67 ± 2.30 cm, a significant difference compared to the control group ($F = 5.42$; $p < 0.0001$). Circumference in infants with moderate BPD was 22.09 ± 2.91 cm, and in infants with severe BPD, 23.75 ± 2.26 cm.

Assessment of respiratory manifestations based on BPD severity revealed intercostal retractions in 100% of infants with mild BPD, compared to 73.1% in the control group without BPD, 100% in moderate BPD, and 100% in severe BPD. Subcostal retractions, indicative of respiratory insufficiency, were observed in all premature infants with varying degrees of BPD severity, versus 32.7% in the control group ($\chi2 = 53.51$; $p < 0.0001$).

Depending on severity, coarse rales were present in 41.7% of children with mild BPD, compared to 65.5% in the control group, 53.8% in moderate BPD, and 56.3% in severe BPD, with no statistically significant difference ($\chi^2=3.202$; df=3; p=0.361). Wheezing was detected on auscultation in 66.7% of preterm infants with mild BPD, compared to 28.8% in those without BPD, 30.8% in moderate BPD, and 68.8% in severe BPD ($\chi^2=18.104$; df=3; $p<0.0001$). However, mixed rales were identified in 29.2% of infants with mild BPD, 13.5% in the control group, 7.7% in moderate BPD, and 43.8% in severe BPD, without statistically significant differences between groups ($\chi^2=9.14$; df=3; p=0.027). Data are presented in Table 8.

Table 8. **Respiratory manifestations in children with different BPD severity levels.**

Respiratory characteristics	**Children with the following BPD severity levels:**						**Non-BPD children**		X^2, Gl-3, P
	mild		**moderate**		**severe**				**P**
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**χ2=53,51; p<0,0001**
Intercostal retractions	16	100	17	100	20	100	38	73,1	
Subcostal retractions	21	100	16	100	15	100	17	32,7	
Coarse rales	10	41,7	7	53,8	9	56,3	33	65,5	χ2=3,202; p=0,361
Weezing rales	16	66,7	4	30,8	11	68,8	15	28,8	**χ2=18,104; p<0,0001**
Mixed rales	7	29,2	1	7,7	7	43,8	7	13,5	χ2=9,14; p=0,027

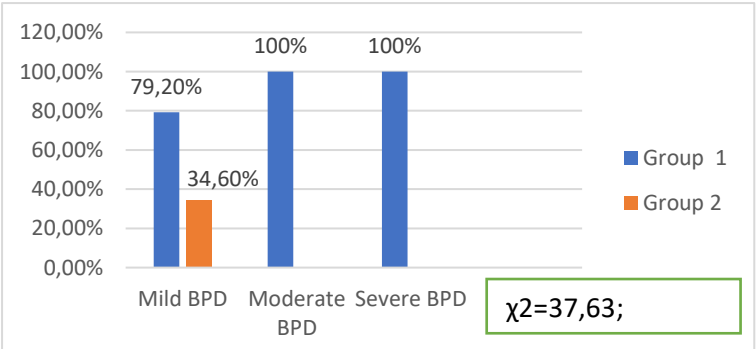

Figure 18. **Respiratory distress syndrome assessment in premature infants by BPD severity.**

The assessment of respiratory distress syndrome in preterm infants with BPD showed an incidence of 79.2% in mild cases, and 100% in both moderate and severe cases, compared to 34.6% in the control group. The association between BPD severity and neonatal factors, particularly RDS, was statistically significant ($\chi^2 = 37.63$, $p < 0.0001$), as shown in Figure 18.

Another identified neonatal risk factor is neonatal sepsis in preterm infants, which has been previously reported. The present study revealed a 100% incidence of neonatal sepsis in infants who developed severe BPD, a 38.5% incidence in those with moderate BPD, and a single case (8.3%) among those with mild BPD. In the control group, only one isolated case of neonatal sepsis was observed. Statistical analysis showed a significant difference in the incidence of neonatal sepsis according to the severity of BPD ($\chi^2 = 71.590$; df = 3; $p < 0.0001$), with the highest prevalence occurring in severe cases (100%), followed by moderate (38.5%) and mild forms (8.3%). The difference between groups was statistically significant ($\chi^2 = 71.590$; df = 3; $p < 0.0001$) (Figure 19).

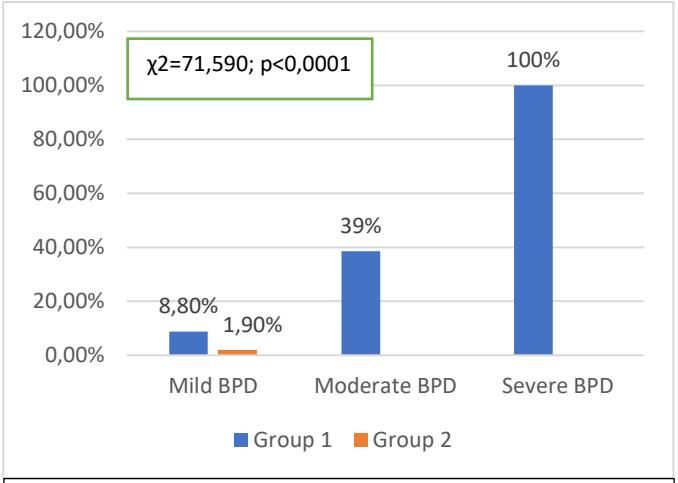

Figure 19. **Sepsis assessment in preterm infants by BPD severity**

The BPD severity level based on neonatal risk factors.

To determine BPD severity, the study analysed the duration (in days) of oxygen (O_2) concentration administered via positive pressure respiratory support. In the BPD group, the following was observed: mild BPD in 7.48% of cases (ranging from 2 to 14 days); moderate BPD in 10.45% of cases (ranging from 4 to 20 days); and severe BPD in 30.10% of cases (ranging from 4 to 64 days). For comparison, the control group exhibited durations ranging from 2 to 45 days in 9.50% of cases. The differences between the groups proved to be statistically significant (F=11.52; p<0.0001). The study also evaluated the maximum O_2 concentration required during nCPAP, based on BPD severity. In the premature infant group, the findings were as follows: mild BPD required an O_2 concentration averaging 30.24% (ranging from 30% to 35%); moderate BPD required an average of 34.0% O_2 (ranging from 30% to 45%); and severe BPD required an average of 33.50% O_2 (ranging from 30% to 40%). The control group required an average of 30.68% O2 (ranging from 21% to 45%). This particular difference did not reach statistical significance (F=3.981; p=0.011), and these data are presented in Table 9. Finally, the analysis of the minimum O_2 concentration during nCPAP by BPD severity, revealed the following: a value of 21.67% in the mild BPD group, 22.09% in the moderate BPD group, 21.60% in the severe BPD group, and 21.38% in the control group (F=0.351; p=0.789).

Table 9. **nCPAP assessment, days, max/min O_2 concentration with BPD severity levels.**

nCPAP parameters	Mild BPD (n=21)		95% CI	Moderate BPD (n=11)		95% CI	Severe BPD (n=10)		95% CI	Control (n=52)		95% CI
	M	SD		M	SD		M	SD		M	SD	
nCPAP, days	7,48	3,66	5,81-9,15	10,45	4,88	7,17-13,74	30,10	24,79	12,36-47,84	9,50	8,67	6,73-12,27
	F=11,50 ; p<0,0001											
nCPAP, maximum O_2 amount	30,24	1,09	29,74-30,73	34,00	5,74	30,14-37,86	33,50	4,74	30,11-36,89	30,68	3,71	29,49-31,86
	F=3,981; p=0,011											
nCPAP manimum O_2 amount	21,67	2,30	20,62-22,72	22,09	2,91	20,13-24,05	21,60	1,89	20,24-22,96	21,38	1,79	20,80-21,95
	F=0,351; p=0,789											

The length of respiratory support via VAP in neonates with mild BPD was 7.26 days. It doubled to 15.46 days in those with moderate BPD, whereas infants with severe BPD required a considerably longer period of VAP, averaging 54.75 days. In contrast, the duration of oxygen therapy via VAP in the control group of infants without BPD was 8.11 days (F=31.27; p<0.0001). Regarding VAP parameters, the required oxygen concentration in premature infants with mild BPD was 31.16%, rising to 39.08% in those with moderate BPD, and reaching maximal concentrations of 51.50% in premature infants with severe BPD, indicating significant differences between the severity levels. The oxygen concentration in the control group was 42.37% (F=5.21; p>0.003), the summary results being presented in Table 10.

Table 10. **Correlations between VAP duration, O2 concentration, and BPD severity level.**

VAP parameters	**Mild BPD (n=19)**		**95% CI**	**Moderate BPD (n=13)**		**95% IC**	**Severe BPD (n=16)**		**95% CI**	**Control (n=52)**		**95% CI**
	M	**DD**		**M**	**SD**		**M**	**SD**		**M**	**SD**	
VAP, days	7,26	5,12	4,78-9,75	15,46	11,57	8,47-22,46	54,75	33,21	37,05-72,45	8,11	7,25	5
	F=31,277; p<0,0001											
VAP O_2 amount	31,16	15,62	23,63 - 38,69	39,08	13,68	30,81 - 47,35	51,50	19,71	41,00-62,00	42,37	12,92	37,26 - 47,48
	F=5,21; p>0,003											

High-Frequency Oscillatory Ventilation (HFOV) represents another modern approach to oxygen therapy for neonates, especially premature infants. It was employed in treating 92.9% of infants diagnosed with mild BPD. Use of HFOV decreased with the severity of BPD in 80% of moderate cases and 62.5% of severe cases. The therapy was also sometimes applied to infants without BPD (5.9% of cases), a statistically significant difference among the groups ($\chi 2$=64.432; p<0.0001) as detailed in Table 11.

Table 11. **Use of HFOV oxygen therapy in children with BPD based on severity level**

HFOV	**BPD children (n=53)**		**Non-BPD children (n=52)**		**x^2, gl=1, p**
	Da	**%**	**Da**	**%**	
Mild BPD	26	92,9	3	5,9	$\chi 2$=64,432; p<0,001
Moderate BPD	8	80			
Severe BPD	10	62,5			

3.6 Assessing radiographic changes in children with bronchopulmonary dysplasia

Chest X-rays have been a standard tool in clinical practice for detecting BPD, leading to the development of radiographic scoring systems to assess its clinical severity [19, 20, 21]. However, chest radiography suffers from inherent limitations due to structural interference and overlapping images, which has fueled ongoing debate regarding its reliability in diagnosing BPD [21, 23]. Consequently, radiographic techniques may not offer sufficient detail to accurately represent abnormalities within the lung parenchyma, nor reliably predict the clinical severity of BPD [19, 20].

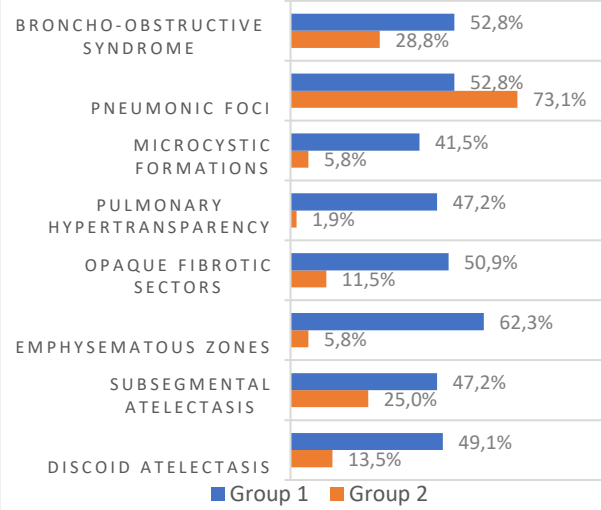

Figure 20. **Chest radiographic changes in children with bronchopulmonary dysplasia.**

In accordance with the research design, chest X-rays were performed on all participating children to confirm their diagnoses. Analysis of the radiographic findings showed that discoid atelectasis was significantly more prevalent in children with BPD at 49.1%, compared to the 13.5% observed in those without BPD ($\chi2=15.431$; $p<0.0001$). Similarly, subsegmental atelectasis was visualized in 47.2% of the BPD group, double the rate of 25.0% in the non-BPD group ($\chi2=5.586$; $p=0.018$).

Areas of emphysema, characterized by imaging signs of localized bronchial obstruction, were found in 62.3% of premature infants with BPD, but only occasionally in children without BPD (5.8%). These differences between the groups were statistically significant ($\chi2=37.182$; $p<0.0001$).

Areas of fibrotic opacity were observed in 50.9% of children with BPD, a significantly higher rate than the 11.5% seen in children without BPD ($\chi2=18.911$; $p<0.0001$).

Pulmonary hyperlucency was detected in 47.2% of children with BPD, while isolated cases occurred in only 1.9% of the control group. Microcystic formations were also more common in children with BPD, observed in 41.5% compared to just 5.8% in the control group ($\chi2=18.482$; $p<0.0001$).

Hospitalizations resulted in radiological changes indicative of pneumonic foci in 52.8% of children with BPD. This was lower than the 73.1% observed in children without BPD who developed pneumonia ($\chi2=4.609$; $p=0.032$). Similarly, broncho-obstructive syndrome was more prevalent in children with BPD (58.5%) than in those without (28.8%) ($\chi2=9.370$; $p=0.002$). Frequency and differences between these groups are further detailed in Figure 20.

Analysis of pulmonary radiological investigations revealed statistically significant differences in all types of bronchopulmonary substrate alterations, except for pneumonic foci. While these foci were more frequently detected in children without BPD, bronchopneumonia was present as a distinct condition in this group.

3.7 Assessing pulmonary computed tomography changes in children with bronchopulmonary dysplasia

Computed tomography provides more objective and definitive evidence of structural lung lesions, useful for guiding future interventions and establishing baseline lung imaging [22, 23].

Specifically, evaluating changes on pulmonary CT scans of the children in the study group revealed the following statistically significant differences: ground-glass opacities were present in 75.5% of preterm infants with BPD, compared to only 9.6% of children without BPD ($\chi2=46.484$; $p<0.0001$). Similarly, linear reticular opacities were found in 67.9% of children with BPD, compared to 11.5% of children without BPD ($\chi2=34.771$; $p<0.0001$). These differences were highly significant.

Infiltrative atelectatic areas on CT imaging are a potential diagnostic criterion for BPD, observed in 79.2% of the study group, but only half as frequently in the control group (32.7%) ($\chi2$=23.108; p<0.0001). Mosaic attenuation patterns were reported in 71.7% of children with BPD, a statistically significant difference from the 32.7% observed in the control group ($\chi2$=16.010; p<0.0001). Pleuropulmonary adhesions were frequently indicated by the pulmonary CT protocol, seen in 69.8% of premature infants with BPD and 44.2% of those without, a difference of slight statistical significance ($\chi2$=7.013; p=0.008). Hyperinflation was visualized in 37.7% of the study group and 34.6% of the control group ($\chi2$=0.111; p=0.739). Bronchial tree involvement, manifested as peribronchial thickening on imaging, was found in over two-thirds of children with BPD (67.9%), compared to 42.3% of children without BPD ($\chi2$=6.966; p=0.008). Pulmonary emphysema was detected in 62.3% of children with BPD and 17.3% of premature infants who did not develop BPD ($\chi2$=22.104; p<0.0001).

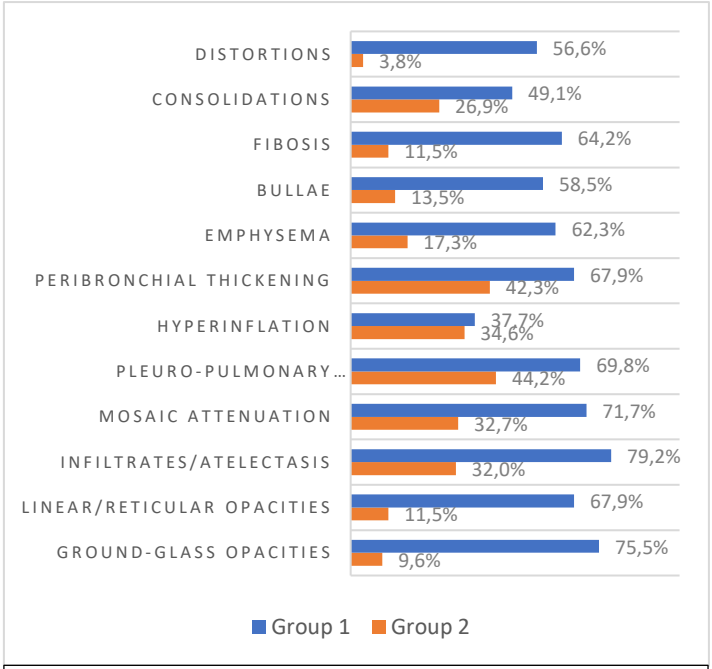

Figure 21. **CT Scan Findings in Children with BPD**

Air bubbles are a significant CT imaging criterion for BPD. The bullae, a pathophysiological consequence of lung injury from assisted ventilation and oxygen therapy in premature infants, were frequently found in children with BPD, occurring in 58.5% of cases. This was sharply in contrast with the control group, where they were rarely seen, appearing in only 13.5% of cases ($\chi2$=23.046; p<0.0001).

The underlying causes of BPD seem to trigger processes that led to pulmonary fibrosis. Fibrosis was observed in two-thirds of the children with BPD 64.2% of cases—a rate significantly higher than the 11.5% seen in the control group ($\chi2$=30.809; p<0.0001).

Table 12. **Modeling risk and etiology for BPD potential**

Criteria	B	P	Exp. (B)	95% CI
Cesarean delivery	5,96	0,006	389,36	5,679-2,66
5-Minute Apgar score	2,22	0,55	9,242	0,953-89,622
Birth weight (g)	-0,01	0,004	0,990	0,983-0.997
Duration on VAP (days)	0,13	0,025	1,145	1,017-1,290
SpO_2	-0,47	0,003	0,625	0,457-0,855
Respiratory rate	0,38	0,47	1,47	1,005-2,157

Consolidation areas were also more prevalent in the BPD study group, identified in 49.1% of cases, compared to just 26.9% in the control group ($\chi2$=5.453; p=0.020). Moreover, signs of distorted bronchopulmonary structures were frequently reported in the CT scans of children with BPD, present in 56.6% of cases, while being almost absent in the control group, seen in only 3.8% of cases, thus, representing a highly statistically significant difference ($\chi2$=34.480; p<0.0001) (Figure 21).

3.8. Prognostic factors in the development of BPD in premature infants

Evaluating prognostic factors for BPD development allows for the early identification of high-risk patient groups and the implementation of preventative measures to potentially minimize the severity of the condition. To investigate the complex interplay of these risk factors, multiple logistic regression modelling was employed. Regression coefficients are presented in Table 12 (R^2=0.855). The data indicates that each day spent on mechanical ventilation is associated with a higher probability of developing BPD (OR=1.06), while a higher SpO_2 value is associated with a reduced risk of developing early clinical characteristics of BPD.

Logistic regression was employed to evaluate the impact of various risk factors on the severity of BPD that developed. The study population was divided into two groups viz: the first included infants from group 2 and those from group 1 with mild BPD, while the second included infants from group 1 exhibiting moderate to severe BPD. The regression coefficients are displayed in Table 44 (R^2=0.679).

Unlike model 2, birth weight emerged as a key factor in predicting the likelihood of BPD development. Lower birth weight significantly correlated with an increased risk of BPD, as shown in Table 13. The logistic regression analysis, examining factors involved in pulmonary injury mechanisms in premature infants with BPD, yielded significant results.

Table 13. **Modeling BPD severity in the neonatal period**

Variable	**B**	**P**	**Exp. (B)**	**95% CI**
Gestational age	-0,192	0,237	0,825	0,600-1,135
Duration on nCPAP (days)	0,095	0,026	1,099	1,011-1,195
Duration on VAP (days)	0,158	0,000	1.172	1,073-1,280
SpO_2	-0,102	0,011	0,903	0,835-0,977

The findings include a detailed analysis of the collected data. This complex analysis enabled the development of a diagnostic algorithm for children with bronchopulmonary dysplasia, facilitating the diagnostic process and optimizing patient management, as presented in Figure 22.

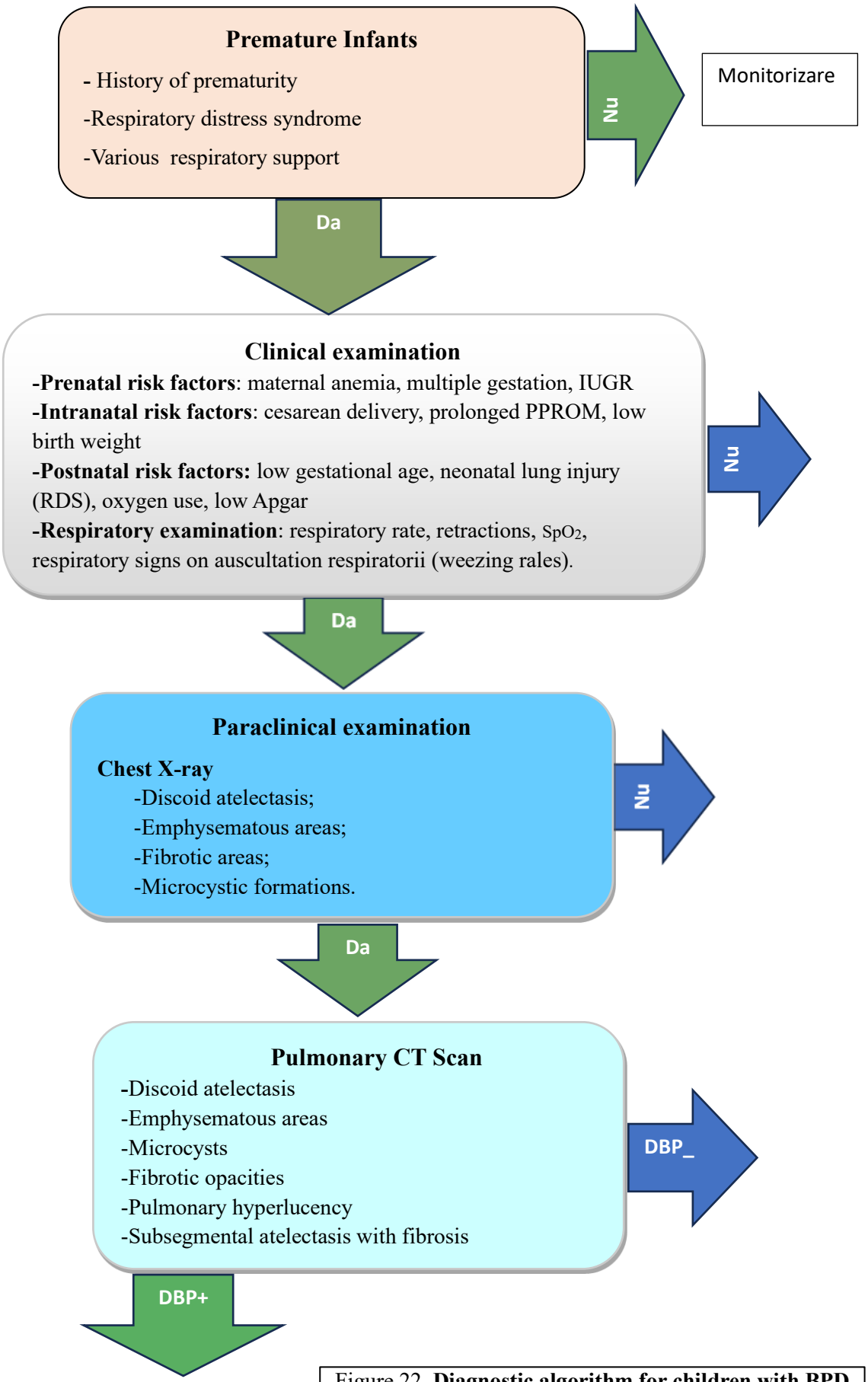

Figure 22. **Diagnostic algorithm for children with BPD**

GENERAL CONCLUSIONS

1. Bronchopulmonary dysplasia in preterm infants is significantly associated with specific perinatal risk factors. These include a mean gestational age of less than 27.28 ± 2.24 weeks, a mean birth weight below 1006.46 ± 239.51 grams, and low Apgar scores at 1 minute ($p < 0.0001$) and 5 minutes ($p = 0.028$).

2. The severity of lung damage in premature infants with BPD is significantly influenced by several postnatal factors. These include mechanical ventilation, which was used in 90.6% of cases ($p < 0.0001$), as well as prolonged oxygen therapy, lasting an average of 25.3 ± 29.2 days ($p > 0.004$), and exposure to elevated oxygen concentrations, averaging 40.1 ± 18.5% ($p = 0.57$). The negative effects of oxygen therapy were also observed via CPAP in 79.2% of children with BPD ($p = 0.77$), with mean oxygen concentrations of 32 ± 4.1% ($p = 0.130$).

3. Clinical signs of BPD in children include rapid breathing ($p < 0.001$), subcostal retractions at rest ($p < 0.0001$), intercostal retractions ($p < 0.0001$), wheezing ($p < 0.0001$), and peripheral oxygen saturation levels below 90%. These clinical features correlate with the severity of the disease ($p < 0.0001$) and serve as important indicators for assessing acute respiratory failure in children with BPD.

4. Radiological findings in children with BPD included discoid atelectasis (49.1%, $p < 0.0001$), subsegmental atelectasis (47.2%, $p = 0.018$), areas of emphysema (62.3%, $p < 0.0001$), opaque fibrotic areas (50.9%, $p < 0.0001$), and microcystic formations (41.5%, $p < 0.0001$). These findings are characteristic of BPD and reflect its severity.

5. Pulmonary computed tomography confirmed BPD through several characteristic findings: ground-glass opacities (75.5% of cases, $p < 0.0001$), reticular linear opacities (67.9%, $p < 0.0001$), infiltrative atelectatic areas (79.2%, $p < 0.0001$), mosaic attenuation (71.7%, $p < 0.0001$), pleuropulmonary adhesions (69.8%, $p = 0.008$), emphysema (62.3%, $p < 0.0001$), bullae (58.5%, $p < 0.0001$), fibrosis (64.2%, $p < 0.0001$), and distortion (56.6%, $p < 0.0001$). The presence of these features on CT provided a definitive diagnosis of the disease.

6. This study identified several neonatal factors with significant prognostic value for the development of BPD. Extremely low birth weight, gestational age, and Apgar scores below 4 in the first minute of life showed the strongest predictive associations.

RECOMMENDATIONS

1. Gestational age, birth weight, and other anthropometric measurements, along with the Apgar score, are important indicators of BPD risk. These factors can be used in healthcare settings to identify infants who may be at risk for bronchopulmonary dysplasia. Evaluating these risk factors aids in the early detection of infants at risk of developing BPD and allows for the timely initiation of appropriate preventative or therapeutic interventions.

2. Clinical signs indicative of lung involvement, such as rapid breathing, intercostal and thoracic retractions, and reduced arterial blood oxygen saturation (hypoxemia), suggest significant pulmonary impairment and are suggestive of BPD.

3. Chest X-rays can reveal characteristic lung changes associated with bronchopulmonary dysplasia, including pulmonary opacities, hyperexpansion, or a characteristic "ground-glass" appearance. Chest X-rays are recommended for evaluating premature infants who have been exposed to oxygen therapy during the neonatal period, especially at the primary healthcare level.

4. At a specialized or tertiary care level, pulmonary computed tomography scanning is recommended. CT provides definitive imaging criteria for bronchopulmonary dysplasia through findings like ground-glass opacities, reticular linear opacities, areas of atelectasis and infiltration, mosaic attenuation, pleuropulmonary adhesions, emphysema, air cysts, fibrosis, and distortion of the lung's architecture.

REFERENCES

1. Bancalari E., Claure N. *Definitions and Diagnostic Criteria for Bronchopulmonary Dysplasia.* Vol. 30, Seminars in Perinatology. 2006.

2. Greenough A., Cox S., Alexander J., Lenney W., Turnbull F., Burgess S, et al. *Health care utilisation of infants with chronic lung disease, related to hospitalisatio.n for RSV infection. Arch Dis Child*. 2001;85(6).

3. Beitler JR., Malhotra A., Thompson BT. *Ventilator-induced Lung Injury*. Vol. 37, Clinics in Chest Medicine. 2016.

4. Cunha GS., Mezzacappa Filho F., Ribeiro JD. *Fatores maternos e neonatais na incidência de displasia broncopulmonar em recém-nascidos de muito baixo peso*. J Pediatr (Rio J). 2003;79(6).

5. Ernest Cutz., David Chiasson. *Chronic Lung Disease After Premature Birth. Survey of Anesthesiology*. 2008;52(4).

6. Cokyaman T. *Bronchopulmonary Dysplasia Frequency and Risk Factors in Very Low Birth Weight İnfants:* a 3-Year Retrospective Study. North Clin Istanb. 2019;

7. Laughon MM., Langer JC., Bose CL., Smith PB., Ambalavanan N., Kennedy KA, et al. *Prediction of bronchopulmonary dysplasia by postnatal age in extremely premature infants*. Am J Respir Crit Care Med. 2011;183(12).

8. Kim SH., Han YS., Chun J., Lee MH., Sung TJ. *Risk factors that affect the degree of bronchopulmonary dysplasia: Comparison by severity in the same gestational age*. PLoS One. 2020;15(7).

9. Bodnar LM., Himes KP., Abrams B., Lash TL., Parisi SM,. Eckhardt CL, et al. *Gestational Weight Gain and Adverse Birth Outcomes in Twin Pregnancies*. Obstetrics and Gynecology. 2019;134(5).

10. Stoelhorst GMSJ., Rijken M., Martens SE., Brand R., Den Ouden AL, Wit JM, et al. *Changes in neonatology: Comparison of two cohorts of very preterm infants (Gestational Age <32 weeks): The Project On Preterm and Small for Gestational Age Infants 1983 and the Leiden Follow-up Project on Prematurity* 1996-1997. Pediatrics. 2005;115(2).

11. Lee JH., Noh OK., Chang YS. *Neonatal outcomes of very low birth weight infants in Korean Neonatal Network* from 2013 to 2016. J Korean Med Sci. 2019;34(5).

12. Cotoman A., Selevestru R., Sciuca S., Ceahlău M., Curteanu A. Ministerul sănătăţii, muncii şi protecţiei sociale al republicii moldova *Displazia bronhopulmonară la copii Protocol clinic naţional*. Chișinău; 2021 Jun.

13. Aleem S., Do BT., Gantz M., Hibbs AM., Jensen EA., Cotten CM., et al. Assessing 3 *Bronchopulmonary Dysplasia Definitions: Associations between Room Air Challenge Results and Respiratory Outcomes.* Pediatrics. 2021;147(3_MeetingAbstract).

14. Higgins RD., Jobe AH., Koso-Thomas M., Bancalari E., Viscardi RM., Hartert T V., et al. *Bronchopulmonary dysplasia: executive summary of a workshop*. Vol. 7, Neonatology. 2019.

15. Ndonyi J. *Utilization of Free Skilled Birth Attendance Services Among Women of Reproductive Age in Public Health Facilities in Kitui County*, Kenya. Front Neurosci. 2021;14(1).

16. Solans Pérez De Larraya AM., Ortega Molina JM., Uberos Fernández J., González Ramírez AR, Garcia Serrano JL. *Speed of Retinal Vascularization in Retinopathy of Prematurity: Risk and Protective Factors*. Biomed Res Int. 2019;2019.

17. Zin A., Gole GA. *Retinopathy of Prematurity-Incidence* Today. Vol. 40, Clinics in Perinatology. 2013.

18. Griscom NT., Wheeler WB., Sweezey NB., Kim YC., Lindsey JC., Wohl MEB. *Bronchopulmonary dysplasia: radiographic appearance in middle childhood*. Radiology. 1989;171(3).

19. Edwards DK. *Radiographic aspects of bronchopulmonary dysplasia.* J Pediatr. 1979;95(5 PART 2).

20. May C., Prendergast M., Salman S., Rafferty GF., Greenough A. Chest radiograph thoracic areas and lung volumes in infants developing bronchopulmonary dysplasia. Pediatr Pulmonol. 2009;44(1).

21. Boechat MCB., de Mello RR., da Silva KS., Daltro P., Marchiori E., Ramos EG., et al. *A computed tomography scoring system to assess pulmonary disease among premature infants. Sao Paulo* Medical Journal. 2010;128(6).

LIST OF PUBLICATIONS AND PARTICIPATION IN SCIENTIFIC FORUMS

Cotoman Aliona, PhD graduate, Department of Paediatrics, "Nicolae Testemițanu" State University of Medicine and Pharmacy, Republic of Moldova. The Ph.D. research was carried out on **"Bronchopulmonary Dysplasia in Children: Etiological Factors and Clinical–Paraclinical Diagnosis"**, within the specialty 322.01 – Paediatrics and Neonatology.

Scientific papers:

- **Monography**

1. **Cotoman A**. Bronșiectaziile în displazia bronhopulmonară, Subcapitolul VIII, pp. 241-263. În: *Șciuca S.; Petrovici V.; Selevestru R.; Adam I.; Neamțu L.; Cotoman A.; Balanețchi L.; Tomacinschi C.Bronșiectaziile la copii.* Chișinău: „Tipografia Centrală". 2018; 352 p. ISBN: 978-9975-53-972-2.

- **Publications in international scientific journals::**
  - ✓ **articles published in ISI, SCOPUS, or other internationally indexed databases**

2. **Cotoman A.,** Selevestru R., Şciuca S., Guduman E., Curteanu A. Clinical-imaging aspects in premature infants with bronchopulmonary dysplasia. In: *Archives of the Balkan Medical Union*. 2024; nr. 4(59): pp. 357-364. DOI:10.31688/ABMU.2024.59.4.05.

- **Publications in accredited national scientific journals:**
  - ✓ **articles published in Category B journals**

3. **Cotoman A**., Selevestru R., Bratu E., Rotaru-Cojocari D., Pînzari L., Ceahlău M., Șciuca S. Displazia bronhopulmonară la copil prematur cu malformaţie congenitală pulmonară. În: *Buletin de Perinatologie.* 2018; nr. 5 (81): pp. 82-86. ISSN: 1810-5289.
4. Sciuca S., Rașcov V., Selevestru R., **Cotoman A**., Crivceanschi E. Tracheobronchomalacia primară la copii (prezentarea unui caz clinic). În*: Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale*. 2019; nr 3(63): ISSN: 1857-0011.
5. Ceahlău M., Selevestru R., **Cotoman A**., Șciuca S. Predictorii displaziei bronhopulmonare la copiii prematuri. În: *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale.* 2020; nr. 2(66): pp. 132-134. ISSN: 1857-0011.
6. **Cotoman A**., Șciuca S., Selevestru R. Sindromul bronho-obstructiv la copii cu displazie bronhopulmonară. În: *Buletinul de Perinatologi.* 2022; 1(93): pp. 201-206. ISSN 1810-5289.
7. Șciuca S., Ceahlău M., **Cotoman A**., Selevestru R. Impactul antecedentelor perinatale în realizarea displaziei bronhopulmonare la copiii născuți prematuri. În: *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale.* 2023; nr. 2(76): pp. 56-62. ISSN: 1857-0011.
8. Sciuca S., Ceahlău M., **Cotoman A**., Selevestru R. Evaluarea clinică a severității displaziei bronhopulmonare la copiii din naşterile premature. În: *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale*. 2023; nr. 3(77): pp. 127-132. ISSN: 1857-0011.
9. **Cotoman A**., Selevestru R., Sciuca S. Evaluation of pulmonary imaging data by radiography in children with bronchopulmonary dysplasia. În*: Revista de Ştiinţe ale Sănătăţii din Moldova*. 2024; nr. 1(11): pp. 32-36. ISSN: 2345-1467.
10. **Cotoman A**., Selevestru R., Şciuca S. Evaluarea factorilor de risc prenatali la copiii cu displazie bronhopulmonară. În: *Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale.* 2024; nr. 2(79): pp.112-115. nr. 3(77). ISSN: 1857-0011.
11. **Cotoman A**., Selevestru R., Şciuca S. Impactul ventilației pulmonare și oxigenoterapiei în etiopatogenia displaziei bronhopulmonare la copilul prematur. *În: Buletinul Academiei de Ştiinţe a Moldovei. Ştiinţe Medicale*. 2024; nr. 3(80): pp.90-93. ISSN: 1857-0011.

  - ✓ **articles published in Category C journals**

12. **Cotoman** A., Șciuca S., Pînzari L., Selevestru R., Bratu E., Rotaru-Cojocari D., Particularităţi ale imunităţii prematurului. În*: Arta Medica*. 2017; nr. 4(65): pp. 45-47. ISSN: 1810-1852.

13. **Cotoman A**., Maladia respiratorie a prematurului. În: *Arta Medica,* 2017; nr. 4(65): pp. 48-50. ISSN: 1810-1852.

- ✓ **papers included in the proceedings of international or national scientific conferences**

14. **Cotoman A.,** Selevestru R., Șciuca S. Sindromul bronhoobstructiv la copii cu displazie bronhopulmonară. În: *Culegerea materialelor științifice a Conf. Naționale cu participare internaț. „IMSP Institutul Mamei și Copilului –40 ani activitate”,* 3-5.11.2022, p.201-206, ISSN 1810-5289
15. **Cotoman A**., Ceahlau M., Șciuca S. Repere diagnostice prin examen radiologic la copiii cu Displazie bronhopulmonară. În: *Culegerea de lucrări Conf. part. intern.„Actualități în pneumologia copilului”,* USMF„Nicolae Testemiţanu". Chișinău, 2023; pp.62-67. ISSN: 978-9975-82-328-9.
16. Șciuca S., Balan A., **Cotoman A**., Conica C., Ceahlau M., Spînu T. Displazia bronhopulmonară la copilul prematur și impactul infecției COVID-19. În: *Culegerea de lucrări a conf. part. Internaț. „Actualități în pneumologia copilului*”, Chișinău, 2023; pp. 123-129. ISSN: 978-9975-82-328-9.
17. **Cotoman A**., Curteanu A., Șciuca S., Selevestru R., Ceahlau M., Conica C., Pînzari L., Braniște N. Evaluarea semnelor clinice de afectare respiratorie la copii cu displazia bronhopulmonară. În: *Conferința "Imunodeficiențe primare în Republica Moldova – succese și provocări",* USMF „Nicolae Testemiţanu". Chișinău, 2023; pp. 78-83.
18. **Cotoman** A., Selevestru R., Șciuca S. Displazia bronhopulmonară la copilul prematur – abordări clinico-imagistice. În: *Conferința „Copilul prematur – realităţi şi perspective în conduita medicală multidisciplinară"*, 28 noiem., Chișinău: „Print-Caro", 2024; pp. 43-49. ISSN: 978-5-85748-085-4
19. **Cotoman A.,** Țurcan A., Mighic C., Coropceanu I., Gaina A., Șciuca S. Diversitatea clinico-imagistică a displaziei bronhopulmonare la copii prematuri din triplex. În: *Copilul prematur – realităţi şi perspective în conduita medicală multidisciplinară*, 28 noiembrie 2024; Chișinău. Chișinău: „Print-Caro”, 2024; pp. 110-114. ISBN: 978-5-85748-085-4.
20. **Cotoman** A., Șciuca S., Gudumac E. Displazia bronhopulmonară la copiii prematuri: aspecte patogenice. În: *Actualităţi în pediatrie – abordări multidisciplinare în conduita medicală a copilului,* 1 noiembrie 2024, Chișinău:"Print-Caro"SRL, 2024; pp.87-93. ISSN:978-5-85748-062-5
21. **Cotoman A**., Șciuca S., Selevestru R., Curteanu A. Displazia bronhopulmonară la copii din nașterile premature – o perspectivă istorică. În: *Culegerea de lucrări a conferinţei cu participare internaţională „Anomalii congenitale și afecțiuni chirugicale la copii. Probleme perspective”,* USMF „Nicolae Testemiţanu". Chișinău, 2024; pp. 49-61. ISBN: 978-5-85748-118-9.

- ✓ **Abstracts, summaries, theses, or posters published in the proceedings of national and international scientific meetings:**

22. Sciuca S., Eremciuc R., Pînzaru L., Rotaru D., **Cotoman A**. Clinical and evolutive peculiarities of the bronchopulmonary dysplasia and Wilson-Mikity syndrome in premature children. In: *Arch Dis Child*. 2014; 99(Suppl 2). 10.1136/archdischild-2014-307384.1400, PO-0761.
23. Crivceanschi M., Selevestru R., **Cotoman A**., Crivceanschi E., Chiriac N., Sciuca S. Chest CT findings in premature born children with bronchopulmonary dysplasia. In: *European Resiratory Jurnal*, 2016; Vol.48, Iss.Supll. 60, Ann. Congr. European Respiratory Society, London, ISSN: 0903-1936 DOI: 10.1183/13993003. congress-2016 PA3825 IF 8,332.
24. **Cotoman A**., Tomacinschii C., Selevestru R., Aioani O., Sciuca S. The impact of oxygen therapy in preterm infants with bronchopulmonary dysplasia. In: *European Respiratory Journal*, Milano, Italia, 2017; 50 (suppl 61) PA 4787.
25. Șciuca S., **Cotoman A**. Bronhopulmonary dysplasia in premature neonates. In: *Journal of Pediatric and Neonatal Individualized Medicine*. *Abstracts of the 8 International Congress of UENPS.* Bucharest, Romania, 2018, Vol. 7(2), pp. 40-41. doi: 10.7363/070230
26. Selevestru R., Șciuca S., Pînzari L., **Cotoman A**. Respiratory affectation in premature newborns. In*: Journal of Pediatric and Neonatal Individualized Medicine*. Abstracts of the 8 International Congress of UENPS, Bucharest, Romania, 2018; 7(2): p. 42. doi: 10.7363/07023.

27. **Cotoman A**., Selevestru R., Sciuca S. Insuficienţa respiratorie în displaziile bronhopulmonare la copii. În: *Rezum. Congr. Pediatrie, Chişinau*. *Bul. Perinatol.* 2018; 4(80): p.83. ISBN 1810-5289.
28. **Cotoman A**., Selevestru R., Sciuca S. Insuficienţa respiratorie în displaziile bronhopulmonare la copii. În: *Buletin de Perinatologie. Chisinau,* 2018; nr 4(80): p. 82. ISBN: 1810-5289.
29. **Cotoman A**., Ceahlău M., Selevestru R., Sciuca S. Bronchopulmonary displasia in children: analytical cohort study. B: *Сборник Трудов XXIX Конгресса. Национальный Конгресс по болезням органов дыхания*. Москва, Россия, 2019; с. 188.
30. Sciuca S., Selevestru R., **Cotoman A**., Ceahlau M. Premature infant with A(H1N1) flu during 2018-2019 season. In: *Abstract, International Conference on Clinical Neonatology. Venice*, 2019; p. 154.
31. **Cotoman A**., Ceahlau M., Selevestru R., Sciuca S. Significance of oxigenotherapy in the bronchopulmonary dysplasia in premature infant**s.** In: *Abstract, International Congerence on Clinical Neonatology*. Venice, 2019; p. 234.
32. **Cotoman A**., Selevestru R., Ceahlau M., Şciuca S. Displazia bronhopulmonară la copii. În: *Materialele Conf. Naţionale a Societăţii Române de Pneumologie.* Bucureşti, România, 2019; p. 67.
33. **Cotoman A**., Ceahlău M., Crivceanschi E., Tomacinschi C., Balanețchi L., Selevestru R., Sciuca S. Modificările la tomografia computerizată la copiii cu displazia bronhopulmonară. Conf. Naţională de Pediatrie. În: *Revista Română de Pediatrie*. Bucureşti, România, 2020; vol. LXIXs: p. 55.
34. Ceahlău M., **Cotoman A**., Selevestru R., Șciuca S. Mycoplasma pneumonia infection in premature infants with bronchopulmonary dysplasia. În: *Lucrările Congresului Naţional XXVI-lea al Societăţii Române de Pneumologie*. Bucuresti, România, 2020; p. 378. ISBN: 978-606-8463-68-1.
35. Ceahlău M., Selevestru R., **Cotoman A.,** Șciuca S. Predictorii displaziei bronhopulmonare la copiii premature. În: *Abstract book. Congresul consacrat aniversării a 75-a de la fondarea Universităţii de Stat de Medicină şi Farmacie "Nicolae Testemiţanu".* Chișinău, 2020, p. 552.
36. **Cotoman A**., Ceahlau M., Selevestru R., Gudumac E., Curteanu A., Sciuca S. Neonatal sepsis - a major risk for bronchopulmonary dysplasia in children born prematurely. In: *Allergy. Abstracts from the Eur. Academy Aller. Clinical Immunol. Congr.*, 2022; Vol.79, Iss. S109, p.82. ISBN:1398-9995.
37. **Cotoman A**., Selevestru R., Grosu V., Goloborodico A. Impactul infecției COVID-19 asociate cu citomegalovirus și herpes virus la copil nou-născut. Particularitățile unui caz clinic. În*: Revista de Ştiinţe ale Sănătăţii din Moldova*. 2022, nr. 3, 1(29), p.140. ISSN 2345-1467.
38. **Cotoman A**., Ceahlău M., Selevestru R., Crivceanschi E., Șciuca S. Displazia bronhopulmonară la copii în imagini tomografice. Conferința Universității de Stat de Medicină şi Farmacie „Nicolae Testemiţanu". În: *MJHS*. Chișinău, 2022; vol. 29; nr. 3, p. 395. ISSN 2345-1467.
39. Ceahlau M., **Cotoman A**., Conica C., Selevestru R., Șciuca S. Antecedente cu potențial de risc pentru dispalzia bronhopulmonară la prematuri. În: *Materialele Conf. Naționale Zilele Pediatriei Ieșene „N.N. Trifan",* ediția a XXXV-a. Iași, România. 2023; p. 57. ISBN: 978-606-13-7701-5.
40. Ceahlau M., Tagadiuc O., **Cotoman A**., Conica C., Selevestru R., Șciuca S. Activitatea prooxidantă în displazia bronhopulmonară la copiii din născterile premature. În: *Materialele Conf. Naț. Zilele Pediatriei Ieşene „N.N. Trifan"*, ed. XXXV. Iași, România. 2023; p.58. ISBN: 978-606-13-7701-5.
41. Șciuca S., Selevestru R., **Cotoman A.,** Filimon-Ceahlău M., Tomacinschi C. Morbiditatea respiratorie în wheezing recurent la copilul sugar. În: *Pediatria – specialitate multidisciplinară:* Congresul Internațional al Societății de Pediatrie din RM, 6-8 iunie 2024, Chișinău, ediția 8, p. 63.
42. Șciuca S., **Cotoman A**. Copilul prematur și afecțiunile pulmonare evolutive. În: *Materialele conf. internaționale* „Patrimoniul cultural de ieri – implicații în dezvoltarea societății de mâine", În: *Supliment al revistei științifice „Authentication and Conservation of Cultural Heritage. Research and Technique"*, Iași-Chișinău-Lviv, 2025, p.295.
43. Șciuca S., **Cotoman A**. The premature infant and evolving pulmonary diseases. In:„*Cultural heritage of yesterday – contribution to the development of sustainable society of tomorrow*" 11-

12.02.2025, ed.11. In: *„Authentication and Conservation of Cultural Heritage. Research and Technique”*, Iași-Chișinău-Lviv, p.296.

- **Scientific, methodological, and educational works:**

44. Șciuca S., Curteanu A., **Cotoman A.** Displazia bronhopulmonară. Managementul pacientului pediatric. ***Ghid științifico-metodic*** *și didactic*. Chișinău, 2025; 76 p. ISBN: 978-9975-58-213-1.

45. Șciuca S., Curteanu A., Selevestru R., **Cotoman A**., Ceahlău M. *Displazia bronhopulmonară la copii***. *PCN-393*.** Chișinău, 2021; 48 p.

46. Șciuca S., **Cotoman A.,** Ceahlău M., Selevestru R**.** Displazia bronhopulmonară. Capitol în: *Compendiu de boli rare.* Sub red. Mazur-Nicorici L., Diaconu C. Chișinău, tipografia „Impressium”, 2020, p.281-300. ISBN 978-9975-3426-6-7

- **Patents, innovation certificates, registration documents, and materials presented at invention exhibitions**:
  - ✓ **Certificate of innovation**

47. **Cotoman A**., Sciuca S., Selevestru R. *Algoritmul monitorzării evoluției clinice la copii cu displazie bronhopulmonară.* Nr.6210 din 07.03.2024, acordat în conf. cu art. 1 al Legii 138-XV; 10.08.2001.

48. **Cotoman A**., Sciuca S., Selevestru R. *Metoda de apreciere a diagnosticului precoce în dispazia bronhopulmonară la copii prematur*i. Nr. 6208 din 07 martie 2024, acordat în conformitate cu art. 1 al Legii 138-XV din 10.08.2001.

49. **Cotoman A**., Sciuca S., Selevestru R. *Evaluarea modificărilor imagistice la copii cu displazie bronhopulmonară*. Nr. 6209 din 07.03.2024, acordat în confor. cu art.1 al Legii 138-XV;10.08.2001

  - ✓ **Implementation documentation**

50. **Cotoman A**., Sciuca S., Selevestru R. *Algoritmul monitorzării evoluției clinice la copii cu displazie bronhopulmonară*. Nr.28 din 07.03.2024, acordat în conform. cu art.1, Legea 138-XV; 10.08.2001.

51. **Cotoman A**., Sciuca S., Selevestru R. *Metoda de apreciere a diagnosticului precoce în dispazia bronho-pulmonară la copii prematuri*. Nr.26 din 07.03.2024, acordat în conformitate cu art.1 al Legii 138-XV din 10.08.2001

52. **Cotoman A**., Sciuca S., Selevestru R. *Evaluarea modificărilor imagistice la copii cu displazie bronhopulmonară*. Nr. 27 din 07.03.2024, acordat în conform. cu art.1, Legea 138-XV; 10.08.2001.

- **Oral presentations at scientific forums:**
  - ✓ **international**

53. **Cotoman A**., Sciuca S. Impactul oxigenoterapiei la copiii prematuri cu displazie bronhopulmonară. În: *Conf. națională cu participare Internațională de Pediatrie* Chișinău, 15-16 sept. 2017.

54. **Cotoman A**., Sciuca S. Sindromul Wiskott-Aldrich. În: *Conf. Științifico-practică cu participare internațională. Imunitatea copilului și imunodeficiențele primare.* Chisinau, 3 noiembrie 2017.

55. **Cotoman A**., Sciuca S. Modificările la tomografia computerizate la copii cu displazie bronhopulmonară. În: *Conferința Națională de pediatrie*. Bucuresti, România, 20 septembrie 2020.

56. **Cotoman A.,** Sciuca S. Обструктивный синдром у детей с бронхолегочной дисплазией. В: *XXIX Конгресс по болезням органов дыхания,* Украина, 2020

57. **Cotoman A**., Sciuca S., Ceahlău M. Displazia bronhopulmonară repere diagnostice imagistice În: *Conferința cu part.internaț.„Actualități în pneumologia copilului”*,USMF„Nicolae Testemițanu”Chișinău, 22 iunie 2023

58. **Cotoman A.,** Sciuca S., Criterii dagnostice radioimagistice la copiii cu displazie bronhopulmonară. În: *Congresul internațional de pediatrie, ediția VIII-a*, Chișinău, 06-08 iunie 2024.

59. **Cotoman A**., Sciuca S., Displazia bronhopulmonară la copilul prematur – abordări clinico-imagistice – În: *Conferința cu participare intrenațională „Copilul prematur – realități și perspective în conduita medicală multidisciplinară”*. Academia de Științe a Moldove, Chișinău, 28

noiembrie 2024.

60. Șciuca S., **Cotoman A**. Copilul prematur și afecțiunile pulmonare evolutive. În: *Conf. internaț.* „Patrimoniul cultural de ieri – implicații în dezvoltarea societății de mâine", Iași-Chișinău-Lviv, 11-12 februarie 2025

- ✓ **naţional**

61. **Cotoman A**., Sciuca S. Displazia bronhopulmonară - factorii de risc și criterii diagnostice prognostic. În: *Conferința „Maladii ale sistemului bronhopulmonar la copii".* Chișinău, 22 oct. 2018.
62. **Cotoman A**., Sciuca S., Selevestru R. Insuficiența respiratorie la copii cu displazie bronhopulmonară*. În:Congresul național de pediatrie ediția VII-a*", Chișinău, 2018.
63. **Cotoman A**., Sciuca S., Selevestru R. Infectiile virale la copii cu DBP. În: *Conf. Ştiinţifică Anuală Zilele Universităţii de Stat de Medicină şi Farmacie ,,Nicolae Testemiţanu,,.* Chișinău, 17.10.2019.
64. Ceahlău M., Selevestru R., **Cotoman A**., Șciuca S. Predictorii displaziei bronhopulmonare la copiii prematuri. În: *Congresul aniversar USMF „Nicolae Testemițanu*", 21-23 octombrie, 2020
65. **Cotoman A**., Sciuca S., Selevestru R. Modificările tomografiei computerizate la copiii cu displazie bronhopulmonară În: *Zilele USMF ,,Nicolae Testemiţanu".* Chișinău, 20 octombrie 2022.
66. **Cotoman A.,** Șciuca S., Sindromul bronho-obstructiv la copii cu displazie bronhopulmonară. În: *Conferința națională* „*Ziua pneumoniei"*. Chișinau, 2022.

- **Poster presentations at scientific forums:**
  - ✓ **Internațional**

67. Crivceanschi M., Selevestru R., **Cotoman A**., Crivceanschi E., Chiriac N., Sciuca S. Chest CT findings in premature born children with bronchopulmonary dysplasia. *Congr. Europ.Respiratory Society*, London, 2016.
68. **Cotoman A**., Tomacinschii C., Selevestru R., Aioani O., Sciuca S. The impact of oxygen therapy in preterm infants with bronchopulmonary dysplasia. *Congr. Eur.Respir.Sosiety*, Milano, Italia, 2017
69. **Cotoman A**., Ceahlau M., Selevestru R., Sciuca S. Significance of oxigenotherapy in the bronchopulmonary dysplasia in premature infants. *Conf. on Clinical Neonatology.* Venice, Italia, 2019.
70. **Cotoman A**., Ceahlau M., Selevestru R., Gudumac E., Curteanu A., Sciuca S. Neonatal sepsis - a major risk for bronchopulmonary dysplasia in children born prematurely. In: *Eur.Acad.Aller. Clin.Immun.Congr.*, 2022
71. Ceahlau M., **Cotoman A**., Conica C., Selevestru R., Şciuca S. Antecedente cu potențial de risc pentru dispalzia bronhopulmonară la prematuri. *Conferința Națională Zilele Pediatriei Ieșene „N.N. Trifan", ediția a XXXV-a.* Iași, România, 2023.
72. Ceahlau M., Tagadiuc O., **Cotoman A**., Conica C., Selevestru R., Şciuca S. Activitatea prooxidantă în displazia bronhopulmonară la copiii din nașterile premature. *Conferința Națională Zilele Pediatriei Ieșene „N.N. Trifan", ediția a XXXV-a.* Iași, România, 2023.

ANNOTATION

Cotoman Aliona, "Bronchopulmonary Dysplasia in Children – Etiological Factors and Clinical-Paraclinical Diagnosis", PhD thesis in medical sciences, Chișinău, 2025.

Structure of the thesis: The thesis is presented on 134 page and comprises the following sections: introduction, 3 chapters, synthesis of obtained results, general conclusions, practical recommendations, bibliography with 217 titles, and 7 annexes. The illustrative material includes 37 tables and 27 figures.

Keywords: bronchopulmonary dysplasia, preterm infants, risk factors, chest X-ray, pulmonary CT.

Aim of the research: To evaluate the etiological factors and clinical-paraclinical diagnosis of bronchopulmonary dysplasia (BPD) in preterm infants to develop prognostic criteria for the disease.

Research objectives: 1) To study the risk and causal factors involved in bronchopulmonary dysplasia in children; 2) To evaluate the clinical manifestations of children with bronchoulmonary dysplasia; 3) To investigate pulmonary imaging changes in children with bronchopulmonary dysplasia; 4) To develop prognostic criteria for the evolution and severity of bronchopulmonary dysplasia in preterm infants.

Scientific novelty and originality: The scientific novelty focuses on identifying determinants and predictive factors in children with bronchopulmonary dysplasia, highlighting specific clinical forms. An analytical observational cohort study was conducted through a multifactorial etiological approach to BPD in children with a history of prematurity. The research provided original national data regarding risk factors for BPD in preterm infants hospitalized at the IMSP Institute of Mother and Child, as well as data related to bronchopulmonary sequelae in BPD. New insights were gained regarding the role of pathogens in BPD, enabling a deeper correlation with the degree of prematurity, birth weight, gestational age, and oxygen therapy level. Risk factors, clinical features, and imaging characteristics were analyzed according to the severity of BPD in children.

Theoretical significance: The theoretical significance of the research lies in the in-depth exploration of the etiopathogenic mechanisms involved in the development of BPD in preterm infants, using a comprehensive and integrative approach to the determining factors. The study enriched the existing theoretical framework by identifying and classifying risk and predictive factors based on disease severity and highlighting the relationship between perinatal, infectious factors and the need for respiratory support. The findings significantly contributed to the understanding of the relationship between prematurity, postnatal insults (infections, oxygen therapy, mechanical ventilation), and the development of bronchopulmonary sequelae, offering a conceptual framework that can support the development of predictive models and follow-up guidelines for children at high risk of BPD.

Practical value: Programs were developed with clear criteria for early diagnosis and prognosis of the evolution of bronchopulmonary dysplasia in children. For practitioners, a well-structured laboratory diagnostic algorithm was proposed to enable the earliest possible detection of this nosological entity. The application of this algorithm facilitates the assessment of BPD's impact on pediatric respiratory morbidity, contributing to faster and more effective clinical interventions.

Implementation of results: The results of the study were implemented in the clinical practice of the Pneumonology Clinic within the IMSP Institute of Mother and Child. Additionally, these findings were incorporated into the educational process at the Department of Pediatrics, "Nicolae Testemițanu" State University of Medicine and Pharmacy, and contributed to the update of the National Clinical Protocol (PCN-393) on "Bronchopulmonary Dysplasia in Children." These initiatives highlight the practical applicability of the research in improving patient care and continuous professional development.