

UDC: 616.832.9-002.2

**CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF PNEUMOCOCCAL MENINGITIS IN ADULTS**

Rabbimova Nodira Tashtemirovna, Yarmuhamedova Nargiza Anvarovna,  
Rustamova Shakhlo Abduhakimovna, Oripova Pokiza Olimovna  
Samarkand State Medical Institute, Republic of Uzbekistan, Samarkand

**КАТТАЛАРДА ПНЕВМОКОКК МЕНИНГИТНИНГ КЛИНИК ВА ЭПИДЕМИОЛОГИК АСПЕКТЛАРИ**

Раббимова Нодира Таштемировна, Ярмухамедова Наргиза Анваровна,  
Рустамова Шахло Абдухакимовна, Орипова Покиза Олимовна  
Самарқанд давлат тиббиёт институти, Ўзбекистон Республикаси, Самарқанд ш.

**КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ АСПЕКТЫ ПНЕВМОКОККОВОГО МЕНИНГИТА У ВЗРОСЛЫХ**

Раббимова Нодира Таштемировна, Ярмухамедова Наргиза Анваровна,  
Рустамова Шахло Абдухакимовна, Орипова Покиза Олимовна  
Самаркандский государственный медицинский институт, Республика Узбекистан, г. Самарканд

e-mail: [nodira.rabbimova@mail.ru](mailto:nodira.rabbimova@mail.ru)

**Аннотация.** Долзарблиги: Этиологияси пневмококк бўлган касалликларнинг оғир кечганлиги сабабли дунёнинг кўплаб мамлакатларида долзарб тиббий ва ижтимоий муаммо бўлиб хисобланади. Тадқиқот мақсади: сўнгги 10 йилдаги Самарқанд вилояти бўйича катталарда пневмококкли менингитнинг клиник-эпидемиологик хусусиятларини ўрганиш. Тадқиқот материали ва усуллари: Самарқанд вилоят юқумли касалликлар клиник шифохонасидаги реанимация ва хаво-томчи инфекциялари бўлимларига 2008 йилдан 2018 йилгача мурожаат қилган жами 209 нафар бактериал йирингли менингит билан даволанган беморларнинг стационар карталари ўрганилди. Хулоса: ПМлар асосан спорадик холатларда учраган. Касалликнинг келиб чиқиши кўпинча совқотиши билан боғланган (56%). Катталарда ПМ оғир кечиши билан характерланган (85,7%). 70,3% беморларда пневмококк инфекциясининг бирламчи ўчоги бўлган касалликлар аниқланган (пневмония – 27,7%, сепсис – 3,7%, ўрта отит – 11%, синусит – 9,2%). 18,5% беморларда анамнезида бошқа касалликлар ўтказганлиги аниқланган (бош мия травмаси, респиратор касалликлар, менингит). 66,5% холларда оғир касалликлар фонида ривожланган. Бирламчи ўчоқ бўлмаган холатларда (29,7%) жиддий асоратлар ва оқибатлар кузатилмаган.

**Калит сўзлар:** пневмококк, менингит, клиник кўриниши, катталар.

**Abstract.** Relevance. Diseases of pneumococcal etiology, due to the particular severity of the course, are one of the significant medical and social problems for many countries in the world. Objective: to study the clinical and epidemiological features of the course of pneumococcal meningitis in adults in the Samarkand region over the past 10 years. Materials and methods: In total, 209 hospital records of patients with bacterial purulent meningitis were processed, in the period from 2008 to 2018. They were admitted to the intensive care unit and the department of airborne infections of the regional clinical infectious diseases hospital in Samarkand. Conclusions: The disease was most often associated with hypothermia (56%). In adults, PM had mainly a severe course (85.7%). 70.3% of identified patients had the primary focus of pneumococcal infection (pneumonia - 27.7%, sepsis - 3.7%, otitis media - 11.0%, sinusitis - 9.2%). An unfavorable history of life was revealed in 18.5% (traumatic brain injuries, numerous respiratory diseases, previous meningitis) of patients. In 66.5%, the disease developed as the result of severe concomitant diseases. In the scarcity of the primary focus of the disease (29.7%), serious complications and consequences were not recorded.

**Key words:** pneumococcus, meningitis, clinical manifestations, adults.

**Relevance.** Diseases of pneumococcal etiology, due to the special severity of the course, are a significant medical and social problem for many countries in the world [1, 2]. Pneumococcal infection (PI) is a group of diseases caused by Streptococcus pneumoniae bacterium. There are a number of pathologies in pneumococcal etiology such as acute otitis media

(nearly 25% of all otitis media), pneumococcal pneumonia (around 70% of all cases of pneumonia), purulent pneumococcal meningitis (from 5% to 15% of all bacterial meningitis), endocarditis (about 3%), sepsis, arthritis, sinusitis, otitis, pleurisy, mastoiditis and others [3]. Pneumococcal meningitis is characterized by high rates of mortality and disability, signifi-

cant socio-economic losses. Among adults, the most vulnerable are people over 40-50. Clinical features include fever, critical initial toxicosis with accompaniment of cerebral phenomena (impaired consciousness), sudden onset, and encephalitic reactions (convulsions, tremor of limbs). The significance of vaccine prophylaxis in adults can be measured depending on the rate of severity of the disease, the period of hospitalization, as well as antibiotic therapy of meningitis caused by *Str.pneumoniae*.

Feature of the disease is a non-epidemic nature of the spread, as a rule, it affects people with weakened factors of immune protection in the background current focal pneumococcal infection (middle ear infections, sinusitis, pneumonia, and so on, etc.). There are cases of pneumococcal meningitis as a primary disease when the pathogen enters directly into the cerebrospinal fluid during cerebrospinal fluid, and brain injuries [7,8]. Despite significant progress in the diagnosis and treatment of neurological infectious diseases, the use of modern intensive care methods and the latest antibacterial drugs, the disease is characterized by a severe course, high mortality rates, the development of late complications, often leading to disability of patients. [6]. Mortality during the PM in different age groups may reach from 30% to 70%, about 35 - 45% of patients required to provide assistance in terms intensive care department, a third, convalescents suffer from late complications and residual phenomena (hydrocephalus, deafness, ataxia, neurological and psychic deficits varying degrees of severity, and others.) This disease has no clear seasonality, however there is a tendency to an increase in winter-spring period [4]. In regions with a temperate climate, the peak incidence occurs in the autumn-winter period [5]. The most vulnerable groups of pneumococcal disease are children under 5 years, older people over 65, immunocompromised individuals (HIV-infected persons, with cancer) and chronic pathologies: chronic kidney disease and sickle cell disease [4, 5]. Pneumococcal meningitis is more common in males, with a ratio to the incidence in females of 3:1. Pneumococcal meningitis and meningoencephalitis commonly derive on the ground of generalization of infection and are usually detected in the sporadic diseases form, accounting for 1/3 of all purulent meningitis. Development of meningitis can be also contributed by old skull injuries. In such cases, development of pneumococcal meningitis is led by respiratory infections, usually even after long period of injury. The elaboration of the disease is preceded by the presence of a purulent focus: sinusitis, tracheobronchitis, otitis media, and pneumonia [6]. Most of the deaths are due to pneumococcal meningitis, rather than meningitis caused by meningococcus or hemophilic bacillus. The following clinical syndromes are characteristic of the classical clinical picture of PM: general infection, cerebral, meningeal, syndrome of inflammatory changes in cerebrospinal fluid (CSF). At the same time, the febrile intoxication syndrome and central nervous system (CNS) lesions characteristic of meningococcal infection do not develop as rapidly

as PM with meningococcal meningitis; in about a half of the patients, PM is preceded by rhinosinusitis, otitis media, pneumonia, so patients are hospitalized later, which also adversely affects the effectiveness of treatment. Thus, according to the literature, a severe course of PM in 43.2% was accompanied by the involvement of brain matter in the pathological process, while in meningococcal meningitis this was 28.6%, in case of meningitis due to hemophilic bacillus it contained 30%. The disease was characterized by severe and significant flow of meningeal syndrome, stem and focal symptoms, convulsive syndrome, damage to II, VI, VII, XII pairs of cranial nerves. These features of PM create serious difficulties in diagnosis.

The study of the pathology became significant due to an increase in the frequency of PM and pathogenesis of pneumococcal meningitis, which is similar to the clinical signs with meningitis of another etiology, however there is an adequate data on the properties of pneumococcus.

**Objective:** to investigate the clinical and epidemiological aspects of pneumococcal meningitis in adults in the Samarkand region over the past 10 years.

**Material and methods of research.** From 2008 to 2018 we conducted a retrospective analysis of statistical data on archived medical history of patients with pneumococcal etiology meningitis, which entered the intensive care unit and the airborne infections department of the regional clinical infectious diseases hospital in Samarkand. Diagnoses were made on the basis of clinical manifestations, epidemiological data and laboratory etiological studies in the context of a standard case definition.

In total, 209 inpatient records of patients with bacterial purulent meningitis were processed, of which 124 (59%) were diagnosed with meningococcal meningitis, 54 (26%) pneumococcal meningitis, 13 (6%) hemophilic meningitis. The diagnosis of pneumococcal meningitis in only 23 (46.6%) patients was confirmed only by bacteriological culture. Since 2012, the BinaxNOW immunochromatographic test in combination with bacteriological culture was used for diagnosis in practice, which was positive in 31 (57.4%) patients with pneumococcal meningitis.

**Results of the study:** The ratio of meningitis of pneumococcal etiology in contrast with meningitis of other etiologies was 26%, meningitis with meningococcal etiology was the second (59%), hemophilic etiology meningitis made up 6%, while meningitis of unknown etiology was 9% of the total number of bacterial purulent meningitis (figure 1.).

When analyzing the age-related composition of patients, it was found that infants before 1 year were 24%, from 2 to 6 years old - 14.8%, 7-15 years old children made up 22.2%, teenagers from 16 to 18 years old - 13%, over 19 years old adults - 25.9% of the total number of hospitalized patients.

The age-related analysis of patients showed that patients 19–25 years old accounted for 7.8%, 25–

30 years old –26.9%, 30–40 years old –19.7 %%, over 40 years old — 45.6%, of the total number hospitalized patients. Among adults, the majority of patients were people older than 40 years of working age (69.1%). Among the studied patients, men accounted for 55.7%, women 44.3% of the total number of patients. When analyzing the main place of residence of the patients who applied, it was found that the prima-

ry treatment from the regions of the Samarkand region was 87.3%, while only 12.7% of patients came from the Samarkand city (Figure 2).

Analysis of seasonality in patients over 18 years of age showed that seasonality is not typical for this category of patients. Diseases in the form of sporadic cases were mainly observed. The disease was most often associated with hypothermia (56%).

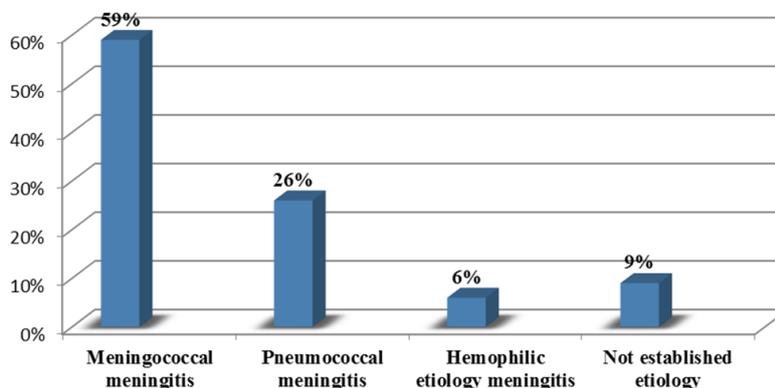


Fig. 1. Distribution of patients with BPM.

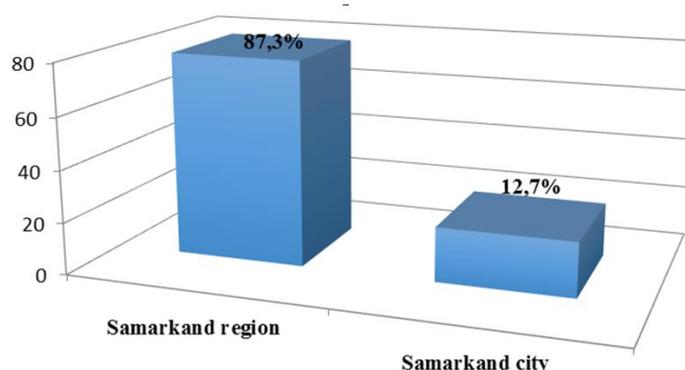


Fig. 2. Distribution of patients by place of residence.

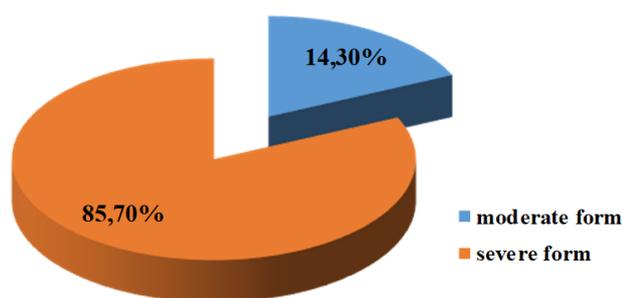


Fig. 3. Severity distribution of patients.

By occupation, patients were divided into the following groups: wage workers (15.3%), unemployed (26.4%), pensioners (18.7%), disabled people (12.2%), university students (9.6 %), college students (15.2%), office employees (2.6%).

The incidence of PM in recent years has been wavelike, with a decreasing tendency since 2015 - while the number of hospitalized patients diagnosed with pneumococcal meningitis decreased by half. Analysis of fluctuations in the annual dynamics of PM incidence showed that 7.4% of cases were detected in 2008, in 2009 – 11%, in 2010 – 7.4%, in 2011

and 2012 – around 11%, 2013. - 9.25%, 2014 - 7.4%, 2015 and 2016 it contained 3.7%, and 5.6% respectively, 2017 - 3.7%, 2018 - 1.9% of patients with PM out of the total number of patients with acute bacterial purulent meningitis. The decrease in the number of patients since 2015 is apparently associated with the inclusion of vaccinations in the National Calendar of Active Immunization of the Population. While at the same time, in adults, the incidence does not tend to reduce.

When analyzing anamnestic data, 70.3% of patient’s pneumococcal infection revealed. Out of that number, pneumonia was detected in 27.7% of patients, sepsis in 3.7%, otitis media in 11.0%, sinusitis in 9.2% of patients. The ratio of patients with an unfavorable history of life (numerous respiratory diseases, traumatic brain injuries, previous meningitis) was 18.5%.

In 66.5% of cases in adult patients, the disease developed on the ground of severe concomitant diseases. So, in 22.3% of patients, the phenomena of chronic bronchitis were determined, in 2.7% of patients severe cardiovascular pathology, in 5.3% of patients - diseases of the nervous system, in 6.7% -

allergic diseases, in 4.9% - diabetes mellitus, in 28.9% - viral hepatitis, in 13.4% - chronic tonsillitis, in 1.2% - rheumatoid arthritis, in 12.1% of patients with ARI, in 2.5% of herpes infection. The severity of the disease in many cases depended on the primary focus of pneumococcal infection. In turn, it is necessary to conduct a clinical examination in primary care, in which diseases caused by pneumococcal infection and severe concomitant diseases occur in order to prevent common forms of PM.

The largest number (74%) of patients was received on the 2nd – 3rd day from the first symptoms of the disease to the intensive care unit, where treatment measures were in average  $7.2 \pm 1.76$  days. The clinical form of preceding focal pneumococcal infection was the main cause of the terms of hospitalization of patients. Late hospitalization, in the majority of cases, caused severe course of the disease. In 40% of cases with primary PI, a rapid onset of the disease was noted. The problem of belated pre-hospital diagnostics and, accordingly, late hospitalization of patients in an infectious hospital, which exists to this day, is possibly associated with a more gradual onset of the disease, which affects the severity of the condition of patients upon admission and requires caution by practical doctors. The distribution of patients according to the severity of the course of the disease showed that, an aggressive flow was observed in 85.7% of cases, while a moderate course was observed only in - 14.3% of cases (Figure 3).

Patients were hospitalized with the following diagnoses: «Acute respiratory infection» (47.3%), «Chronic tonsillitis» (13.1%), «Meningococcus oic infection» (7.8%), «Acute intestinal infection. Bronchopneumonia» (12, 3%), «Purulent Meningitis» (19.5%) More often (25.3% of cases), it was severe in patients with concomitant diseases. Also, high mortality rates were observed in patients with concomitant diseases (2.4%). In patients who did not identify the primary focus of the disease, serious complications and consequences were not recorded (29.7%).

When analyzing the clinical course of the disease it has been found that meningeal syndrome, in various rates of severity, cerebral syndrome in - 94% and general infection syndrome in 96% of patients was observed

In the clinic of the disease, general infectious syndrome, cerebral and meningeal syndromes were found with the same frequency, in adults, unlike children, cranial nerve damage was recorded more early in the disease and was more common. In 2.3% of patients, focal symptoms were observed in the form of smoothing of the nasolabial fold, ptosis, anisocoria, paresis of the gaze. In 23.8% of patients, psychomotor agitation was noted, 1.3% of patients lack of consciousness, 5.4% of patients with clinic convulsions, a decrease in sensitivity to external stimulus was observed in 9.5% of patients.

In 59.7 % of patients, the disease was characterized by a sudden onset with fever around  $38^{\circ}\text{C}$ , not often to higher numbers, severe initial toxicosis (in 60-70% of patients) with cerebral phenomena (severe headache, repeated vomiting, impaired consciousness - psychomotor agitation, somnolence, stupor, coma) and encephalitic reactions (tremor of limbs, convulsions). In the first days of the disease revealed paresis of cranial nerves, most often abducant and oculomotor was detected in 23.5% of cases. 18.3% had mono- and hemiparesis.

Clinical symptoms of the general infection syndrome were manifested by an increase in body temperature of varying severity, pallor of the skin, refusal to eat, weakness, lethargy. The above symptoms were recorded with different frequencies in different study groups. Thus, an increase in body temperature to subfebrile numbers was observed in 36.8% of patients, in 40.7% of patients an increase in temperature to  $39.5^{\circ}\text{C}$  was detected, an increase in temperature to hyperpyretic numbers was most often recorded in patients with complicated course - in 22.5% of patients. Pallor of the skin, weakness, and refusal to eat were observed in all studied groups of patients. Meningeal syndrome was observed in all patients. In all cases, stiff neck was recorded, Kerning's symptom was observed in 75.9% of patients, and Brudzinsky's symptom (upper, middle or lower) was determined in more than 3/4 of patients.

Meningeal syndrome of varying degrees of intensity indicated damage to the soft meninges of the brain and it was positive in all patients, while in 44% of them it was clinically pronounced - a plank-like degree of stiff neck, positive symptoms of Kerning, Brudzinsky and others. In 23 (42.6%) patients, meningeal syndrome was regarded as moderate, with a “flickering” of meningeal signs, and in 9 (16.67%) patients it was mild (stiff neck, dubious, other symptoms are unstable).

Another feature of PM is a high percentage of complications. The following complications were observed in 85.7% of patients: cerebral edema, impaired consciousness, and hemodynamic disorders. High mortality rates were soaked in patients with late hospitalization. In 11.1% of hospitalized patients, subarachnoid hemorrhages were observed in the period from 2<sup>nd</sup> to 9<sup>th</sup> day of hospitalization, which led to death. Pneumococcal meningitis, which occurred on the ground of the existing primary focus of inflammation (purulent sinusitis, pneumonia, otitis media, mastoiditis), slightly symptomatic, begins sub-acute, while it varies in a particularly severe flow and more often than primary pneumococcal meningitis, it ends lethally. The consequences of pneumococcal meningitis largely depend on adequately initiated treatment and diagnosis in time. Residual effects due to PM were manifested by asthenoneurotic syndrome

(26.7%), cardiopathy (33.2%), arthritis (12.5%), ataxic syndrome (8.7%), hypertensive syndrome (18.9%).

**Conclusion:** Analysis of seasonality in adults showed that PM was mainly found in the form of sporadic cases. The disease was most often associated with hypothermia (56%). The incidence of PM in recent years has been wavelike, with a decreasing tendency since 2015 - while the number of hospitalized patients diagnosed with pneumococcal meningitis has decreased by half. The reduction in the number of patients since 2015 is apparently associated with the inclusion of vaccinations in the National Calendar of Active Immunization of the Population. While at the same time, in adults, the incidence does not tend to decrease. The importance to introduce pneumococcal vaccines in the practice of standard vaccination of adult patients aged 50 years and older as the way to prevent invasive pneumococcal infection was emphasized by the world's leading experts in the field of infectology. In adults, PM was mainly characterized by a severe course (85.7%). In 70.3% of patients, identification of the disease became the primary focus of pneumococcal infection (pneumonia - 27.7%, sepsis - 3.7%, otitis media - 11.0%, sinusitis - 9.2%). An unfavorable history of life was revealed in 18.5% (traumatic brain injuries, numerous respiratory diseases, previous meningitis). In 66.5%, the disease developed against the background of severe concomitant diseases. In the absence of a primary focus of the disease (29.7%), serious complications and consequences were not recorded. The severity of the disease in many cases depended on the primary focus of pneumococcal infection. This, in turn, necessitates the organization of medical examination in the primary care in a planned manner in order to identify patients with primary foci of pneumococcal infection and severe concomitant diseases to prevent common forms of PM.

#### Literature:

1. Koroleva I. S., Beloshitsky G. V., Koroleva M. A., Mel'nikova A. A. Epidemiological aspects of pneumococcal meningitis in the Russian Federation. *Epidemiologia i Vaccinoprofilactica*. [Epidemiology and Vaccinal Prevention]. 2016; 15 (5): 6–13 (in Russian).
2. Martynova GP, Kutishcheva IA, Bogvilene Ya. A., Solovieva IA, Kuznetsova NF, Alyieva LP Actuality of vaccination against pneumococcal infection for children in Krasnoyarsk. *Epidemiologia i Vaccinoprofilactica*. [Epidemiology and Vaccinal Prevention]. 2015; 14 (2): 60–65 (in Russian).
3. National association of specialists in healthcare associated infections (NASKI). The current situation of pneumococcal infections in the world and in the Russian Federation. Available on: <http://nasci.ru> (in Russian).
4. Epidemiology and vaccine prevention of infection

caused by *Streptococcus pneumoniae*. Methodical guidelines 3.3.1.0027-11. Available on: <http://rospotrebnadzor>.

5. Pneumococcal Diseases in Adults after Vaccinations in Children, Japan, 2010–2013. *Emerging Infectious Diseases*. 2015; 11: 1956–1965.
6. Kastenbauer S. Pneumococcal meningitis in adults: Spectrum of complications and prognostic factors in a series of 87 cases. 2003; 5: 1015–1025.
7. Weisfelt M, van de Beek D, Spanjaard L, Reitsma JB, de Gans J. Clinical features, complications, and outcome in adults with pneumococcal meningitis: a prospective case series. *The Lancet Neurology*. 2006; 2: 104–105.
8. Joo-Yeon, Engelen-Lee. Engelen-Lee J-Y, Brouwer MC, Aronica E, van de Beek D. Pneumococcal meningitis: Clinical pathological correlations (meningene-path) *Acta Neuropathologica Communications Neuroscience of Disease*. 2016; 4: 26. <https://doi.org/10.1186/s40478-016-0297-4>.

### КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ АСПЕКТЫ ПНЕВМОКОККОВОГО МЕНИНГИТА У ВЗРОСЛЫХ

Раббимова Н.Т., Ярмухамедова Н.А., Рустамова Ш.А., Орипова П.О.

**Аннотация.** Актуальность. Болезни пневмококковой этиологии, в связи с особой тяжестью течения, являются значимой медицинской и социальной проблемой для многих стран в мире. Цель работы: изучить клинико-эпидемиологические особенности течения пневмококкового менингита у взрослых по Самаркандской области за последние 10 лет. Материалы и методы. Всего обработано 209 стационарных карт больных с бактериальным гнойным менингитом, в период с 2008 по 2018 гг., которые поступали в отделение реанимации и отделение воздушно-капельных инфекций областной клинической инфекционной больницы города Самарканда. Выводы: ПМ в основном встречался в виде sporadических случаев. Заболевание чаще всего связывалось с переохлаждением (56%). У взрослых ПМ в основном (85,7%) характеризовался тяжелым течением. В более половине случаев (70,3%) выявлялись заболевания, ставшие первичным очагом пневмококковой инфекции (сепсис - 3,7%, синусит - 9,2%, средний отит - 11,0%, пневмония - 27,7%). У 18,5% больных выявлялся неблагоприятный анамнез жизни (частые респираторные заболевания, перенесенный ранее менингит, черепно-мозговые травмы). В 66,5 % случаев заболевание развивалось на фоне тяжелых сопутствующих заболеваний. При отсутствии первичного очага заболевания (29,7%), серьезных осложнений и последствий не регистрировалось.

**Ключевые слова:** пневмококк, менингит, клинические проявления, взрослые.