



PROGNOSTICALLY SIGNIFICANT RISK FACTORS FOR BRONCHIAL ASTHMA IN CHILDREN WITH BRONCHOOBSTRUCTIVE SYNDROME

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Article history:	Abstract:
Received: 2 th April 2021	A long-term prospective observation of children who underwent repeated episodes of bronchial obstruction at an early age was carried out. The structure of diseases occurring with broncho-obstructive syndrome, diagnostic criteria for differential diagnosis have been determined. It has been shown that the main clinical criteria for the transformation of diseases of ongoing biofeedback into bronchial asthma are the presence of a hereditary predisposition for allergic and bronchopulmonary diseases, TM and DST in history, their combination with low CD95, g-INF and high IL-4 and IgE values.
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RELEVANCE.

Bronchoobstructive syndrome (BOS) is quite common in infant pathology (30-35%), but to date there are no unified approaches to the differential diagnosis of bronchoobstructive syndrome, interpretation of its pathogenesis, prognosis and treatment assessment [3,12,15,16].

(BOS is not a stand-alone nosological form and may be associated with many pathological conditions, and the same bronchoobstruction may be due to different diseases. All children with (BOS) require a comprehensive evaluation to identify the underlying disease and to provide timely differential treatment [1,2,9,10,11]. The literature on the characteristics of immunological reactivity in children with bronchoobstructive syndrome is inconsistent. An in-depth assessment of the immunological status of young children with respiratory pathology has been initiated, but the available studies reflect only the features of individual parts of the immune system.

In view of the above, studying how to improve the detection and medical care of children with bronchial asthma, as well as carrying out preventive measures to prevent the transformation (BOS) into bronchial asthma, is now a major medical and social problem.

PURPOSE OF THE STUDY:

To examine the clinical and anamnestic parameters in children with bronchoobstructive syndrome and to identify prognostically relevant risk factors for the transformation of the disease into bronchial asthma.

MATERIALS AND METHODS OF RESEARCH

To solve the tasks set in the work 284 children aged 7 to 14 years old were examined.

The study group included children who had repeatedly had respiratory diseases with obstructive syndrome (acute respiratory infections, ARI, SARS pneumonia) at an early age. 230 children were selected in outpatient clinics, and the remaining 54 children were followed up for a long time in children's disease clinics of the Tashkent Medical Academy with a verified diagnosis of obstructive bronchitis, recurrent obstructive bronchitis, and bronchial asthma.

The work was carried out in two stages. Stage I involved a retrospective study of the developmental histories of children (form 112/u) who had been in the dispensary for recurrent respiratory diseases with (BOS) at an early age.

At stage II, a thorough clinical and laboratory examination of the selected cohort of children was carried out.

The clinical examination involved the collection of anamnestic data, including maternal obstetric history, hereditary predisposition to certain diseases, life history of the child, past medical history, allergic history, premorbid background of the child and assessment of general condition at the time of the examination.

The history of the first episode of obstruction, at what age it appeared, its duration, the dynamics of the disease, how many times before the age of 3 the child was hospitalised for bronchial obstruction, what treatment he received, and whether rehabilitation measures were taken.

All children were divided into 3 groups as a result of a thorough examination:

Group 1 - 33 children with a verified diagnosis of atopic bronchial asthma;

Group 2 - 113 children with airway hyperresponsiveness in the absence of bronchial obstruction symptoms;

Group 3 - 138 "conditionally healthy" children at the time of examination (no chronic bronchopulmonary disease).

Table 1 shows the sex characteristics of the children observed. As can be seen from Table 1, while Group 1 was dominated by girls (54.5%), Group 2 and 3 were dominated by boys (60.1% and 60.8% respectively).

During the study of child development histories we paid attention to the structure (BOS) .

Table 1
Gender characteristics of the children surveyed

Gender	Group 1 n=33	Group 2 n=113	Group 3 n=138
Boys	<u>15</u> 45,5	<u>68</u> 60,2	<u>84</u> 60,8
Girls	<u>18</u> 54,5	<u>45</u> 39,8	<u>54</u> 39,2

*In numerator - abs, in denominator - % of value

It was found that 54.3% of children were diagnosed with AOB, 21.6% of children had pneumonia with obstructive syndrome, 12.4% of children had ARI with obstructive syndrome and 11.7% had recurrent obstructive bronchitis.

In all children observed the debut of the disease was accompanied by a catarrhal syndrome, moderately pronounced symptoms of intoxication, subfebrile body temperature, and cough. On 3-5 days from the beginning of the disease symptoms of bronchial obstruction appeared as moderate expiratory dyspnea, increased cough, "oral crepitations". The duration (BOS) ranged from 5 to 14 days. The anamnestic history showed that shortly after discharge, the children presented with moderate BOS without significant impairment. The standard conservative therapy was ineffective, and the children did not have clinical remission of the disease. The inpatients received similar treatment including antibiotics, mucolytics and physiotherapy. After successful management of SLE, children were discharged from the hospital. However, a short time later (2-3 weeks after discharge), children were hospitalized again for increased symptoms of bronchial asthma.

Allergological examination included determination of total serum IgE levels by enzyme immunoassay. The peak flowmetry was carried out according to the conventional method. The obtained data were compared with the proper values corresponding to the age, sex and height of the examinee or with the individual best PSV value.

Standard (MS Excel2002, Statistica 6.0) and specially designed programs were used for statistical calculations. Pearson's correlation analysis and discriminant analysis were applied. Differences were assessed by Student's t-test. The following significance levels were adopted to assess the statistical validity of the results obtained: p<0.001, p<0.01 p<0.05. All studies were conducted with parental consent and participation.

RESULTS AND DISCUSSION

One of the objectives of our study was to develop a principle for identifying children at increased risk of bronchial asthma based on exogenous and endogenous factors. To this end, we retrospectively evaluated the anamnestic data, which included the features of intrauterine development, premorbid background, hereditary predisposition, the first clinical manifestations of bronchial obstruction, and the further dynamics of the disease. The clinical and anamnestic findings were compared in groups of children with bronchial asthma, with airway hyperresponsiveness with no symptoms of bronchial obstruction, and currently healthy children who suffered recurrent attacks of bronchial obstruction at an early age.

We selected what we thought were the most informative features from our examination of the children's history and from discussion with parents (Table 2)

Table 2
Clinical and anamnestic findings of the children examined (%)

Signs	Group 1 n=33	Group 2 n=113	Group 3 n=138
Childbirth: - first	60,6 27,2 12,2	55,75 41,59 2,65	58,7 40,58 0,72
- second	63,6 27,2	54,8 12,3	23,1 13,1
-thirdormore	33,0	46,3	18,0
Gestosis: firsthalf	66,7 30,3	10,6 49,56	2,17 42,75

	3,03	38,9	15,07
secondhalf	87,8	58,41	21,04
Asphyxiainchildbirth	69,6	58,4	21,01
Hereditaryburden:	-	9,7	28,2
- Allergicdiseases	63,6	52,2	39,1
-Bronchopulmonarypathology	78,7	56,6	27,5
-cardiovascular diseases	33,3	15,9	3,6
ECD	45,4	21,2	7,9
Paratrophy of the first degree	30,3	7,7	-
Hypotrophy of the first degree			
	39,4	21,2	17,4
	12,12	15,9	14,5
	15,15	31,8	16,2
	33,3	30,9	31,8
Anaemia of I-II degree			
	42,4	49,5	58,7
	21,2	8,8	2,1
	36,4	41,6	39,13
PEP			
	81,8	33,6	20,2
	18,2	66,3	79,7
DST			
	15,15	97,3	99,2
	84,85	2,65	0,72
Timomegaly (TM)	60,6	9,4	-
Combination of DST and TM	12,12	7,1	-
Allergiesin a child:	36,3	63,7	-
-food	30,3	10,6	-
-insectallergies	48,4	42,4	23,9

As can be seen from Table 2, the data in the compared groups differed in many respects. We focused on children in groups 1 and 2, as children in group 3 were considered "conditionally healthy" at the time of the examination.

18 children of the 1st group (54.5%) were under our observation for a long time and were diagnosed with AD. 15 children were registered in the dispensary with the diagnosis of recurrent obstructive bronchitis. Subsequently, on the basis of clinical and laboratory data we made a provisional diagnosis of AD, atopic form.

Group 2 consisted of children with bronchial hyperresponsiveness and no symptoms of bronchial obstruction. These children were considered conditionally healthy at the time of examination and were not observed in the dispensary group. We diagnosed GDM in these children by PSV after exercise.

The examination of anamnestic data revealed that 60.6% of group 1 children and 55.75% of group 2 children had their first pregnancy and first birth. In the majority of cases the mothers had first half gestosis (63.6% and 54.8% respectively).

18 children in group 1 (54.5%) had been under long-term observation and had been diagnosed with BA. Fifteen children were under outpatient care with a diagnosis of recurrent obstructive bronchitis. Subsequently, based on clinical and laboratory data, we made an expert diagnosis of BA, atopic form.

Group 2 consisted of children with bronchial hyperresponsiveness in the absence of symptoms of bronchial obstruction. These children were considered conditionally healthy at the time of examination and were not observed in the dispensary group. We diagnosed GDM in these children by PSV after exercise.

The examination of anamnestic data revealed that 60.6% of group 1 children and 55.75% of group 2 children had their first pregnancy and first birth. In the majority of cases their mothers had a history of first half gestosis (63.6% and 54.8% respectively). 33% of children with BA and 46.3% of children with GDM were born asphyxiated. PEP was diagnosed in 78.7% of Group 1 children and 56.6% of Group 2 children, for which the diagnosis was registered by a neurologist. 57.6% of Group 1 children were on early artificial and mixed feeding. Group 2 breastfed 49.5% of the children. In our opinion, this contributed to the fact that in most children of this group the first episode of bronchial obstruction was diagnosed after 6 months of age (66.3%), while in 81.8% of group 1 children the first episode of bronchial obstruction was diagnosed before 6 months of age.

Heredity and constitutional predisposition play an important role in the recurrence of obstructive syndrome, which contribute to the occurrence of the disease when etiological factors intervene against a background of altered immune reactivity.

In children of the 1st group the hereditary predisposition was noted for allergic (66,3%) and bronchopulmonary diseases (30,3%) whereas in children of the 2nd group there were bronchopulmonary (49,56%) and cardiovascular diseases (38,9%). Group 3 children mostly had chronic bronchopulmonary disease in their parents (42.75%).

Interesting in our view is the fact that allergic predisposition in Group 1 children was predominantly maternal (64.3%) while in Group 2 children it was more often paternal (62.4%).

A retrospective study of the premorbid background of the examined children also revealed differences in the compared groups.

Group 1 and 2 had more frequent ECD (87.8 and 58.4% respectively), paratrophy (69.6 and 58.4% respectively), anemia (63.6 and 52.2% respectively). In Group 3 the incidence of these conditions was significantly lower than in the compared groups ($p < 0.05$).

The study of the developmental histories of children showed that most children in Groups 1 and 2 had thymomegaly diagnosed at an early age.

45.4% of group 1 children were diagnosed with grade I-III thymomegaly at an early age. And 8 children (24.2%) were treated for it. Group 2 children were diagnosed with grade I-II thymomegaly in 21.2% of cases. According to the literature data in children with bronchopulmonary pathology a special place is occupied by the frequency of connective tissue dysplasia, in which changes in the muscular-cartilaginous framework, tracheobronchial tree and alveolar system are noted. All this leads to disorders of pulmonary tissue integrity, associated with increased elasticity and decreased elasticity, forming the main changes of the respiratory organs, causing the development of recurrent obstructive bronchitis and bronchial asthma in children [5,14].

Signs of connective tissue dysplasia were found in 33.3% of group 1 children and 15.9% of group 2 children. But in the questionnaire data, this diagnosis was not made. DST was diagnosed by the presence of external phenotypic features. The most common clinical manifestations of external phenotypic features in the examined children were as follows: Large protruding ears (13%), hypertelorism (12%), hypertrichosis (28%), sparse teeth (48%), gothic palate (33%), ingrown lobes (3-4%), blue sclerae (7%), postural abnormality (19%), chest deformity (7%), joint hypermobility (50%), muscle hypotonia (17%), flat feet (18%), high palate (33%), ingrown lobe (3-4%), blue sclerae (7%), bad posture (19%), sandal cleft (38%).

A combination of thymomegaly and DST was observed in 30.3% of group 1 children, which in our opinion is an aggravating factor adversely affecting both the functioning of the immune system and bronchopulmonary system. When analyzing the course of the disease at an early age, the following symptoms, characteristic of children with AD, can be distinguished: increase in the severity of obstruction over time; cough, dyspnea at physical and emotional stress. In most children the first episode of bronchial obstruction developed against the background of acute respiratory infections, only later on the attacks of difficult breathing under the influence of non-infectious factors began to occur. In the compared group of currently healthy children, respiratory symptoms were largely absent between illnesses, and obstructive episodes occurred much less frequently and solely against the background of acute respiratory infections. Group 2 children had episodes of bronchoobstruction due to non-infectious factors. An important role in the formation of recurrent obstructive syndrome is played by unnecessarily massive and irrational antibiotic therapy, which depresses the already suppressed cellular immune system by infectious pathogens [4,6,7,8].

A study of the histories of children in groups 1 and 2 revealed that on each hospital admission for (BOS) they were prescribed broad-spectrum antibiotics, sometimes a combination of these, often against a background of normal or subfebrile fever.

In our opinion, such neo-(BOS)-induced iatrogenic interventions lead to decreased function not only of the immune system, but also of the parenchymatous organs.

In children of groups 1 and 2 there were chronic foci of infection (48,4% and 42,5% respectively). These were mainly chronic tonsillitis and dental caries.

Main complaints of children in groups 1 and 2, and their parents at the moment of examination were persistent cough (60,6 and 9,4% respectively), shortness of breath after physical effort (36,3 and 63,7% respectively), shortness of breath after emotional stress (12,12 and 7,1% respectively), shortness of breath when inhaling cold air (30,3 and 10,6% respectively).

Thus, a thorough analysis of anamnestic data and objective examination of children helped to identify the most informative risk factors of recurrent obstructive syndrome. According to our data, such factors include unfavourable pregnancy period, unfavourable premorbid background, hereditary predisposition for allergic and bronchopulmonary diseases, presence of chronic foci of infection, unjustified prescription of antibiotics.

The introduction of modern mathematical methods into health care practice has allowed us to approach the question of differential diagnosis in a deeper way, as it excludes subjective evaluation of information.

We had the following objectives:

1. To determine the similarities and differences between the compared groups;
2. Determine the similarities and differences between anamnestic data;
3. Determine the similarities and differences between laboratory data;
4. Identify the trait which has the greatest contribution to the development (BOS).

The main criterion for symptom selection was their informative weight, which was defined as the ratio of the frequency of each symptom in children with a history of (BOS).

All signs were divided into qualitative and quantitative signs.

The most important qualitative anamnestic signs for differential diagnosis are shown in Table 3.

Table 3
Most informative anamnestic signs contributing to transformation (BOS) into Bronchial asthma

Synonym	Detectionrate
Family history of allergies and allergic diseases:	
	66,7%
	30,3%
- Allergic diseases	63,6%
- Bronchopulmonary disease	87,8%
Maternal gestosis in the first half of pregnancy	69,6%
Exudative catarrhal diathesis	63,6%
Paratrophy	33,3%
Grade I-II anemia	45,5%
Connective tissue dysplasia	30,3%
Thymomegaly	
	39,4%
	33,3%
Age of 1st episode (BOS)	
	81,8%
-Up to 6 months of life	84,85%
(BOS) more than 3 times a year	48,4%
Presence of chronic foci of infection	60,6%
Prolonged cough, especially at night	36,3%
Dyspnea on exertion	30,3%

The structural components of organs or systems, when presented with functional requirements, distribute this functional load among themselves, selecting such a quantity and quality of structural components that will be adequate to these specific requirements. This principle is called the principle of mosaicism of organ and system functioning [12,17]. If the functional demands are too great, all structural components become involved. However, such a state cannot last for a long time and, as a rule, this degree of prolonged functional load leads to a breakdown of adaptive capabilities. Thus, for the first time a long-term prospective observation of children who had repeated episodes of bronchoobstruction at an early age was carried out. The structure of diseases with bronchoobstructive syndrome and diagnostic criteria for differential diagnosis were determined. It was shown that the main clinical criteria of transformation of bronchial obstruction diseases (BOS) into bronchial asthma are genetic predisposition for allergic and bronchopulmonary diseases, TM and DST in anamnesis, their combination with low indices of CD95, g-INF and high indices of IL-4 and IgE. The clinical and functional features of the airways of children who suffered repeated episodes of bronchial obstruction syndrome at an early age were revealed. It is shown that 39% of children with a history of frequent episodes (BOS) have a hidden bronchial hyperactivity, detected by peak flowmetry with physical exercise.

CONCLUSIONS

1. Children with hereditary burden of allergic and bronchopulmonary diseases, unfavourable premorbid background (thymomegaly, DST, paratrophy, ECD), with prolonged cough and shortness of breath after physical activity are at high risk for transformation of BOS into AD.
2. Peak flowmetry is the most informative, accessible and prognostically significant method of PSV determination in children with bronchial hyperresponsiveness and bronchial asthma in outpatient settings.
3. marker activation and cytokine level evaluation can be used as additional and prognostic criteria of severity (BOS) and serve as a method for immunomonitoring of children with AD.

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