НЕОНАТОЛОГІЯ, ХІРУРГІЯ ТА ПЕРИНАТАЛЬНА МЕДИЦИНА
NEONATOLOGY, SURGERY AND PERINATAL MEDICINE
ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)
Т. XIV, № 3(53), 2024
VOL. XIV, № 3(53), 2024
KEY TITLE: NEONATOLOGÌÂ, HÌRURGÌÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)

АНАЛІТИЧНІ ОГЛЯДИ

UDC 616.248:616.24-006-071-053.2
DOI: 10.24061/2413-4260. XIV.3.53.2024.19

DIAGNOSTIC CRITERIA AND RISK FACTORS FOR PULMONARY FIBROSIS IN PEDIATRIC PATIENTS WITH BRONCHIAL ASTHMA

T. O. Kryuchko, D. O. Klymko

Poltava State Medical University
(Poltava, Ukraine)

Summary

The diagnosis of pulmonary fibrosis represents a significant and urgent concern, particularly within the context of pediatric practice. A review of the scientific literature reveals that pulmonary fibrosis can be a complication of bronchial asthma in pediatric patients. Among pediatric patients, there is currently a trend towards a steady increase in the prevalence of allergic diseases, in particular bronchial asthma. An additional crucial area of investigation is the advanced study of asthma predictors, which include children with a history of extreme prematurity. Concurrently, prematurity and low birth weight represent risk factors for the onset of bronchopulmonary dysplasia. A substantial body of evidence from clinical trials of uncontrolled asthma substantiates the necessity for further investigation into the influence of additional adverse environmental factors, including electronic smoking. Despite the growing importance of diagnosing pulmonary fibrosis in adult patients in recent years, many questions remain regarding the relevance of this issue in pediatric patients.

Key words: *Children; Bronchial Asthma; Pulmonary Fibrosis; Premature Infants; Vaping; Microrna.*

In recent years, there has been a notable increase in the scientific community's interest in the study of fibrosis in adult patients. Concurrently, no literature sources currently exist that provide information on the status of this issue in pediatric patients. The prevalence of pulmonary fibrosis in adults worldwide is variable, with an average of 17.4 % per 100,000. [1] The pathogenic link of pulmonary fibrosis is represented by a structure called the extracellular matrix, which plays a crucial role in maintaining the lung architecture in a state of balance between synthesis and degradation. The extracellular matrix is comprised of a diverse array of proteins and glycoproteins, including structural proteins (collagen and elastin), adhesive proteins (fibronectin and tenascin), and glycosaminoglycans/ proteoglycans. The extracellular matrix of the lungs is primarily composed of collagen fibres, which are made up of collagen types I, II, III, V and IX. These fibres provide the lungs with flexibility and elasticity. Adhesive proteins of the extracellular matrix, such as fibronectin and tenascin, serve as ligands for cell adhesion receptors. Meanwhile, glycosaminoglycans and proteoglycans represent the primary structural components of the extracellular matrix, forming the stroma of nearly all tissue types (2, 3). In physiological conditions, proteins provide structural and mechanical support for lung tissue, thereby establishing the foundation for normal cellular activities, including adhesion, migration, and proliferation. However, in pathological conditions, they become one of the contributing factors to the initiation and progression of fibrosis in lung tissue. This conclusion is supported by several experiments in which extracellular lung matrix obtained from patients with pulmonary fibrosis led to the differentiation of normal fibroblasts into myofibroblasts, even in the absence of cellular components and cytokines. Furthermore, evidence indicates that elevated synthesis of extracellular matrix components driven by myofibroblasts can result in reduced elasticity, which in turn stimulates the expression of a mechanosensitive effector protein, leading to increased deposition of matrix components and a further decline in lung elasticity. This represents a key mechanism in the fibrotic cycle. An increase in the deposition of extracellular matrix proteins is a hallmark of irreversible changes in lung tissue. In patients with chronic inflammatory lung diseases, such as chronic obstructive pulmonary disease and bronchial asthma, this can often result in the development of pulmonary fibrosis. In the present context, the issue of the rising prevalence of allergic diseases, particularly bronchial asthma, represents a significant challenge in the field of pediatric medicine. The global prevalence of asthma among children ranges from 10 to 15 %. [6] The observed increase in this pathology can be attributed to the influence of various etiological factors that can precipitate the onset of the disease at a younger age and complicate its course during adolescence. The pathological changes observed in the lungs of patients with asthma can be classified into two main categories: alterations in the bronchial epithelium and smooth muscles, and the presence of distinct signs indicative of an asthma exacerbation, as well as subepithelial fibrosis. The presence of pathological changes can result in bronchial obstruction, which is reversible in the early stages of the disease but irreversible in the later stages. [7,8].

The development of bronchial asthma is characterised by hyperplasia and metaplasia of goblet and epithelial cells of the bronchial epithelium, which results in an increase in mucus production, airway thickening and bronchial obstruction. Furthermore, in severe exacerbations of asthma, both the large and small airways are frequently obstructed by mucus plugs containing an admixture of inflammatory cells, predominantly eosinophils in cases of allergic asthma. Furthermore, mucus plug formation is exacerbated by ciliary cell dysfunction resulting from airway inflammation. This is evidenced by a reduction in the frequency of ciliary cell oscillations, as well as ciliary dyskinesia and disorientation. [9] Another factor that contributes to airway obstruction is bronchial smooth muscle spasms, which result in bronchoconstriction. In physiological conditions, the bronchial smooth muscle provides mechanical stability to the airways without the

presence of cartilage. Nevertheless, in cases of bronchial asthma, the threshold for smooth muscle sensitivity is reduced following spasms and reversible airway obstruction. [10]. Another component of the pathomorphological changes in bronchial asthma is the accumulation of smooth muscle cells due to their hypertrophy and hyperplasia, which leads to airway thickening. [14]. Moreover, it is postulated that smooth muscle cells may facilitate airway remodeling through the secretion of proinflammatory mediators, matrix and cell adhesion proteins, and other stimulatory molecules, which may influence the subsequent migration and activity of inflammatory cells. [15] The progression of irreversible airway narrowing and the associated increase in airway hyperresponsiveness represent the primary factors contributing to the development of severe asthma. Notwithstanding considerable advances in the comprehension of the aetiology, pathogenesis and clinical management of asthma, a proportion of patients may exhibit severe disease and poor control. A substantial body of evidence from clinical trials of uncontrolled asthma substantiates the necessity for a comprehensive analysis of the factors that contribute to the development of severe forms. The current challenge is to control the course of the disease and to identify risk factors for the development and progression of asthma in pediatric patients.

In recent years, an increasing number of scientific papers have established a correlation between the occurrence of allergic pathology, particularly bronchial asthma, in children with a history of extreme prematurity. The results of a meta-analysis indicated that the prevalence of bronchial asthma was 1.37-1.71 % higher among preterm infants compared to full-term infants. [11] Prematurity and low birth weight are identified as risk factors for the development of bronchopulmonary dysplasia (BPD). The development of this disease is associated with a high concentration of toxic oxygen and the use of artificial lung ventilation (ALV), which directly affect the immature lungs, thereby contributing to the disease's progression. [12]. It has been observed by researchers that the utilization of mechanical ventilation in a premature infant for a period exceeding 10-14 days is associated with an elevated risk of developing bronchopulmonary dysplasia. The most common indication for supplemental oxygen is respiratory failure, which may result from congenital pneumonia or respiratory distress syndrome. The highest risk of bronchopulmonary dysplasia is observed in infants born at a gestational age of less than 28 weeks, as this is the period during which the processes of alveolarization of the distal lung sacs and formation of the alveolar vascular system commence. The consequence of this disease is the development of an immature lung, which is characterised by interstitial changes involving collagen formation disorders. This results in the underdevelopment of arterioles and capillaries, which subsequently leads to fibrosis. [13, 14]. Furthermore, a reduction in the surface alveolar area is observed, which is linked to a dysmorphologically altered pulmonary microcirculatory pathway. This is evidenced by the presence of inflammatory markers in the airways, resulting in an increased neutrophil count and proinflammatory cytokine levels. The specific characteristics of cytokine release and the response of immature lungs to harmful factors are influenced by differences in the genetic predictors, particularly single-nucleotide polymorphisms (SNPs), fibroblast growth factor receptor 4 (FGFR-4), and surfactant protein B (SP-B), in low-birth-weight infants who exhibit a genetic predisposition to the development of bronchopulmonary dysplasia (BPD) in the future. Alterations in the structure of the small and large alveolar septa, in addition to an insufficient number and altered configuration of pulmonary capillaries, can result in the development of pulmonary hypertension. At present, the pathogenesis of bronchopulmonary dysplasia remains incompletely understood. Impairment of lung function, a hallmark of moderate to severe bronchopulmonary dysplasia in infants, may serve as a foundation for the subsequent development of asthma. Furthermore, both bronchopulmonary dysplasia and asthma present with analogous respiratory symptoms, including bronchial hyperreactivity, inflammation, and airflow restriction. The pathogenic course of BD is typified by a prevalence of neutrophils and macrophages, which is characteristic of a Th1-mediated response. Conversely, in asthma, inflammation is accompanied by the activation of mast cells and eosinophils, which is typical of Th2-mediated responses. [15]. Therefore, children with a history of extreme prematurity are at risk for serious bronchopulmonary diseases, such as bronchopulmonary dysplasia and bronchial asthma. These children require dynamic monitoring and a personalized set of preventive measures.

The management of asthma in children continues to present a significant challenge in the field of pediatric practice. The uncontrolled course of the disease is typically attributable to a combination of factors, including allergens and additional environmental influences such as air pollution, particularly passive and active smoking. The use of second-generation electronic systems, colloquially known as «vapes,» is becoming increasingly prevalent among adolescents. There has been a notable surge in the demand for vaping over the past decade. Initially, the sale of electronic systems was intended to reduce smoking among adult smokers. However, the product's designation as a «safe alternative» and its availability in a wide variety of flavors attracted the attention of teenagers. An electronic system is defined as a device comprising a battery and a cartridge. The heating element is situated within the cigarette itself, and its function is to convert the liquid into a vapor that is then inhaled by the smoker. The liquid contained within the cartridge is composed of propylene glycol and vegetable glycerin, which serve as a solvent, in addition to nicotine and flavorings. The chemical process of thermal dehydration of propylene glycol can yield a range of products, including acetaldehyde, formaldehyde, propylene oxide, acetol, allyl alcohol, glyoxal, and methyl glyoxal. The majority of the liquids contained within the cartridges are flavored. [16]. A growing body of scientific literature is documenting the deleterious effects of diacetol and benzaldehyde compounds on lung tissue. A significant component of the cartridge liquid is flavorings, including tobacco, fruit, and floral, which enhance the appeal of vaping. The aforementioned characteristics, in conjunction with the affordability of these devices and the availability of bespoke handmade models, serve to pique the interest of adolescents, fostering a desire to purchase and utilize these products. As evidenced by recent research, the prevalence of

ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

e-cigarettes among Ukrainian adolescents aged 13-15 is 22 % among boys and 14 % among girls. [17] Adolescents who used vapes exhibited elevated levels of neutrophils, including myeloperoxidase, neutrophil elastase, and proteinase-3, in sputum. When dysregulated, pulmonary proteases have the potential to destroy basement membranes, thereby contributing to the development of chronic obstructive pulmonary disease. Adolescents who regularly utilize vaping devices have been observed to exhibit a heightened degree of exposure to nicotine vapor within the respiratory tract, accompanied by the manifestation of symptoms such as coughing, wheezing, and shortness of breath when compared to their counterparts who did not engage in vaping. [18,19]. It is therefore evident that the aforementioned alterations may prove hazardous for both healthy children and those afflicted with bronchopulmonary disorders, particularly for patients with asthma. Consequently, the investigation of the influence of e-smoking as a potential exacerbating factor in pediatric asthma is a crucial domain within the field of pediatric pulmonology.

The diagnosis of pulmonary fibrosis in adult patients is based on a comprehensive history and an accurate description of the presenting symptoms, a thorough physical examination, an evaluation of the clinical manifestations, and instrumental methods of examination and biopsy. The issue of diagnosing pulmonary fibrosis in pediatric patients has prompted the development of additional non-invasive research methods. Modern, highly informative methods of molecular genetic research, such as microRNA biomarkers, represent a promising avenue for confirming the diagnosis of pulmonary fibrosis. MicroRNAs are a class of non-coding RNA molecules comprising 21-23 nucleotides. They regulate gene expression at the post-transcriptional level by binding to the 5'-untranslated region (UTR) and the 3'UTR target site of the hairpin end. [20, 21]. To date, more than 2,500 types of microRNAs have been identified, with this list continually expanding in response to the expression changes observed in a range of pathological conditions affecting the body. It has been demonstrated that microRNA-29 (miR-29b) plays a pivotal role in the regulation of fibrosis, not only in the lungs but also in a number of other organs, including the liver and kidneys. [22,23] MiR-29b plays a pivotal role in maintaining homeostasis, as reduced levels of this microRNA are frequently observed in numerous respiratory disorders, including pulmonary fibrosis, pulmonary hypertension, and lung cancer. MiR-29b has been the subject of considerable interest in the context of fibrosis due to its effects on genomic material, particularly through genes encoding extracellular matrix proteins such as collagens, fibronectin, and elastin. The levels of miR-29b are decreased in mesenchymal cells/fibroblasts, which are the primary effectors that mediate this pathology. [24]. A substantial body of evidence suggests that abnormalities are present not only in pulmonary fibroblasts, but also in alveolar epithelial cells, immune cells, and even endothelial cells in this complication. Therefore, microRNA biomarkers possess significant diagnostic value for the early detection of pulmonary fibrosis. Furthermore, given the minimally invasive nature of this technique, it may be a promising avenue for pediatric patients. Despite the extensive research conducted on the cellular and molecular processes underlying pulmonary fibrosis, the search for reliable markers for early diagnosis and the prevention of disease progression remains a crucial and ongoing endeavor. [25].

Immunological methods of research play an equally important role in the diagnosis of pulmonary fibrosis, in particular, the marker of fibroblast activity, transforming growth factor beta. Transforming growth factor β (TGF-β) represents a large family of polypeptides that modulate several biological processes, including cell proliferation, differentiation and apoptosis in internal organs. The TGF-β superfamily has more than 30 components, including TGF-β isoforms, antimullerian hormone, and bone morphogenic proteins. [26,27] They are important regulators of inflammation, injury, and repair, but their role largely depends on the context of their expression and other parallel cellular processes. TGFβ1 is involved in lung extension during development, while overexpression stops lung morphogenesis. TGF-β is secreted in a latent form, and its transition from the latent to the active phase is one of the main mechanisms regulating its activity during pulmonary fibrosis. TGF-β through Smad-dependent signal transduction stimulates the synthesis of endoplasmic reticulum components, inhibits their degradation by matrix metalloproteinases, and regulates the differentiation of fibroblasts into myofibroblasts. [28] In humans, TGFβ isoforms continue to be expressed in healthy lungs in adulthood. TGFβ has been described in human airway epithelium, alveolar macrophages, and airway smooth muscle cells. In various pulmonary diseases, TGFβ signaling has been reported to be enhanced in airway epithelium, fibroblasts, macrophages, and smooth muscle cells.TGF-β affects macrophages, which are among the most important regulators of the fibrotic response, by secreting cytokines, growth factors, and proteins that regulate the endoplasmic reticulum. Lymphocytes are also one of the targets of TGF-β during the development of fibrosis and affect their proliferation, activation, and function. TGF-β is involved in the repair of lung tissue (especially alveolar type II cells), which are damaged by prolonged fibrosis. The TGF-β signaling pathway is activated during the development of fibrosis in any tissue of the body, regardless of its localization and etiology. Activation of TGF-β leads to the release of various cell types from the endoplasmic reticulum, namely macrophages, platelets, and T-cells. The cytokine TGFβ1 plays a multifactorial and complex role in the pathogenesis of asthma and chronic obstructive pulmonary disease (COPD). These diseases are characterized by airway obstruction, inflammation, and remodeling. TGFβ1 levels were elevated in bronchoalveolar lavage fluid from patients with asthma, as well as in the airways and alveolar epithelium of patients with COPD. Higher levels of TGFβ1 isoforms are associated with asthma severity. TGFβ1 causes pathological effects in these diseases by promoting goblet cell hyperplasia, subepithelial fibrosis, epithelial damage, and airway smooth muscle hypertrophy.

A review of the literature indicates that the diagnosis of pulmonary fibrosis remains a significant challenge, particularly in the context of pediatric practice. The need for non-invasive, highly informative markers is paramount in this regard. The incidence of diseases that lead to the formation of pulmonary fibrosis is on the

rise in the pediatric population. In particular, the number of patients with bronchial asthma has increased by 2.5 times over the past three years, underscoring the necessity for a comprehensive analysis of the predictors of this allergopathology. The risk of developing asthma in infancy is significantly elevated in infants born at less than 31 weeks of gestation, with a reported range of 3.2 to 6.2 times higher compared to full-term infants. At 32 to 36 weeks of gestation, this risk is observed to be 1.5 to 2.5 times higher than in full-term infants (29). Prematurity and low birth weight are identified as risk factors for the subsequent development of bronchopulmonary dysplasia.

Conclusions. A review of the scientific literature reveals that one in three infants born before the 25th week of gestation is susceptible to developing bronchopulmonary dysplasia. Bronchopulmonary dysplasia (BPD) is the most prevalent disease among premature infants, occurring when the process of alveolarization, the final stage of lung development, is disrupted. An additional area of concern is the investigation of factors associated with uncontrolled asthma in children, which encompasses the use of electronic vaping devices. Statistical data indicates that the prevalence of electronic system use among adolescents is 17-21 %, with an upward trend that warrants further investigation into the impact of smoking on children. [30].

References:

1. Mustafin RN. Molecular genetics of idiopathic pulmonary fibrosis. Vavilovskii Zhurnal Genet Selektsii. 2022;26(3):308-18. DOI: https://doi.org/10.18699/vjgb-22-37

2. Savin IA, Zenkova MA, Sen'kova AV. Pulmonary Fibrosis as a Result of Acute Lung Inflammation: Molecular Mechanisms, Relevant In Vivo Models, Prognostic and Therapeutic Approaches. Int J Mol Sci [Internet]. 2022 [cited 2024 Jun 8];23(23):14959. Available from: https://www.mdpi.com/1422-0067/23/23/14959DOI: https://doi.org/10.3390/ijms232314959

3. Gu S, Liang J, Zhang J, Liu Z, Miao Y, Wei Y, et al. Baricitinib Attenuates Bleomycin-Induced Pulmonary Fibrosis in Mice by Inhibiting TGF-β1 Signaling Pathway. Molecules [Internet]. 2023 [cited 2024 Jun 7];28(5):2195. Available from: https://www.mdpi.com/1420-3049/28/5/2195 DOI: https://doi.org/10.3390/molecules28052195

4. Hariri LP, Flashner BM, Kanarek DJ, O'Donnell WJ, Soskis A, Ziehr DR, et al. E-Cigarette Use, Small Airway Fibrosis, and Constrictive Bronchiolitis. NEJM Evid [Internet]. 2022 [cited 2024 Jul 1];1(6):10.1056/evidoa2100051. Available from: https://evidence.nejm.org/doi/10.1056/evidoa2100051?url_ver=Z39.88-2003&rfr_id=ori: rid: crossref.org&rfr_dat=cr_pub%20 %200pubmed DOI: https://doi.org/10.1056/evidoa2100051

5. Yu D, Xiang Y, Gou T, Tong R, Xu C, Chen L, et al. New therapeutic approaches against pulmonary fibrosis. Bioorg Chem [Internet]. 2023 [cited 2024 Jun 1];138:106592. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0045-2068(23)00253-5 DOI: https://doi.org/10.1016/j.bioorg.2023.106592

6. van de Griendt EJ, Tuut MK, de Groot H, Brand PLP. Applicability of evidence from previous systematic reviews on immunotherapy in current practice of childhood asthma treatment: a GRADE (Grading of Recommendations Assessment, Development and Evaluation) systematic review. BMJ Open [Internet]. 2017 [cited 2024 Jun 1];7(12): e016326. Available from: https://bmjopen.bmj.com/content/7/12/e016326.long DOI: https://doi.org/10.1136/bmjopen-2017-016326

7. Onubogu U, West B. The Pattern of Comorbidities of Childhood Asthma as Seen in the Rivers State University Teaching Hospital, Nigeria. Open J Respir Dis [Internet]. 2021 [cited 2024 Jul 3];11:1-18. Available from: https://www.scirp.org/journal/paperinformation?paperid=107325 DOI: https://doi.org/10.4236/ojrd.2021.111001

8. Toskala E, Kennedy DW. Asthma risk factors. Int Forum Allergy Rhinol. 2015;5(1): S11-6. DOI: https://doi.org/10.1002/alr.21557

9. Conrad LA, Cabana MD, Rastogi D. Defining pediatric asthma: phenotypes to endotypes and beyond. Pediatr Res. 2021;90(1):45-51. DOI: https://doi.org/10.1038/s41390-020-01231-6

10. Bousquet J, Pfaar O, Agache I, Bedbrook A, Akdis CA, Canonica GW, et al. ARIA-EAACIcarepath ways for allergen immune therapy in respiratory allergy. Clin Transl Allergy [Internet]. 2021 [cited 2024 Jun 9];11(4): e12014. Available from: https://onlinelibrary.wiley.com/doi/10.1002/clt2.12014 DOI: https://doi.org/10.1002/clt2.12014

11. Sun T, Yu HY, Yang M, Song YF, Fu JH. Risk of asthma in preterm infants with bronchopulmonary dysplasia: a systematic review and meta-analysis. World J Pediatr. 2023;19(6):549-56. DOI: https://doi.org/10.1007/s12519-023-00701-1

12. Pierro M, Van Mechelen K, van Westering-Kroon E, Villamor-Martínez E, Villamor E. Endotypes of Prematurity and Phenotypes of Bronchopulmonary Dysplasia: Toward Personalized Neonatology. J Pers Med. 2022;12(5):687. DOI: https://doi.org/10.3390/jpm12050687

13. Gonçalves Eda S, Mezzacappa-Filho F, Severino SD, Ribeiro MÂ, Marson FA, Morcilo AM, et al. Association between clinical variables related to asthma in schoolchildren born with very low birth weight with and without bronchopulmonary dysplasia. Rev Paul Pediatr. 2016;34(3):271-80. DOI: https://doi.org/10.1016/j.rpped.2015.12.005

14. Shin JE, Jang H, Han JH, Park J, Kim SY, Kim YH, et al. Association between bronchopulmonary dysplasia and early respiratory morbidity in children with respiratory distress syndrome: a case-control study using nationwide data. Sci Rep [Internet]. 2022 [cited 2024 Jun 8];12(1):7578. Available from: https://www.nature.com/articles/s41598-022-11657-z DOI: https://doi.org/10.1038/s41598-022-11657-z

15. Um-Bergström P, Hallberg J, Pourbazargan M, Berggren-Broström E, Ferrara G, Eriksson MJ, et al. Pulmonary outcomes in adults with a history of Bronchopulmonary Dysplasia differ from patients with asthma. Respir Res [Internet]. 2019 [cited 2024 Jul 9];20(1):102. Available from: https://respiratory-research.biomedcentral.com/articles/10.1186/s12931-019-1075-1 DOI: https://doi.org/10.1186/s12931-019-1075-1

16. ThorpeAE, DonovanC, KimRY, Vindin H. Third-Hand Exposure to E-Cigarette Vapour Induces Pulmonary Effects in Mice. Toxics [Internet]. 2023[cited 2024 May 19];11(9):749. Available from: https://www.mdpi.com/2305-6304/11/9/749 DOI: https://doi.org/10.3390/toxics11090749

17. Tsentr hromads'koho zdorov'ia MOZ Ukrainy. Maizhe kozhen p'iatyi pidlitok «paryt'» e-syharety – dani doslidzhennia VOOZ [Almost every fifth teenager «vapes» e-cigarettes – WHO study] [Internet]. 2019 [tsytovano 2024 Cher 8]. Dostupno: https://phc.org.ua/news/mayzhe-kozhen-pyatiy-pidlitok-parit-e-sigareti-dani-doslidzhennya-vooz (in Ukrainian)

18. Auschwitz E, Almeda J, Andl CD. Mechanisms of E-Cigarette Vape-Induced Epithelial Cell Damage. Cells [Internet]. 2023 [cited 2024 Jul 1];12(21):2552. Available from: https://www.mdpi.com/2073-4409/12/21/2552 DOI: https://doi.org/10.3390/cells12212552

19. Tsai M, Byun MK, Shin J, Crotty Alexander LE. Effects of e-cigarettes and vaping devices on cardiac and pulmonary physiology. J Physiol. 2020;598(22):5039-62. DOI: https://doi.org/10.1113/jp279754

ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

20. Wang M, Huo Z, He X, Liu F, Liang J, Wu L, et al. The Role of MiR-29 in the Mechanism of Fibrosis. Mini Rev Med Chem. 2023;23(19):1846-58. DOI: https://doi.org/10.2174/1389557523666230328125031

21. Budakoti M, Panwar AS, Molpa D, Singh RK, Büsselberg D, Mishra AP, et al. Micro-RNA: The darkhorse of cancer. Cell Signal [Internet]. 2021 [cited 2024 May 17];83:109995. Available from: https://www.eurekaselect.com/article/130411 DOI: https://doi.org/10.2174/1389557523666230328125031

22. Liu G, Thannickal VJ. The Lung Likes the Little Fella miR-29. Am J Respir Cell Mol Biol. 2017;57(6):637-8. DOI: https://doi.org/10.1165/rcmb.2017-0266ed

23. Deng Z, He Y, Yang X, Shi H, Shi A, Lu L, et al. MicroRNA-29: A Crucial Player in Fibrotic Disease. Mol Diagn Ther. 2017;21(3):285-94. DOI: https://doi.org/10.1007/s40291-016-0253-9

24. Cushing L, Kuang P, Lü J. The role of miR-29 in pulmonary fibrosis. Biochem Cell Biol. 2015;93(2):109-18. DOI: https://doi.org/10.1139/bcb-2014-0095

25. Durrani-Kolarik S, Pool CA, Gray A, Heyob KM, Cismowski MJ, Pryhuber G, et al. miR-29b supplementation decreases expression of matrix proteins and improves alveolarization in mice exposed to maternal inflammation and neonatal hyperoxia. Am J Physiol Lung Cell Mol Physiol. 2017;313(2): L339-49. DOI: https://doi.org/10.1152/ajplung.00273.2016

26. Frangogiannis N. Transforming growth factor-β in tissue fibrosis. J Exp Med [Internet]. 2020 [cited 2024 Jun 7];217(3): e20190103. Available from: https://rupress.org/jem/article/217/3/e20190103/133821/Transforming-growth-factor-in-tissue-fibrosisTGF DOI: https://doi.org/10.1084/jem.20190103

27. Poniatowski ŁA, Wojdasiewicz P, Gasik R, Szukiewicz D. Transforming growth factor Beta family: insight into the role of growth factors in regulation of fracture healing biology and potential clinical applications. Mediators Inflamm [Internet]. 2015 [cited 2024 Jul 9];2015:137823. Available from: https://onlinelibrary.wiley.com/doi/10.1155/2015/137823 DOI: https://doi.org/10.1155/2015/137823

28. Caja L, Dituri F, Mancarella S, Caballero-Diaz D, Moustakas A, Giannelli G, et al. TGF-β and the Tissue Microenvironment: Relevance in Fibrosis and Cancer. Int J Mol Sci [Internet]. 2018 [cited 2024 May 16];19(5):1294. Available from: https://www.mdpi.com/1422-0067/19/5/1294 DOI: https://doi.org/10.3390/ijms19051294

29. He H, Butz A, Keet CA, Minkovitz CS, Hong X, Caruso DM, etal. Pretermbirthwithchildhoodasthma: Theroleofdegreeofprematurityandasthmadefinitions.Am J RespirCritCareMed.2015;192(4):520-3. DOI: https://doi.org/10.1164/rccm.201503-0522le

30. Collaco JM, McGrath-Morrow SA. Electronic Cigarettes: Exposureand Use Among Pediatric Populations. J Aerosol Med Pulm Drug Deliv. 2018;31(2):71-7. DOI: https://doi.org/10.1089/jamp.2017.1418

ДІАГНОСТИЧНІ КРИТЕРІЇ ТА ФАКТОРИ РИЗИКУ ЛЕГЕНЕВОГО ФІБРОЗУ У ПЕДІАТРИЧНИХ ПАЦІЄНТІВ З БРОНХІАЛЬНОЮ АСТМОЮ

Т.О. Крючко, Д. О. Климко

Полтавський державний медичний університет
(м. Полтава, Україна)

Резюме.

Діагностика легеневого фіброзу представляється надзвичайно актуальною проблемою, особливо в педіатричній практиці. Дані наукової літератури свідчать, що у педіатричних пацієнтів легеневий фіброз може бути ускладненням бронхіальної астми. Серед педіатричних пацієнтів на сьогоднішній день відмічається тенденція до постійного росту алергічних захворювань, зокрема бронхіальної астми. Не менш важливим аспектом являється поглиблене вивчення предикторів бронхіальної астми, до яких можна віднести дітей з глибокою недоношеністю в анамнезі. У свою чергу, недоношеність та мала вага при народженні є факторами ризику розвитку бронхолегеневої дисплазії. Численні клінічні дослідження неконтрольованого перебігу бронхіальної астми підтверджують необхідність вивчення впливу додаткових несприятливих чинників зовнішнього середовища, до яких можна віднести паління електронних систем. Незважаючи на те, що останніми роками проблема діагностики легеневого фіброзу у пацієнтів дорослої популяції набуває все більшої актуальності, залишається багато питань щодо доцільності вивчення даної проблеми у педіатричних пацієнтів.

Ключові слова: діти; бронхіальна астма; легеневий фіброз; недоношені діти, вейп, мікроРНК.

Contact Information:
Tetyana Kryuchko – MD, Professor, Head of the Department of Pediatrics № 2 of Poltava State Medical University (Poltava, Ukraine).
e-mail: drkryuchko@gmail.com
ORCID: https://orcid.org/0000-0002-5034-4181
ResearcherID: W-4506-2017
Scopus Author ID: 57194855000

Dariia Klymko, – assistant of Pediatrics № 2 of Poltava State Medical University (Poltava, Ukraine).
e-mail: dklimko0307@gmail.com.
ORCID: https://orcid.org/0000-0003-2981-5804

Контактна інформація:
Крючко Тетяна Олександрівна – доктор медичних наук, професор, завідувачка кафедри педіатрії № 2 Полтавського державного медичного університету (м. Полтава, Україна).
e-mail: drkryuchko@gmail.com
ORCID: https://orcid.org/0000-0002-5034-4181
ResearcherID: W-4506-2017
Scopus Author ID: 57194855000

Климко Дарія Олександрівна – асистентка кафедри педіатрії № 2 Полтавського державного медичного університету (м. Полтава, Україна).
e-mail: dklimko0307@gmail.com.
ORCID: https://orcid.org/0000-0003-2981-5804

Received for editorial office on 27/07/2024
Signed for printing on 15/09/2024