The American Journal of Medical Sciences and Pharmaceutical Research
(ISSN – 2689-1026)
Published: May 31, 2021 | **Pages:** 51-57
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue05-09

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

Genetic Predisposition To Out-Of-Hospital Pneumonia In Children: A Modern Interpretation Of The Problem

Karimjonov I.A.
Doctor Of Medical Sciences, Professor, Tashkent Medical Academy, Uzbekistan

Fayzieva U.R.
Candidate Of Medical Sciences, Associate Professor, Termez Branch Of The Tashkent Medical Academy, Uzbekistan

ABSTRACT

The article provides a review of the literature devoted to modern data, as well as the impact of genetic predisposition on the development of pneumonia in children. It is known that timely, innovative diagnosis, treatment and prevention of pneumonia in children today is one of the most pressing problems in pediatrics. Timely identification of the etiological cause of pneumonia, treatment is carried out only by early diagnosis, adequate assessment of the severity of the patient's condition, reasonable choice of treatment with antibiotics, taking into account the background disease, age and weight of the child.

KEYWORDS

Children, pneumonia, genes, predisposition, prevention.

INTRODUCTION

Today, the achievements of molecular genetics are very effectively used by clinicians in such branches of medicine as oncology, surgery, transplantology, psychiatry, pediatrics, pulmonology, etc. processes and the creation

The American Journal of Medical Sciences and Pharmaceutical Research
(ISSN – 2689-1026)
Published: May 31, 2021 | **Pages:** 51-57
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue05-09

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

of predictive models and verification of criteria for the effectiveness of treatment of diseases.

The scientific work identified three polymorphic markers in the genes CYP1A1, GSTM1 and ACE, associated with the development and course of acute community-acquired pneumonia. Allelic variants of these genes can affect the risk of the disease and its complications both by themselves, due to a change in the activity of the enzymes encoded by them, and as a result of linkage with other, as yet unknown, loci. Genetic polymorphism is the presence in a population of different variants of the same gene of an allele. In this case, an allele can be considered polymorphism if the frequency of its occurrence in the population is less than 1%. Alleles occurring less often are called mutations. The structure and activity of the protein products of the gene depend on the allele variant. It is believed that approximately 30% of the genes encoding are polymorphic. The rapid accumulation of knowledge about the genetic basis of many pathological processes enriches the understanding of the etiology and pathogenesis of common human diseases, significantly increases the possibilities of their diagnosis [1, p. 63; 2, pp. 203-206; 3, pp. 5-12; 4, pp. 24-38; 5].

THE MAIN FINDINGS AND RESULTS

Along with the widespread increase in morbidity, mortality rates persist, the number of complicated and protracted forms of acute pulmonary inflammation is increasing. In the structure of mortality, pneumonia is one of the ten most common causes of death, and among infectious diseases it ranks first. The clinical picture of community-acquired pneumonia is characterized by a wide variety: from little or no symptoms to fulminant forms with the development of infectious-toxic or septic shock. In addition to the properties of the pathogen itself, its virulence and pathogenicity, the onset and course of pneumonia is influenced by the body's ability to resist infection. Toll-like receptors are proteins that recognize conservative patterns of microbial structures. One of them, toll-like receptor 9 (TLR9), is a cytoplasmic protein that ensures the functioning of innate immunity. By recognizing GC-rich DNA regions, TLR9 triggers signaling pathways leading to the production of the Stat3 signaling protein, pro-inflammatory cytokines such as interferons, TNFa (tumor necrosis factor alpha), and interleukins: IL-12, IL-1β, IL-6 and etc.

One of the variants of SNP rs352162 (52218953T> C) of the TLR9 gene, namely TLR9 52218953T> C CC, is associated with an increased production of the proinflammatory cytokine TNFa by leukocytes in response to GC-rich bacterial DNA. Prospective studies include: determination of polymorphism of single nucleotides and other variants of the human genome at the level of individual candidate genes and genome-wide scanning to identify regions of chromosomes with genetic markers of diseases or traits [6, p. 243; 7, pp. 5-12; 8, p. 243; 9, p. 41]. The main goal of the genetic study of patients with acute lung injury (ALI) and ARDS is to explain the fact that not all patients in critical conditions (trauma, sepsis) have a detailed clinical and laboratory picture of lung damage, while the action of the risk factor is approximately the same in its strength and duration.

Currently, cytogenetic research methods for the diagnosis of respiratory diseases are aimed primarily at detecting malignant neoplasms, which is dictated by the presence of a high level of chromosomal imbalance accompanying the development of the tumor process [10, pp. 46–55; 11, pp. 188–193; 12, pp. 67-68; 13, pp. 71-73]. At the same time, the high frequency of infectious diseases of the respiratory system, the mortality rate not decreasing in them, is a strong argument for carrying out genetic

The American Journal of Medical Sciences and Pharmaceutical Research
(ISSN – 2689-1026)
Published: May 31, 2021 | **Pages:** 51-57
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue05-09

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

studies in patients with pneumonia, which is a multifactorial disease. Advances in immunology and molecular biology indicate the important role of immune activation and systemic inflammation in the pathogenesis and course of human diseases. According to the WHO, pneumonia is the leading cause of infant mortality worldwide. Among the causes of mortality in children under 5 years of age, her share accounts for 17.5%, which is about 1.1 million deaths annually in the world (this is more than AIDS, malaria and measles taken together).

Thus, the use of molecular genetic tests expands the possibilities of early diagnosis of pneumonia, allows the development of new highly sensitive and accurate criteria for the effectiveness of pathogenetic treatment, and, ultimately, can significantly increase the effectiveness of specialized care, reduce the cost of treatment and examination of this category of patients. Thus, it can be assumed that the development of pathological changes in pneumonia is determined not only by the presence of foci of impaired lung parenchyma function, exudative-destructive and proliferative inflammation, but by a complex of other additional factors. It is possible that an imbalance in the system of anti-inflammatory cytokines of systemic and local origin may be involved in the pathology of the bronchopulmonary system.

The data obtained show that for more effective treatment of patients with pneumonia of various origins, new technologies should be used - medical genetic research. The obtained results of the study can be used as the basis for the development of screening programs to identify persons with an increased risk of developing pneumonia. Thus, the changing profile of low molecular weight phenolic compounds in human blood serum reflects, according to the authors, the existence of poorly studied molecular mechanisms of interaction of cells and tissues of the host organism with its microflora and, probably, plays a role in the development and outcome of critical conditions, which requires further study [14, pp. 61-62; 15, pp. 5-11; 16].

According to the classification adopted in Russia, pneumonia is defined as an acute infectious disease of the pulmonary parenchyma, diagnosed by the syndrome of respiratory disorders and / or physical data in the presence of focal or infiltrative changes on the radiograph. The presence of radiological signs of damage to the pulmonary parenchyma, according to WHO, is the gold standard of diagnosis, since it allows excluding from the range of diseases defined as pneumonia, viral lesions of the lower respiratory tract that do not require antibacterial treatment. The most important classification feature of pneumonia is where it occurs. Community-acquired pneumonia occurs in a child in the normal conditions of his life, nosocomial pneumonia - after 72 hours of stay at a hundred lives, nosocomial - after 72 hours of hospital stay or within 72 hours after discharge from there [17, 18, 19].

According to A. Bakhodirova and other authors (2017), issues of timely diagnosis, treatment and prevention of nosocomial pneumonia are in the focus of attention of doctors and researchers due to the significant prevalence. Nosocomial pulmonary infection ranks second in prevalence after community-acquired pneumonia, but significantly exceeds it in terms of mortality.

According to Aliev A.L., Turaev B.B. et al (2016), the combination of pneumonia with various other diseases is the cause of the unfavorable interaction of various sufferings, not only aggravates their course, but also worsens the prognosis. The effectiveness of the treatment of pneumonia developing against the background of another disease depends on

The American Journal of Medical Sciences and Pharmaceutical Research
(ISSN – 2689-1026)
Published: May 31, 2021 | **Pages:** 51-57
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue05-09

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

how expediently the entire complex of therapeutic measures is built, aimed at combating the entire pathology of the child's body. And also from the individual choice of therapy, taking into account the etiology of the disease, the course and phase of the pathological process, the patient's age, and the degree of extra-pulmonary pathologies of the body.

According to literature data, viral pneumonia has also been frequently encountered in recent years. Pneumonia of viral etiology in children is more difficult than bacterial pneumonia. Of particular danger are diseases of the lower respiratory tract of infectious etiology. These include pneumonia and bronchiolitis. Infectious pneumonia is a dangerous lower respiratory tract disease that can be fatal in children. Until now, the persisting high level of morbidity and mortality determines the urgency of the problem. The state of the immune system plays a leading role in the development, clinical course and outcome of pneumonia in children. The increase in the incidence of nosocomial pneumonia, along with dynamic changes in reactivity and immune response in children, dictates the need to study the immunological aspects of the pathogenesis of nosocomial pneumonia to optimize the diagnosis, prevention and treatment of this disease [20, p. 70; 21].

Immunological diagnostic methods are aimed at detecting the bacterial antigen and / or antibodies of the pathogen.

The genes of the bacteria Enterobacteriaceae, KlebsiellapneumoniaCarbapenemase, and Pseudomonasaeruginosa carry the determinants of resistance to other ABP classes - aminoglycosides and fluoroquinolones.

Thus, the literature data obtained allows us to study in detail the study of the dynamics of the incidence of pneumonia in children, as well as to obtain new statistical data on the characteristics of the growth of pneumonia and a significant excess of the regional level, on the high proportion of children with impaired resistance and mixed viral-bacterial etiology, as well as gene polymorphism in the formation of diseases; it is proposed to supplement the standard recommendations for the diagnosis and rehabilitation of young children.

CONCLUSIONS

1. Timely detection of the disease requires more in-depth development and implementation of active measures for primary and secondary prevention of diseases, as well as the rehabilitation of children.
2. With the timely identification of the implementation of risk factors in community-acquired pneumonia in children, the increase in the incidence of community-acquired pneumonia is studied.
3. Currently, the identification of phenotypes and gene polymorphisms in community-acquired pneumonia in children are coming to the fore, which form the immunodeficiency state.
4. To develop a scientifically grounded set of measures to reduce the health losses of the child population from pneumonia and their complications, it is necessary to study the genetic aspects of the disease.
5. The modern substantiation of the tactics of managing the period of convalescence after the transferred community-acquired pneumonia remains relevant.

REFERENCES

1. Community-acquired pneumonia in children: prevalence, diagnosis, treatment

Published: May 31, 2021 | **Pages:** 51-57
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue05-09

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

and prevention. Scientific and practical program. – Moscow: 2011. – p. 63. (Внебольничная пневмония у детей: распространенность, диагностика, лечение и профилактика. Научно-практическая программа. М., 2011. 63 с.)

2. Morbidity and mortality from community-acquired pneumonia in children and adolescents living in Kuzbass//Pediatrics. Lyutina E.I., Manerov F.K2015. No 2. – pp. 203–206. (Заболеваемость и смертность от внебольничной пневмонии у детей и подростков, проживающих в Кузбассе// Педиатрия. Лютина Е. И., Манеров Ф. К2015. № 2. С. 203–206.)
3. Genetics and Critical Care Medicine: From Theory to Practice. V. V. Moroz, T. V. Smelaya, Research Institute of General Reanimatology named after V.V. V.A.Negovsky. Russian Academy of Medical Sciences, Moscow. Institute of General Genetics. VN Vavilova Russian Academy of Sciences. – Moscow: 2012. – pp. 5-12. (Генетика и медицина критических состояний: от теории к практике. В. В. Мороз, Т. В. Смелая, НИИ общей реаниматологии им. В. А. Неговского РАМН, Москва. Институт общей генетики им. В. Н. Вавилова РАН, Москва. 2012г.С.-5-12.)
4. Molecular genetic markers of nosocomial pneumonia and acute respiratory distress syndrome. T. V. Bold, A. N. Kuzovlev. GENERAL REANIMATOLOGY, 2015, 11; - pp. 24-38. (Молекулярногенетические маркеры нозокомиальной пневмонии и острого респираторного дистресс синдрома. Т. В. Смелая, А. Н. Кузовлев. GENERAL REANIMATOLOGY, 2015, 11; С.-24-38.)
5. Baranov V. S., Baranova E. V., Ivaschenko T. E., Aseev M. V. Human genome and genes of "predisposition". Introduction to Predictive Medicine. – Saint Petersburg: Intermedica; 2000. (Баранов В. С., Баранова Е. В., Иващенко Т. Э., Асеев М. В. Геном человека и гены «предрасположенности». Введение в предиктивную медицину. СПб.: Интермедика; 2000.)
6. Sukhanov V.A., Piruzyan L.A. (2009) Pharmacogenetic problems in medicine. – Moscow: Medicine. – p. 243. (Суханов В. А., Пирузян Л. А. Фармакогенетические проблемы в ме дицине. М.: Медицина; 2009. 243.)
7. Genetics and Critical Care Medicine: From Theory to Practice. V. V. Moroz, T. V. Smelaya, Research Institute of General Reanimatology named after V.V. V.A.Negovsky. Russian Academy of Medical Sciences. – Moscow: Institute of General Genetics. V.N. Vavilov. Russian Academy of Sciences, Moscow. 2012 S.-5-12. (Генетика и медицина критических состояний: от теории к практике. В. В. Мороз, Т. В. Смелая, НИИ общей реаниматологии им. В. А. Неговского РАМН, Москва. Институт общей генетики им. В. Н. Вавилова РАН, Москва. 2012г.С.-5-12.)
8. Sukhanov V.A., Piruzyan L.A. (2009) Pharmacogenetic problems in medicine. - Moscow: Medicine. – p. 243. (Суханов В. А., Пирузян Л. А. Фармакогенетические проблемы в ме дицине. М.: Медицина; 2009. 243.)
9. Kholodok G.N. (2012) Microbiological and pathogenetic aspects of community-acquired pneumonia in children: author. Diss. Doctor of Medical Sciences. – Moscow: - p. 41. (Холодок Г. Н. Микробиологические и патогенетические аспекты внебольничной пневмонии у детей: автореф. дис. докт. мед.наук. Москва, 2012. 41 с.)
10. Spichak T.V., Katosova L.K., Yatsyshina S.B., et al. (2014) A critical look at the results of laboratory diagnostics of

Published: May 31, 2021 | **Pages:** 51-57
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue05-09

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

community-acquired pneumonia of mycoplasma etiology in children. Pediatrics. 93 (3): - pp. 46–55. (Спичак Т. В., Катосова Л. К., Яцышина С. Б., и соав. Критический взгляд на результаты лабораторной диагностики внебольничной пневмонии микоплазменной этиологии у детей. Педиатрия 2014; 93(3): 46–55.)

11. Geppe N.A., Malakhov A.B., Volkov I.K. et al. (2014) On the further development of the scientific and practical program for community-acquired pneumonia in children // Russian medical journal. Vol. 22. No. 3. – pp. 188–193. (Геппе Н. А., Малахов А. Б., Волков И. К. и соав. К вопросу о дальнейшем развитии научно-практической программы по внебольничной пневмонии у детей // Русский медицинский журнал. 2014. Т. 22. № 3. С. 188–193.)
12. Risk factors and features of the course of complicated pneumonia in children with hypoimmune conditions. A.N.Bakhodirova, H.P. Alimova, T.L. Kim. Herald of Emergency Medicine, 2013, No 2. – pp. 67-68. (Факторы риска и особенности течения осложненных пневмоний у детей с гипоиммунными состояниями. А.Н.Баходирова, Х.П.Алимова, Т.Л.Ким. Вестник экстренной медицины, 2013, № 2, стр-67-68.)
13. Some indicators of the immune status in nosocomial pneumonia in children. A.N.Bakhodirova., N.A. Akbarova. / Bulletin of emergency medicine. 2013, No 2. – pp. 71-73. (Некоторые показатели иммунного статуса при нозокомиальных пневмониях у детей. А.Н.Баходирова., Н.А.Акбарова. /Вестник экстренной медицины. 2013, № 2, стр-71-73.)
14. Features of the clinical course of pneumonia in combination with other diseases. Aliev A.L.1, Turaev B. B. 2, Turaeva Yu.Sh. / Bulletin of emergency medicine. 2012. No 1. – pp. 61-62. (Особенности клинического течения пневмонии при сочетании с другими заболеваниями. Алиев А. Л.1, Тураев Б. Б.2, Тураева Ю.Ш./Вестник экстренной медицины, 2012, № 1, стр-61-62.)
15. Salnikova L.E., Brave T.V., Moroz V.V. et al. (2010) Genetic predisposition to the development of acute community-acquired pneumonia. General Reanimatology; VI (1): - pp. 5-11. (Сальникова Л. Е., Смелая Т. В., Мороз В. В. и соавт. Генетическая предрасположенность к развитию острой внебольничной пневмонии. Общая реаниматология 2010; VI (1): 5—11.)
16. RuuskanenO. Viralpneumonia / RuuskanenO., LahtiE., JenningsL. S. // Lancet 377 (9773): 1264-75. 2011 -04-09.
17. Rudan I., O'Brien K.L., Nair H., et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries // J. Glob.Health. 2013. Vol. 3. № 1 — 010401.
18. Mayanskiy N., Alyabieva N., Ponomarenko O., et al. Serotype distribution and antibiotic-resistance of paediatric Streptococcus pneumoniae in Moscow. ECCMID 2014. P2173.
19. Lodha R., Kabra S. K., Pandey R. M. Antibiotics for community-acquired pneumonia in children // Cochrane Database Syst. Rev. 2013. Vol. 4.№ 6. CD004874.
20. Wang K., Shun-Shin M., Gill P., et al. Neuraminidase inhibitors for preventing and treating influenza in children (published trials only) // Cochrane DatabaseSyst. Rev., 2012.70 p.
21. Belopolskaya O.B., Smelaya T.V., Moroz V.V., Golubev A.M., Salnikova L.E. Clinical associations of host genetic variations in

Published: May 31, 2021 | **Pages:** 51-57
Doi: https://doi.org/10.37547/TAJMSPR/Volume03Issue05-09

IMPACT FACTOR
2021: 5. 64
OCLC - 1121105510

the genes of cytokines in critically ill patients. Clin. Exp. Immunol. 2015; 180 (3): 531-541. http://dx.doi.org/10.1111/cei.12592. PMID: 25619315.