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CLINICAL FEATURES AND OUTCOMES OF MENINGITIS FOR CHILDREN IN THE REPUBLIC OF NORTH OSSETIA–ALANIA

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КЛИНИЧЕСКИЕ ОСОБЕННОСТИ И ИСХОДЫ МЕНИНГИТОВ У ДЕТЕЙ В РЕСПУБЛИКЕ СЕВЕРНАЯ ОСЕТИЯ–АЛАНИЯ

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The study was to determine regional characteristics and outcomes of meningitis in 105 children. Purulent meningitis developed in young children (56.7 %) and was accompanied by severe (85.1 %) forms, risks of infectious (29.9 %) and neurological (20.9 %) complications, and a protracted course (65.7 %). Children with serous meningitis had an underlying

pathology (52.6 %), partial meningeal syndrome (79.0 %), and developed meningoencephalitis or meningoencephalomyelitis (55.3 %). During the recovery period, the frequency and range of neurological disorders in purulent and serous meningitis were not different. Still, in the long term, a range of neurological disorders in children with bacterial meningitis and a decrease in QOL was identified.

Keywords: neuroinfection, meningitis, purulent, serous, outcomes, quality of life, children

В работе определялись региональные особенности и исходы менингитов среди 105 детей. Гнойный менингит развивался у детей раннего возраста (56,7 %) и сопровождался тяжелыми (85,1 %) формами, инфекционными (29,9 %) и неврологическими (20,9 %) осложнениями и затяжным течением (65,7 %). У детей с серозным менингитом имела фоническая патология (52,6 %), менингеальный синдромокомплекс был неполным (79,0 %), уровень поражения соответствовал менингоэнцефалиту или менингоэнцефаломиелиту (55,3 %). В периоде реконвалесценции частота и спектр неврологических нарушений при гнойных и серозных менингитах не имели отличий, но в отдаленном периоде у детей с бактериальным менингитом расширялся спектр неврологических расстройств и выявлялись нарушения качества жизни.

Ключевые слова: нейроинфекция, менингит, гнойный, серозный, исходы, качество жизни, дети

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HUI – Health Utilities Index
IF – impairment of function
PM – purulent meningitis

QOL – quality of life
SM – serous meningitis

Neuroinfectious diseases play an essential role in developing most functional and deficient disorders of the nervous system in children. Neuroinfections negatively affect children's social adaptation and decrease quality of life (QOL) during recovery [1]. Adverse effects of bacterial purulent meningitis (PM) in recovery are caused by the development of infectious and cerebral complications (toxic shock syndrome, disseminated intravascular coagulation and respiratory distress syndrome, cerebral edema, ischemic stroke, and intracranial hypertension). Disability and mortality develop in 15–50 % of children, with more «mild» consequences – in 20–30 % of cases [2–4]. Expected outcomes include severe hearing loss, epileptic status, motor impairment, blindness, and mental retardation. Weak results include cognitive, speech, and behavioral impairments, problems with minor motor skills, and poor school performance [1, 5]. Serous meningitis (SM) in children is now more common than bacterial meningitis; climatic and regional characteristics determine its frequency. Cerebral asthenia, reduced «working memory», hypertonic syndrome, diencephalic syndrome, asthenic-neurotic syndrome, and symptomatic epilepsy develop with serous meningitis during recovery [6]. Analysis of the peculiarities of meningitis development in children can provide important practical information for developing preventive measures in the region.

The study aimed to determine regional clinical features and long-term effects of bacterial and serous meningitis in children.

Material and Methods. Clinical database: Republican Children's Clinical Hospital, Vladikavkaz. The object of epidemiological study: 645 cases of meningitis during 15 years (2005–2019). The object of clinical study: 105 patients with meningitis: PM – 67 and SM – 38 children. The median age of children with PM was 4.1±0.5 years, with SM – 5.6±0.7 years. Research

methods: clinical observation, copying of data from patient's medical records, assessment of neurological consequences in short (after 1–6 months) and long-term (after 3–5 years) follow-up periods. Assessment of QOL in 118 children with meningitis. The QOL instrument was a Russian version of the HEALTH UTILITIES INDEX (McMaster University, Canada) Russian questionnaire – Proxy-assessment: HUI23P2RU.15Q, the classification system of which contains eight parameters: Vision, Hearing, Speech, Ability to Move, Fine Motor Skills, Emotions, Cognitive Abilities, and Pain. Each parameter corresponds to a certain degree of impairment of function (IF): absent (IF 0), mild (IF I), moderate (IF II), or severe (IF III). Statistical processing: program «Statistica for Windows 10.0» (StatSoft Inc., USA). Pearson's χ^2 test was used to assess differences between the groups.

Results and Discussion. The epidemiological analysis showed that among 645 children who had meningitis during 2005–2019, PM was diagnosed in 49.9 % (322) cases and SM in 50.1 % (323). It was possible to determine the etiology of PM in 50.6 % (163) of children and SM in 34.3 % (57). The etiology of PM was represented by meningococcal (47.6 %), Haemophilus influenzae (24.5 %), pneumococcal (19.6 %), staphylococcal (3.7 %), streptococcal (2.5 %), acinetobacter (1.2 %) and E. coli (0.3 %) types. Enteroviral meningitis (73.7 %) was the most common type among SM. Herpes meningitis (herpes type 1–2, varicella-zoster, cytomegalovirus, and herpes type 6) accounted for 12.3 % of cases; chlamydia and mycoplasma for 1.8 % each; fungal and secondary traumatic meningitis were seen in 7.0 % and 3.5 % of patients respectively. There was no predominant season among cases of PM. Children were ill in winter (29.9 %), spring (25.4 %), summer (20.9 %), and autumn (23.9 %). The incidence of SM was recorded in summer (51.2 %), autumn (32.5 %), and less often in winter (3.6 %) and spring (12.7 %), $p < 0.05$.

Geosocial characteristics of children with meningitis are presented in Table 1.

Table 1

Table 2

Geosocial characteristics of children with meningitis

Characteristics		PM (n=67)	SM (n=38)
		abs. (%)	abs. (%)
Age	0–12 months	23 (34.3 %)*	4 (10.5 %)
	1–3 years	15 (22.4 %)	10 (26.3 %)
	4–6 years	14 (20.9 %)	13 (34.2 %)
	7–12 years	11 (16.4 %)	8 (21.1 %)
	13–17 years	4 (6.0 %)	3 (7.9 %)
Gender	Boys	36 (53.7 %)	23 (60.5 %)
	Girls	31 (46.3 %)	15 (39.5 %)
Place of residence	Urban area	26 (38.8 %)	17 (44.7 %)
	Rural area	41 (61.2 %)	21 (55.3 %)
Preschool attendance	Attending	28 (41.8 %)	13 (34.2 %)
	Not attending	39 (58.2 %)	25 (65.8 %)*

Note: *p<0.05 – statistical significance of differences between the PM and SM groups (χ^2 test).

Infants (34.3 %) predominated in the PM group, and preschool children (34.2 %) – in the SM group. Gender analysis did not reveal significant differences, but there was a tendency for boys to prevail in the SM group (60.5 %). An analysis of the place of residence revealed a predominance of rural children over urban in the PM group (61.2 %/38.8 %). A study of the disease incidence among occupied and unoccupied children showed that SM was more common in children who did not attend children’s educational institutions (65.8 %).

Unfavorable underlying pathology was detected in a third (29.9 %) of children with PM and half (52.6 %) of children with SM, and was represented by intrauterine infections (22.4 %/15.8 %), congenital malformations (6.0 %/13.2 %), endocrine diseases (1.5 %/0 %), organic (16.4 %/23.7 %) and functional (9.0 %/7.9 %) disorders of the nervous system. Among organic disorders in children with PM and SM, a neurodevelopmental delay (16.4 %/23.7 %), epilepsy (3.0 %/2.6 %), and paresis/paralysis (7.5 %/21.1 %) were diagnosed. A comorbidity index in children with PM was 2.1, and in children with SM – 1.7. A low vaccination rate against Haemophilus influenzae (9.1 %) and pneumococcal (4.5 %) infections in children with PM was found.

A primary diagnosis in children with PM (44.8 %) was incorrect more often than in children with SM (18.4 %), p<0.05. Admission to non-specialized hospital departments was also more common in children with PM (20.9 %) than children with SM (2.6 %). There were no differences in hospitalization rates between the PM and SM groups. On day one, from the onset of the disease, 46.3 %/50.0 % of children were admitted; on days 2–3 – 32.8 %/36.8 %; on days four and later – 20.9 %/13.2 % with PM and SM, respectively.

Features of clinical manifestations of meningitis in children are presented in Table 2. The initial diagnosis in children with PM (44.8 %) was more frequent than in children with SM (18.4 %), p<0.05. Admissions to non-specialized hospital departments are also more common among children with MIL (20.9 percent) than children with SM (2.6 %). There was no difference in hospitalization rates between the PM and SM groups. On the 1st day after the onset of the disease, 46.3 %/50.0 % of children were admitted to the hospital; in 2–3 days – 32.8 %/36.8 %; on the 4th day and later – 20.9 %/13.2 % with PM and SM, respectively.

Clinical signs of purulent and serous meningitis in children

Clinical signs of meningitis		PM (n=67)	SM (n=38)
		abs. (%)	abs. (%)
Fever	37–38 °C	15 (22.4 %)	8 (21.1 %)
	38–39 °C	33 (49.3 %)	20 (52.6 %)
	39–40 °C	18 (26.9 %)	10 (26.3 %)
Meningeal syndrome	full	42 (67.2 %)*	8 (21.1 %)
	partial	25 (37.3 %)	24 (63.2 %)*
Vomiting	1–2 times a day	20 (29.9 %)	25 (65.8 %)*
	3–7 times a day	43 (64.2 %)*	11 (28.9 %)
Convulsions	tonic	14 (20.9 %)	21 (55.3 %)*
	focal	9 (13.4 %)*	0
Level of consciousness	obtundation	26 (38.8 %)	24 (63.2 %)*
	sopor, coma	18 (26.9 %)	6 (15.8 %)
Clinical Severity	moderate	10 (14.9 %)	27 (71.1 %)*
	severe	49 (73.1 %)*	11 (28.9 %)
	very severe	8 (12.0 %)	0
Level of damage	meningitis	49 (73.1 %)*	17 (44.7 %)
	meningoencephalitis	18 (26.9 %)	21 (55.3 %)*
Duration of illness	10–14 days	23 (34.4 %)	30 (78.9 %)*
	3–4 weeks	30 (44.8 %)*	6 (15.7 %)
	more than 4 weeks	14 (20.9 %)	2 (5.3 %)
Course of disease	smooth	37 (55.2 %)	29 (76.3 %)*
	complicated	30 (44.7 %)*	9 (23.7 %)
Complications	infectious	20 (29.9 %)	8 (21.1 %)
	neurological	14 (20.9 %)	9 (23.7 %)

Note: *p<0.05 – statistical significance of differences between the PM and SM groups (χ^2 test).

Fever in children with meningitis was high (39–40 °C) only in a quarter of cases; moderate (38–39 °C) or subfebrile (37–38 °C) temperature was found most often without distinction between groups. Vomiting was seen in most patients, but in children with PM it was frequent, while in CM, it was single or repetitive, p<0.05. The Meningeal syndrome was found in all (100 %) patients with PM and 84.2 % of children with CM. The full range of meningeal signs in children with PM was observed three times more often than in children with SM, p<0.05. Children with CM often had partial meningeal syndrome (63.2 percent) or no symptoms of meningitis (15.8 percent). In 33.4 % of cases, children with PM developed tonic seizures; seizures were less common. Children with SM were more likely to have seizures (55.3 percent) and to be tonic in all cases. In the CM group (63.2 %), the level of consciousness in the form of obtundation was higher than in the PM group (38.8 %).

Patients were admitted to hospitals of varying degrees of clinical severity. Children with PM have a severe form (73.1 %), and children with SM have a moderate form (71.1 %), p<0.05. A severe form was observed only in patients with PM (12.0 %). The level of neural damage in 73.1 percent of children with PM was equivalent to meningitis, in SM to meningoencephalitis/meningoen-

cephalitis (55.3 %). Only one-third of patients (34.4 %) had a PM duration of 10–14 days. Most PM patients lasted 3–4 weeks (44.8 %) or over a month (20.9 %). In most cases, PM (78.9 %) was cleared within 10–14 days.

Infectious complications were detected similarly in children with PM (29.9 %) and SM (21.1 %), but complications differed. In the PM group, toxic shock syndrome – (26.9 %), disseminated intravascular coagulation syndrome (4.5 %), multiple organ failure (3.0 %), and brain abscess (1.5 %) were recorded, and in the SM group – carditis (18.4 %) and arthritis (7.6 %) were registered. 76.1 % of children with PM and 76.3 % of children with SM recovered without residual outcomes. A lethal outcome was seen among children with PM (3.0 %).

Neurological disorders in children with meningitis are presented in Table 3.

Table 3

Neurological disorders in children with purulent and serous meningitis in the short and long term

Organic neurological disorders	Observation periods			
	PM short term (n=67)	PM long term (n=61)	SM short term (n=38)	SM long term (n=38)
	abs. (%)	abs. (%)	abs. (%)	abs. (%)
Total	14 (20.9 %)	24 (39.3 %)*	9 (23.7 %)	15 (39.5 %)
Hydrocephalus	11 (16.4 %)	11 (18.0 %)	4 (10.5 %)	4 (10.5 %)
Paresis, paralysis	8 (11.9 %)	16 (26.2 %)*	8 (21.1 %)	9 (23.7 %)
Neurodevelopmental delay	11 (16.4 %)	14 (23.0 %)	9 (23.7 %)	11 (28.9 %)
Epilepsy	2 (3.0 %)	13 (21.3 %)*	2 (5.3 %)	3 (7.9 %)
Visual impairment	1 (1.5 %)	3 (4.9 %)	4 (10.5 %)	5 (13.2 %)
Hearing impairment	2 (3.0 %)	5 (8.2 %)	2 (5.3 %)	3 (7.9 %)
Ataxia	0	1 (1.6 %)	4 (10.5 %)	2 (5.3 %)
Speech disorders	0	5 (8.2 %)	0	2 (5.3 %)

Note: * $p < 0.05$ – statistical significance of differences between observation periods (χ^2 test).

Neurological consequences in the early follow-up period were detected with the same frequency in children with PM (20.9 %) and SM (23.7 %), including hydrocephalus (16.4 %/10.5 %), movement disorders (11.9 %/21.1 %), neurodevelopmental delay (16.4 %/23.7 %), epilepsy (3.0 %/5.30 %), visual impairment (1.5 %/10.5 %), hearing impairment (3.0 %/5.3 %), fronto-cerebellar ataxia (0 %/10.5 %). However, in the long-term period, the frequency of neurological disorders increased only in the PM group (39.3 %), mainly due to epilepsy (21.3 %) and movement disorders (26.2 %).

QOL analysis showed that dysfunction is more common in children with PM. Thus, according to the parameter «Vision», normal functioning was observed in most children with SM (70.7 %) and only in half of children with PM (58.3 %). IF of varying severity in terms

of «Pain and discomfort» is more common in children with PM (81.7 %) than in children with SM (56.9 %). The parameter «Ability to control pain» was also more frequently impaired in children with PM, $p < 0.05$. Cognitive abilities of memory were normal in a third of children with SM (36.2 %) and in isolated cases of PM (6.7 %). Similar results in SM (36.2 %) and PM (15.0 %) were obtained in the aspect of «Cognitive thinking abilities». Impairments of the ability to «Self-care» were mild in 36.2 % of children with SM and 15.0 % of children with PM. On the contrary, severe IF was detected in 23.3 % of children with PM and 10.3 % with SM. Negative emotions of irritability and depression of a mild degree were more often demonstrated by children with SM (65.5 %) and less frequently by children with PM (45.0 %). Severe IF was found in patients with PM (13.3 %) and rarely (1.7 %) in patients with SM, $p < 0.05$. The aspect of «Emotions of happiness» corresponded to normal functioning in 43.1 % of patients with SM and only in 11.7 % of those with PM.

Despite improvements in diagnosis and treatment, meningitis remains a catastrophic clinical disease with a significant risk of neurological complications and adverse outcomes [7].

The high frequency of long-term consequences in purulent meningitis is explained by several adverse events, among which are essential: the age of the child under three years [8, 9], the start of antibiotic therapy delayed by more than 24–72 hours [10, 11], the untimely administration of dexamethasone [12], and the likelihood of developing immune-mediated neurodegenerative inflammation [13, 14].

Conclusion. The study analyses clinical courses and results of purulent and serous meningitis in children in the Republic of North Ossetia–Alania preceding the coronavirus infection. It was established that children of all ages are susceptible to meningitis, but purulent meningitis more often develops in young children (56.7 %) and serous meningitis in toddlers and preschool children (60.5 %). Risk factors for serious meningitis are an unfavourable underlying pathology (52.6 %), preschool nonattendance (65.8 %), purulent meningitis – living in rural areas (61.2 %), and low vaccination rates with licensed vaccines (4.5–9.1 %). Serous meningitis marked the summer-autumn season (83.7 %), and the lack of seasonality was observed in purulent.

Serous meningitis featured a frequent underlying pathology (52.6 %), partial (63.2 %), or absent (15.8 %) meningeal syndrome and widespread damage to the nervous system with the development of meningoencephalitis or meningoencephalomyelitis (55.3 %).

The features of purulent meningitis include the development of severe (73.1 %) or very severe (12.0 %) forms, complications of infectious (29.9 %) or neurological (20.9 %) nature, a long course (65.7 %) and risk of death (3.0 %). Errors in primary diagnosis (44.8 %), hospitalizations to non-specialized hospital departments (20.9 %), and insufficient interpretation of the disease etiology further contribute to the developing of severe and complicated forms.

The frequency and range of neurological disorders in purulent and serous meningitis are comparable during early recovery (after 1–6 months). However, in the long term (after 1–5 years), the progression of neurological disorders manifests itself in bacterial meningitis with increasing frequency of epilepsy and motor disorders.

In children with a history of bacterial meningitis, deeper functional impairments are also detected during self-examination of health indicators related to visual

function, pain, and ability to control it, cognitive ability of memory and thinking, self-care, and the emotional sphere.

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