Etiological Characteristics of Bronchopulmonary Pathology in Children, Taking into Account the Microbiota of the Lungs and Intestines

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Abstract: The intestinal microbiota is known to influence local immune homeostasis in the intestine and shape the developing immune system towards elimination of pathogens and tolerance to self-antigens. Although the lungs have long been considered sterile, recent evidence using sequencing techniques has confirmed that the lower respiratory tract has its own local microbiota. Since then, there has been increasing evidence that local respiratory and intestinal microbiota play a role in acute and chronic lung disease in children.

Keywords: Respiratory Syndrome infection, causative agents, synobiotic describes, Bacteriological examination, Bronchopulmonary pathologies.

Introduction

The development of the human intestinal microbiota and its impact on health and disease is one of the most studied topics of the last decade. Every human mucosal surface is populated by a more or less complex and diverse microbiota that represents a key player informing immune homeostasis. The fact that the count of bacterial cells outnumbers human cells within our body (1–10:1) further stresses the importance of the microbiome [1]. In animal models using germ-free mice, it was shown that a complete lack of commensal bacteria results in reduced viability due to impaired immune defence against pathogens and increased autoimmunity [2,3].

The individual composition of the microbiota is determined by endogenous (e.g., host genotype) and exogenous (mode of delivery, antibiotic exposure, diet) factors. Once established, the individual composition of the microbiota as well as its metabolic pathways remain stable [4]. The intestinal microbiota is the most studied part of the human microbiome, as it harbours the majority of bacteria and can be investigated by non-invasive sample collection using feces. Furthermore, the intestinal microbiota can be modified by several mechanisms including pre-, post-, and synbiotics. Prebiotics are non-digestive short chain carbohydrates that promote growth and/or activity of beneficial bacteria, whereas probiotics are defined according to the World Health Organization (WHO) as "live microorganisms which when administered in adequate amounts confer a health benefit on the host"

[5]. The term "synbiotic" describes the combination with a prebiotic that specifically favors the accompanying probiotic.

However, next generation sequencing techniques have been applied more and more in these field and enabled researchers to study the microbiome of organs (i.e., the lung) with minor bacterial colonization. It further led to the identification of many bacteria that cannot be cultivated, resulting in a much more detailed and complex image of the human microbiota. There is growing evidence that the respiratory microbiota is altered in human lung diseases. Whether this is a cause or a consequence cannot always be clearly determined, but in some cases, lung dysbiosis was found to be associated with worse disease outcome.

In addition, the intestinal microbiota plays a role in respiratory diseases, as intestinal dysbiosis in early infancy was shown to increase the risk of pulmonary infections and childhood asthma [6]. The inter-organ cross talk between the gut and the lung was named the "gut–lung axis", and knowledge about the underlying mechanisms such as production of short chain fatty acids (SCFA) and signaling through Toll-like receptors (TLR) by the intestinal microbiota has grown recently [7].

Materials and methods

To solve the tasks, during 2017-2020, studies were conducted on the basis of the Department of Hospital Pediatrics №2 of Tashkent Pediatric Medical Institute. We examined 37 children in early age with acute pneumonia and acute bronchitis. All children underwent inpatient treatment in the departments of pathology of young children and pulmonary departments of the TashPMI clinic.

All children were divided into 2 groups:

1. 1st group (experimental group) consisted of children with bronchopulmonary pathology.

2. 2nd group (control group) consisted of children who were conditionally healthy.

The majority of the examined patients were children with pneumonia (59%), in a smaller percentage of cases acute bronchitis (41%).

Boys prevailed among children with acute pneumonia (60%), while among children with acute bronchitis there were more girls (68,18%).

Among children with acute pneumonia, the majority were children under one year old (46,66%), the lowest among these children was among 2-year-old children (6,66%), while among children with acute bronchitis, the highest rate was found in children of 2 years old (31,81%), and children of 3 years old made up the smaller part of this group (9,09%)

All patients were observed by:

1. Objective research methods: assessment of the general condition, examination, percussion to determine the boundaries of the lungs.

2. Laboratory research methods: general clinical tests: blood. Bacterial culture of feces, pharynx and nose.

3. Instrumental research methods: chest x-ray, bronchoscopy.

Results and discussions

According to the objectives, to determine the determinants of health that contribute to the development of bronchopulmonary diseases in children, we studied the anamnestic factors that contribute to the development of bronchopulmonary pathologies in young children (Fig 1).
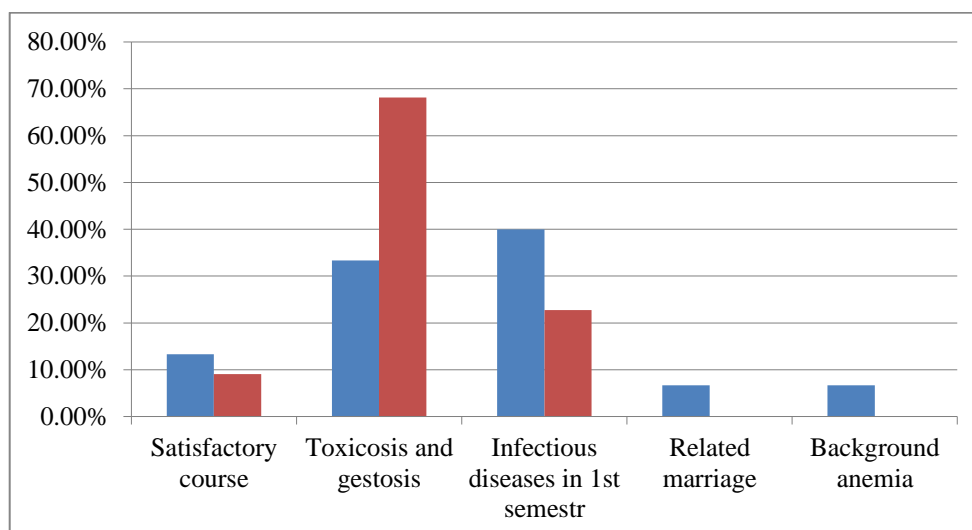
Fig.1. Pregnancy period.

Causes of bronchopulmonary pathologies in children is mostly related to the health of a mother including toxicosis and gestosis, nutritional micronutrient deficiencies, infectious diseases and anemia during pregnancy [1].

The diagram (Fig 1) shows that in the first group, the most influential in the development of bronchopulmonary diseases is the frequent infectious diseases of the mother in the 1st trimester (40%), toxicosis and gestosis take the second place, making up (33.33%), the lowest indicator in this group, related marriages and anemia of pregnant woman during pregnancy are reported, making up the same figures (6.66%). The second group is dominated by toxicosis and gestosis of the mother during pregnancy, accounting for (68.18%), unlike the first group, related marriages and anemia of pregnant women were not registered.

During the examination of children, in addition to the period of mother's pregnancy, attention was paid to the premorbid background of the child, complaints, clinical data, laboratory data, treatment and the course of the preoperative period.

Premorbid diseases in children with bronchopulmonary pathologies are still relevant, as they complicate their course [8]. According to a number of researchers, mainly young children die from complications of premorbid pathology (11.3 per 100 thousand children born alive) [10]. To assess the background diseases, we took the most common diseases in the figure (Fig 2).
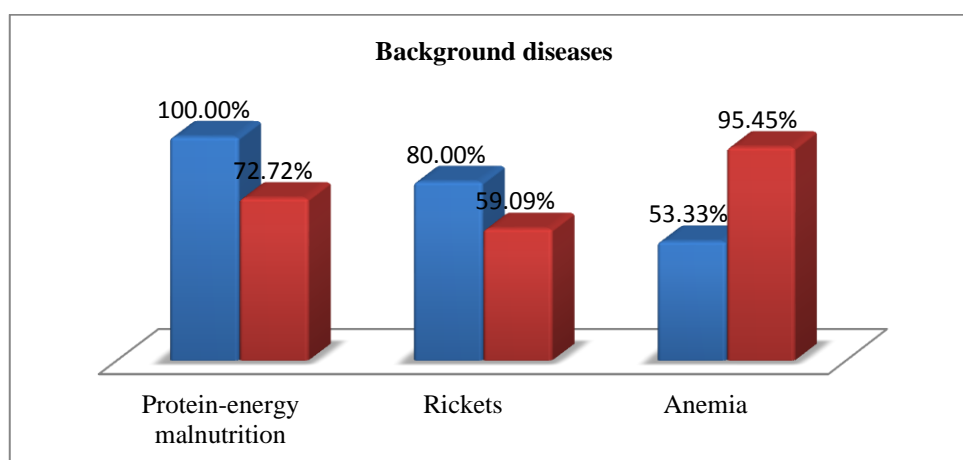
Fig.2. Background diseases.

As the graph shows, in the bronchopulmonary disease group, protein-energy malnutrition (PEM) was found to varying degrees in all 15 (100%) children of this group. Rickets in varying degrees occurred in 12 (80%) children, when anemia was registered in 8 (53.33%) children showing the lowest numbers. In the second group, anemia of varying degrees occurred in 21 (95.45%) children, showing the highest numbers in this group. PEM in this group was found in 16 (72.72%) children, and rickets in different degrees, as a background disease showed the lowest numbers, occurring in 13 (59.13%) children.

Table 3. Results of bacteriological culture of the pharynx and nose.

	Pathogens	**1 group** **n=15**		**2 group** **n=22**	
		n	**%**	**n**	**%**
1.	Streptococcus pneumoniae	10	66.66%	8	36.36%
2.	Staphylococcus aureus	3	20%	5	22.72%
3.	Streptococcus agalactiae	1	6.66%	3	13.63%
4.	H.influenzae	1	6.66%	4	18.18%
5.	Chlamydia trachomatis	-		2	9.09%

Bacteriological examination of the oropharynx and nose, carried out according to indications in patients of the experimental group, revealed that among the causative agents of acute pneumonia, causative agents from the group Streptococcus pneumoniae prevailed, as they were found in 10 (66.66%); among the children of the control group, bacteria from the Streptococcus pneumoniae group also prevailed, and were registered in 8 (36.36%) children. The rarest causative agents of acute pneumonia in the first group were Streptococcus agalactiae 1 (6.66%) and H. influenzae 1 (6.66%). And in the second group, they turned out to be bacteria from the Chlamydia trachomatis group, which were found in 2 (9.09%) children.

Respiratory Infection. Respiratory infection is the most common infectious disease and is a leading cause of morbidity and mortality worldwide. The gut commensal microbiotaprovides essential benefits to pulmonary mucosal immunity and plays protective roles in respiratory infection by distally driving host responses to pneumonia [8]. Depletion or absence of the gut microbiota is believed to influence the host immune response. Schuijt et al. found that microbiota-depleted mice showed increased bacterialdissemination, inflammation, organ damage, and mortality compared with control mice, and FMT reversed the gut microbiota diversity and enhanced the host defense against pneumonia [9]. In addition, the gut microbiota differed between patients with respiratory infection and HCs. It was reported that certain gut microbiota, such as Enterococcaceae, was associated with community-acquired pneumonia (CAP) [10]. Many studies have suggested that oral administration of probiotics can not only protect against bacterial pneumonia [11] but also contribute to accelerated recovery from respiratory viral infection [12, 15], further emphasizing the crucial role of the gut microbiota in respiratory infection.

Conclusions

1. In the first group, the most influential in the development of bronchopulmonary pathology is the frequent infectious diseases of the mother in the 1st trimester (40%). In the second group the dominated feature was toxicosis and gestosis of the mother during pregnancy, accounting for (68.18%).

2. Protein-energy deficiency is the most common premorbid pathology in bronchopulmonary diseases.

3. In the development of simple congenital heart defects, toxicosis and gestosis were the dominant pathology.

4. The features of the bacterial spectrum of acute pneumonia in young children with bronchopulmonary pathology consisted in the fact that Streptococcus pneumoniae was two times more likely to become the causative agent of the disease and amounted to 67%, in 20% of cases the causative agent was Staphylococcus aureus.

5. Increasing evidence suggests an important and complex between the gut and lung, as well as between the gut microbiota and host immunity. Gut microbial dysbiosis is believed to be associated with the etiology or/and development of common respiratory diseases, such as acute pneumonia and acute brochitis. To date, the understanding of the mechanism involving the gut-lung axis is still in its infancy and remains to be further elucidated.

6. Future research into modification and improvement of the gut microbiota and into the balance of gut and lung immunity through diet, probiotics, and FMT is necessary to improve our understanding of the role of gut microbiota in the lung and to provide effective and new therapeutic strategies for respiratory diseases.

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