

PREVALENCE AND CLINICAL CHARACTERISTICS OF HEMOPHILIC INFECTION IN CHILDREN IN UZBEKISTAN

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Аннотация. *Infections caused by Haemophilus influenzae type b (Hib) are widespread in many countries around the world. For this purpose, we have studied the prevalence and peculiarities of the clinical course of the most frequently occurring forms of haemophilus infection in 124 children aged 2 months to 15 years. It was found that Hib infection is most common in children with lower respiratory tract diseases (43.8%), the total incidence of Hib was 38.7% of the total number of children surveyed and depended on clinical forms of hemophilic infection.*

Keywords: *Haemophilus influenzae type b, the prevalence, clinical forms, children vaccination.*

Relevance

Infections caused by Haemophilus influenzae type b are widespread in many countries of the world, causing a high level of invasive diseases, among which the most common are meningitis, sepsis, epiglottitis, pneumonia, most often affecting children of the first 3-5 years of life [1, 2].

Before the introduction of broad immunization, invasive forms of hemophilic infection were a common pathology in children under five years of age. Purulent meningitis, often accompanied by bacteremia, accounted for more than 50% of the total number of invasive forms; epiglottitis was 17%; pneumonia - 15%; the remaining forms were represented by arthritis, cellulitis in the head and neck, sepsis, osteomyelitis, pericarditis [3].

In the USA, the incidence of Hib meningitis in children aged 6-17 months was 122 per 100,000, compared to 65 per 100,000 children aged 18-23 months. A sharp decline in the incidence of Hib meningitis was observed after 23 months of age [7]. The incidence rates in Europe in this age category varied: in Spain and in France - 12 and 21 cases per 100 thousand, respectively. In the Scandinavian countries the incidence rate was higher: in Finland and Sweden - 41 and 54 cases per 100 thousand, respectively [5]. Data for the Asian region per 100 thousand people vary: 4 cases in Thailand, 6 cases in South Korea, from 1 to 10 cases in China (depending on the region), 17 cases in Saudi Arabia, from 18 to 95 cases in the Philippines [7].

Prior to vaccination in Russia, Hib-meningitis was the second (17.5%) in the rating of purulent meningitis, with 95% of the diseases occurring at the age of 2-4 years. According to estimates for Russia as a whole, for one year the number of cases with Hib-meningitis was at the level of 300 cases, while the number of cases with other generalized forms of infection

was at the level of 200 cases. In Russia, the USA and other developed countries, mortality in purulent meningitis caused by H. influenzae type b was 3-4%. A significant proportion of patients with the disease developed residual effects (blindness, deafness, mental retardation, etc.) [8].

At present, at least 3 million cases of invasive Hib infection are registered annually in the world and approximately 386 thousand cases are fatal [7]. The highest morbidity and mortality rates due to Hib infection occur in developing countries. The greatest burden falls on children aged 4 to 18 months of life, however, sometimes the disease can affect infants younger than 3 months and children older than 5 years. In the first year of a child's life, Hib-meningitis dominates among all bacterial meningitis. Even with timely and adequate antibiotic treatment, 3-20% of patients with Hib-meningitis die, and serious neurological complications (up to 30-40%) are often observed in surviving children [10].

In the domestic literature of hemophilic infection, single works are devoted. The prevalence of this infection in Uzbekistan and its significance for the health care of the republic has not been studied. In this regard, the goal of our study was to study the frequency, clinical features of the most common forms of hemophilic infection in children, as well as the development of methods for early diagnosis, treatment and prevention.

Materials and research methods. The results of the study are based on the clinical observation and examination of 124 children aged 2 months to 15 years. Etiological diagnostics was carried out in 35 patients with purulent meningitis, in 39 patients with acute and chronic otitis media, and in 20 patients with acute and chronic sinusitis. 50 patients with croup and 80 patients with lesions of the lower respiratory tract were also examined to identify hemophilic etiology of the disease. To clarify the causative agents of meningitis, patients underwent bacterioscopic, cultural methods, as well as a latex agglutination method with commercial diagnostics for the determination of H. Influenzae type b, N. Meningitidis A, B, C and S. Pneumonia antigens in a liquor produced by bio-Merier (kit-5) (France). Bacterioscopic and cultural methods were performed for patients with lesions of ENT organs. Isolation and cultivation of capsular hemophilic bacteria was carried out on a modified "chocolate" agar with the addition of yeast extract. Patients with croup and lesions of the lower respiratory tract were examined by PCR to detect Haemophilus influenzae DNA. To detect DNA of Haemophilus influenzae in the serum of patients we used a set of reagents "GENTEX-MASTER" - Haemophilus influenzae tm-PCR screen test, intended for qualitative detection of DNA of Haemophilus influenzae from whole blood and other biological materials of human by polymerase chain reaction.

Results and discussion: A study of clinical and laboratory data made it possible to determine the etiology of meningitis in 22 of the 35 examined patients, 20 of them revealed N. Meningitidis of group A, in 2 - H. influenzae type b (Table 1).

Table 1

Etiology of bacterial meningitis in different age groups

Age	Number of patients	Hib-etiology		Meningococcal etiology		Unclear etiology	
		Aбс.	%*	Aбс.	%*	Aбс.	%*
3month- 1year	6	2	5,7	2	5,7	2	5,7
1 -5 years	29	0	0	18	62,0	11	38,0
Total	35	2	5,7	20	57,0	13	37,3

Note: *- to the total number of detected

As can be seen from the table, the frequency of meningitis of hemophilic etiology from the number of verified was 9.1% (2 cases). Both of these cases were presented by children

under 1 year of age. In the group of children older than 1 year, meningococcal meningitis prevailed.

The clinical picture of hemophilic etiology patients with meningitis was characterized by a severe course, the presence of a high fever of a wave-like character, pronounced meningeal signs. Patients had impaired consciousness up to its complete loss, convulsions, intoxication, dry skin. The hemogram in patients with hemophilic meningitis upon admission was characterized by normal leukocyte counts or moderate leukocytosis, which did not correspond to the severity of the patient's condition. Cerebrospinal fluid flowed under pressure, cloudy, marked inflammatory changes were noted - a positive Pandy reaction, an increase in protein content, cytositis of a neutrophilic nature. Clinical, otolaryngological, X-ray, microbiological examination of 59 patients with with otorhinolaryngology diseases in 5 patients (12.8%) was detected Hib, and more often hemophilic infection was detected in patients with acute purulent otitis media, compared to chronic.

In children with lower respiratory tract diseases, Haemophilus influenzae was detected in 56.3% of patients. Pneumonia caused by a hemophilic infection met with a frequency of 35% and was characterized by a benign course, a polysegmental or bilateral nature of lung damage.

In order to study the prevalence of bacterial flora in the etiology of diseases accompanied by croup syndrome in children, we studied the role of Haemophilus influenzae type b.

When making the diagnosis, we were guided by the International Classification of Diseases, 10th revision. To assess the severity of the condition of the children, to determine the degree of stenosis of the larynx, the Westley C scale was used. To assess the severity of the croup, the following symptoms were taken into account: stridor, chest retraction, shortness of breath, cyanosis, consciousness. Each symptom was scored from 0-5. The condition of the children was evaluated in dynamics at admission, then every 10 minutes for 40 minutes, also for another 3 days.

Table 1.1: Grain Grade Grading Scale by Westley C.

Symptoms	Баллы
Stridor:	
not	0
under load	1
at rest	2
Retraction:	
not	0
weak	1
moderate	2
strong	3
Inhale:	
normal	0
hindered	1
Significantly hindered	2
Cyanosis:	
not	0
under load	4
at rest	5
Level of consciousness:	
normal	0
disorientation	5

A study of the etiology of the disease in 50 children with croup in 12% of cases revealed Hib, and in 83.3% of them Hib infection was combined with viral.

The clinical picture of Hib croup syndrome etiology in 80% of cases was characterized by acute onset, the general condition of the patients was severe. Catarrhal phenomena in children were not expressed.

At admission, patients complained of a husky voice, fever, shortness of breath. Objectively noted hyperemia of the pharynx, noisy stridor breathing. Hypersalivation was observed in 80% of children, dysphagia and forced position in almost half of the patients (Fig.2).

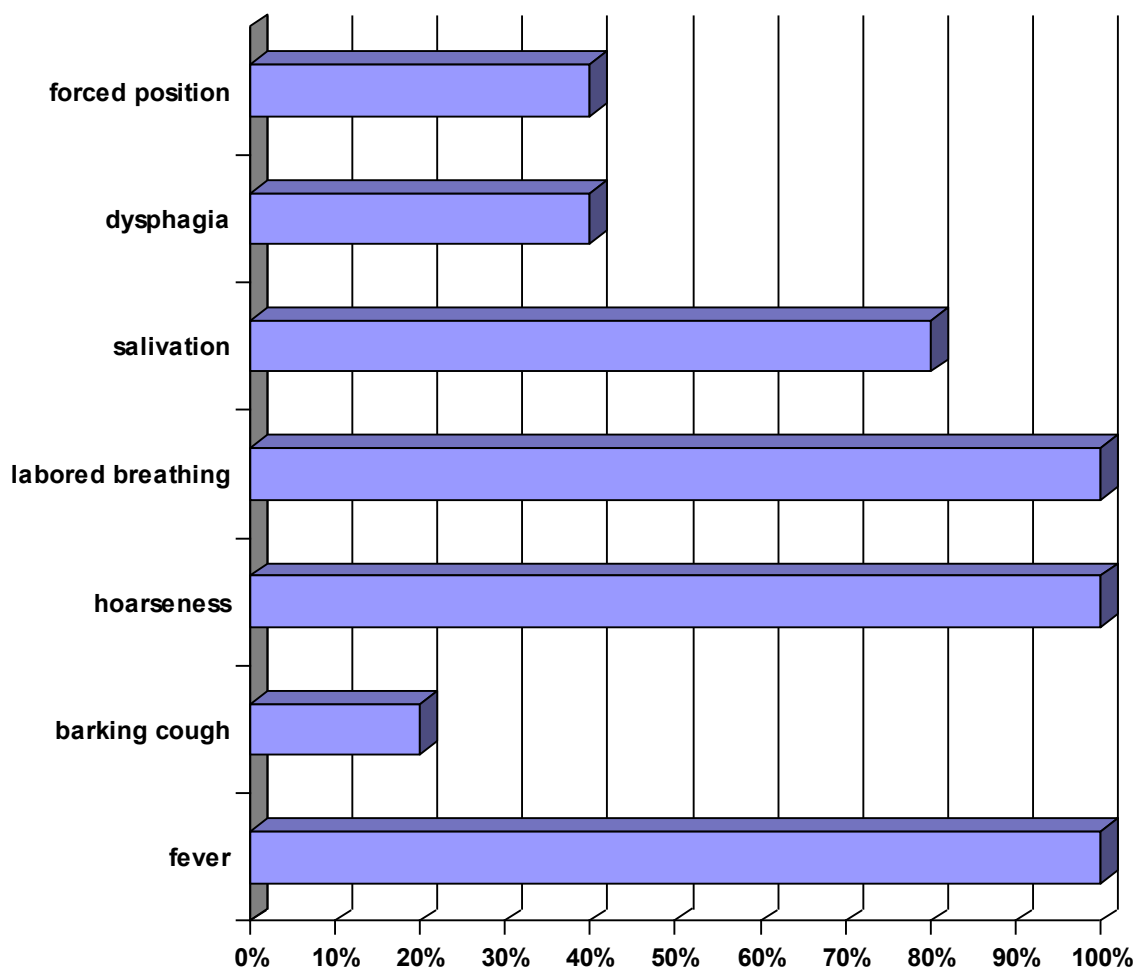


Fig. 2. The severity of clinical symptoms with epiglottitis.

An analysis of the occurrence of an infectious agent depending on gender has shown that the incidence is more often observed among males ($83.3 \pm 6.7\%$; $P < 0.05$). High prevalence of Hib infection was recorded in the age group from 1 to 3 years ($83.3 \pm 6.7\%$ compared to 16.7% in the age group under 1 year), while in the group of children from 3-5 years old - did not meet.

In almost all children, the disease developed against an unfavorable premorbid background, a significant role of which in Hib infection is emphasized by many experts. We found that 50% of children had allergic manifestations (exudative-catarrhal diathesis, food allergy, drug intolerance), and 83.3% showed grade I anemia. Perinatal encephalopathy was noted in 33.3% of children. Among the infectious diseases, frequent acute respiratory viral infections were noted in 83.3% and acute respiratory infections in 50% of children with Hib etiology.

Croup of Hib etiology appeared as epiglottitis. Epiglottitis was characterized by: acute onset of the disease: sore throat, hoarseness, fever and shortness of breath - stridor breathing, which manifests itself mainly when inhaling.

The general condition in all patients with epiglottitis was severe, manifested pronounced symptoms of general intoxication in 83.3% of patients, and moderately in 16.7%.

An increase in body temperature upon admission to high numbers (39⁰C and higher) was observed in 4 patients (66.7%), in 2 children (33.3%), febrile fever (38.2⁰C) was observed. The average duration of the febrile period was 4.2 ± 0.2 days.

In 50% of patients, acute pains were observed in the pharynx, in 33.3% - the head took a forced position. Dry cough was noted in only 1 patient (16.7%), who stopped on the 4th day of illness.

Catarrhal symptoms, in the form of a mucous discharge from the nose, were noted in only 1 child, in other children nasal breathing was free on both sides. During auscultation in 83.3% of children, hard breathing was heard for 3.5 ± 0.2 days, in 1 child vesicular breathing was heard in the lungs. Heart sounds were muffled, tachycardia. Respiratory dyspnea was observed in all children with Hib etiology croup during the first two days.

During the examination, all patients had common hyperemia of the soft palate, temples and mucous membranes of the throat and stricture respiration.

It is noteworthy that 66.7% (4) of patients had hypersalivation, 33.3% had dysphagia (2), which is the result of lesions of IX-X pairs of cranial nerves due to severe intoxication and edema. In order to prevent the development of hemophilic infection and its complications in Uzbekistan, since 2008 Hib vaccination has been introduced into the national preventive vaccination calendar. It is of interest to study the incidence of hemophilic infection after Hib vaccination has been introduced.

Conclusions. Thus, it has been established that Hib infection in most cases occurs in children with lower respiratory diseases including bronchitis and pneumonia (43.8%), the total Hib prevalence rate was 38.7% of the total number of children surveyed and depended on clinical forms of hemophilic infection. We consider it appropriate to vaccinate children against Hib according to the national preventive vaccination calendar.

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