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The incidence of neurological complications of varicella-zoster virus infection in hospitalised children in a population with low vaccination coverage

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ABSTRACT

Introduction: Varicella is an infectious disease with potentially severe and not uncommon complications.

Aim of the study was to assess the occurrence of neurological complications of varicella-zoster virus among hospitalised children and to analyse the specific clinical picture and outcome.

Material and methods: This retrospective study reviewed the medical records and collected post-hospitalisation interviews of children admitted to the hospital for varicella complications between January 2009 and December 2018. None of the patients was vaccinated. Patients were divided into two groups: neurological and non-neurological complications. Statistical analysis of the data was performed, and the results were compared with published data.

Results: Of the 484 patients admitted to the hospital with chickenpox, 71 (14.7%) met the study assumption of neurological complications. The median age of subjects in the study group was 4.3 years old (2 months to 16 years). The leading causes for hospitalisation in the study group were: cerebellar ataxia (39.4%), convulsions (26.8%), meningitis and encephalitis (14.1% each). An association between age and type of neurological complication was found. Rates of hospitalisation decreased with age, and the highest was found in children in the first six years of life. No laboratory parameter was found to be a prognostic factor for the development of neurological consequences. The majority of patients showed no comorbidity and hence were not considered as potentially at risk of a severe course of illness. The clinical outcome at one-year follow-up was favourable in most patients (64 of 71, 91.5%). One child died (1.4%).

Conclusions: The potential severity of neurological complications and sequelae of chickenpox in unvaccinated children is significant. Even though neurological complications of chickenpox may not result in long-term effects, they significantly prolong hospitalisation.

KEY WORDS:

chickenpox, neurological complications, pediatric, varicella-zoster virus.

INTRODUCTION

Varicella (chickenpox) is a highly infectious disease caused by airborne spread of the varicella-zoster virus (VZV), occurring primarily in childhood and, as it is usually self-limiting, is perceived as a common but harmless

condition. Nevertheless, complications are frequently described: mainly cutaneous bacterial superinfections, pulmonary, hepatic and haematological disorders, and central nervous system disturbances. The neurological complications of chickenpox may be caused either by the primary infection or virus reactivation, the latter being more common

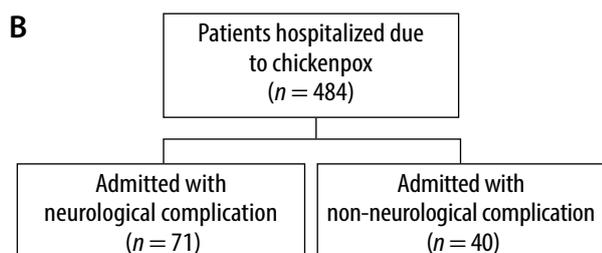
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TABLE 1. A) Definitions and diagnostic criteria of the clinical syndromes. **B)** Process of recruiting patients to the study

A

Ischaemic stroke	An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction defined as cell death attributable to ischaemia, based on clinical evidence of cerebral, spinal cord, or retinal focal ischaemic injury with symptoms persisting ≥ 24 hours and other aetiologies excluded
Meningitis	≥ 2 of following: fever $> 38^{\circ}\text{C}$; meningeal signs; headache; nausea/vomiting plus: <ul style="list-style-type: none"> • pleocytosis with leucocytes $> 5/\mu\text{l}$ • negative CSF bacterial culture • no signs of brain parenchymal involvement
Encephalitis	≥ 2 of following: fever $> 38^{\circ}\text{C}$; pleocytosis with leucocytes $> 5/\mu\text{l}$; abnormality in EEG; abnormal neuroimaging Signs of brain parenchymal involvement: <ul style="list-style-type: none"> • altered mental status or decreased consciousness • focal neurological deficit • seizures



among elderly and immunocompromised patients. These include meningoencephalitis, acute cerebellar ataxia, post-infectious encephalitis, stroke or stroke-like episodes, vasculopathy and convulsions. The neurological sequelae rates vary among different studies, from 7.8% to 25.4% [1–5].

There are around 150,000 cases of varicella annually in Poland, with an increase in the number of noted cases every few years and seasonal patterns typical for the temperate climate. In 2018, the last year of the analysed period, 149,565 cases of VZV infection were registered nationally, with a hospitalisation rate of 0.73%. The majority of cases, i.e. 72,797, were children aged 0–4 years. 57,178 belonged to the group aged 5–10 years and only 11,275 were children above ten years.

MATERIAL AND METHODS

This single-centre retrospective study was performed to describe the clinical, laboratory and radiological features of neurological complications related to acute VZV infection in non-vaccinated children and determine the role of prognostic factors. Ethics committee clearance was obtained for the study (Protocol No. 1235/18 of 6 December 2018).

Of 484 children admitted to the Department of Infectious Diseases and Child Neurology between January 2009 and December 2018 due to chickenpox diagnosed based on typical clinical symptoms (rash with or without fever), 71 aged 2 months to 16 years, with signs of central or peripheral nervous system involvement associated with VZV infection, were included in the study group. A list of the signs and symptoms is presented in Table 1 A. Patients were identified using the International Statistical Classification of Diseases 10th Revision (ICD-10). Forty patients assigned to the control group presented with clinical features of acute VZV infection and no neurological abnormalities. The control group was admitted to the hospital due to the severe course of disease with high fever, multiple skin lesions, non-neurological complications, bacterial superinfections, inflammation of the lower respiratory tract, and gastroenteric symptoms most common (Table 1 B). Diagnosis of chickenpox made at admission was based on a typical unquestionable clinical picture, causing no need for further molecular testing.

Analysed laboratory parameters included cellular blood count with differential, clinical chemistry parameters, C-reactive protein and cerebrospinal fluid (CSF) analysis when available. Laboratory tests were performed on standard analysers.

Radiological data and electroencephalography (EEG) tests were obtained. Computed tomography (CT) or magnetic resonance imaging (MRI) scans of the brain were performed in the case of suspected meningitis, encephalitis or stroke based on clinical signs and symptoms presented in Table 1 A. Central nervous system imaging was performed based on computed tomography in all patients with suspected neuroinfection prior to lumbar puncture to exclude contraindications for the procedure.

In patients with suspected encephalitis or stroke, MRI as a gold standard was performed. However, due to the reduced availability of the test during the study period, CT was, in most cases, the first imaging performed to exclude, inter alia, a proliferative process.

None of the patients was immunised against VZV due to the parental decision, despite the absence of clear contraindications to vaccination.

Every patient admitted for hospitalisation was treated with intravenous acyclovir.

Data analysis included a detailed history, abnormalities in physical examination, fever duration, neurological features, and hospitalisation duration. The clinical outcome of the patients was determined from the clinical charts and post-hospitalisation questionnaire containing questions regarding the neurological sequelae, including quality of development after diagnosis, the occurrence of epileptic seizures and indications for antiepileptic treatment and the need for neurological and psychological ambulatory care. Analysis of prognostic factors included: age, the severity of general and neurological symptoms,

laboratory findings, and treatment administration time. The follow-up was planned for one year.

STATISTICAL ANALYSIS

Statistica software version 13.3 (TIBCO Software Inc., Palo Alto, USA) was used for statistical analysis. The results are presented as mean, standard deviation (SD), median and interquartile range (IQR) where appropriate. Categorical variables are presented as frequencies. The normality of the analysed data was evaluated by the Shapiro-Wilk test. The differences between groups were assessed by the Mann-Whitney *U*-test and the Student *t*-test for continuous variables (where appropriate). The χ^2 test was used for categorical variables. Results were considered statistically significant with a *p*-value < 0.05.

RESULTS

Of the total of 71 patients included in the study group, peak admission time was noted in the period from December to May with 73.2% (*n* = 52) of hospitalisations. The maximum admission rate was registered in March (*n* = 14) and April (*n* = 10) with a seasonal decline in August and September. The mean age of patients affected by VZV infection neurological complications was 4.8 years (IQR: 3.2–5.7 years); a similar proportion of cases was noted in males and females (*n* = 38, 53.5% and *n* = 33, 46.5% respectively).

The distribution of seasonal pattern, gender and mean age in the control group was similar to that noted in the study group. Table 2 displays the main characteristics of hospitalised patients. The median hospital stay was 10 days (IQR: 6–12 days). In one case of encephalitis with multiple complications, the total hospitalisation time was prolonged to 87 days due to the severity of the disease. Overall, 95.6% (*n* = 66) of patients enrolled in the study

group had no medical condition predisposing to varicella complications. An underlying medical condition was reported in 3 children in the study group (2 had epilepsy, one had developmental delay) and 5 among the control group (two had a diagnosis of genetic disorders, and the remaining 3 had cystic fibrosis, epilepsy and nephritic syndrome).

The majority of patients from the analysed groups recovered from the disease and its complications. 21 of 71 (29.6%) children with neurological complications of chickenpox had sequelae, most commonly prolonged gait disturbances in patients with cerebellar ataxia (*n* = 8, 38%). Three patients with ischaemic stroke and one with encephalitis suffered from unilateral paresis. Three children developed seizure episodes that ultimately resulted in antiepileptic treatment. Other complications reported at follow-up included impaired speech development (*n* = 1), memory impairment (*n* = 1) and attention deficit disorder (*n* = 3). One patient with meningitides suffered from prolonged headaches but fully recovered within two months.

One child with a suspected inborn error of metabolism succumbed after prolonged hospitalisation with multiple complications, with multiorgan failure as a cause of death. Due to a lack of parental consent for the autopsy, the underlying cause of the severity of the disease course is unknown.

Of all neurological complications in the study group, the most frequently diagnosed were: cerebellar ataxia (39.4%, *n* = 28), convulsions found in 19 patients (26.8%), followed by meningitis and encephalitis in 10 children each (14.1%). Three children were diagnosed with ischaemic stroke (4.2%) and one only with unilateral facial nerve palsy (1.4%)

There was a noticeable decline in hospitalisation rates with age in both groups (Figure 1 A). The highest frequency (67.6%, *n* = 48) of neurological complications was

TABLE 2. General characteristics of 111 varicella-zoster virus related hospitalisations in tested groups

Characteristics	Total <i>N</i> = 111	Study group <i>n</i> = 71	Control group <i>n</i> = 40	<i>p</i> -value
Gender: male/female, <i>n</i> (%)	60 (54.1)/51 (45.9)	38 (53.5)/33 (46.5)	22 (55)/18 (45)	0.88
Mean age in years \pm SD	4.8 \pm 3.5	4.8 \pm 2.8	4.8 \pm 4.6	
Median age in years (IQR)	4.1 (2.72–5.84)	4.3 (3.2–5.7)	3.6 (1.1–6.6)	0.15
Median time: start of exanthema to hospital admission in days (IQR)	3 (2–7)	6 (3–9)	2.5 (1–3)	< 0.0001
Median hospital stay in days (IQR)	8 (5–11)	10 (6–12)	5.5 (4–7)	0.0001
Hospital stay \leq 7 days, <i>n</i> (%)	55 (49.5)	22 (31.0)	33 (82.5)	< 0.00001
Hospital stay \geq 14 days, <i>n</i> (%)	17 (15.3)	16 (22.5)	1 (2.5)	0.005
Outcome, <i>n</i> (%)				
Cure	88 (79.3)	48 (67.6)	40 (100)	0.0001
Sequelae	22 (19.8)	22 (31.0)	–	
Death	1 (0.9)	1 (1.4)	–	

IQR – interquartile range, SD – standard deviation

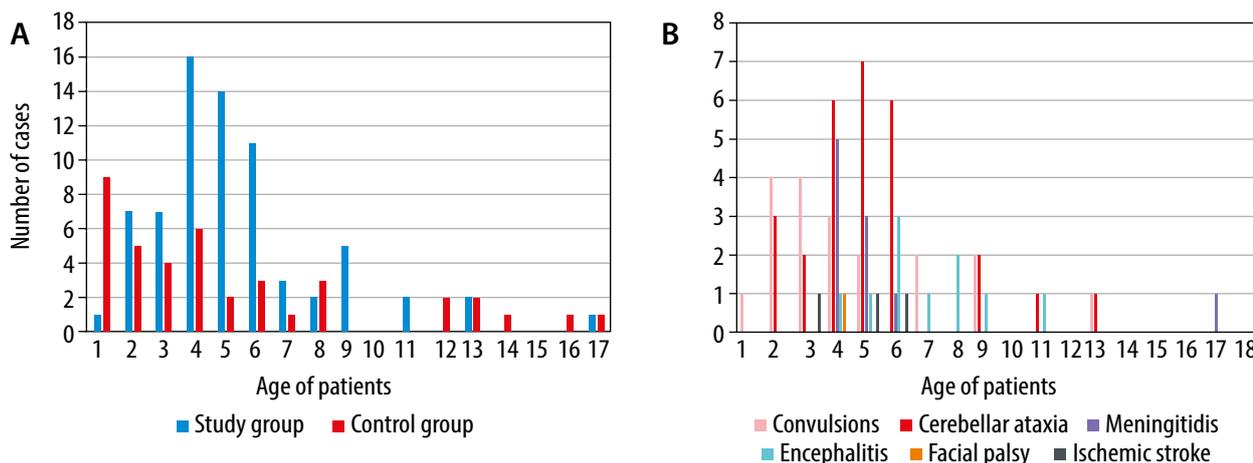


FIGURE 1. A) Number of cases. B) Type of complication

observed in a group of children aged 3-6 years. Younger children, 0-2 years old, constituted 11.2% ($n = 8$), 14.0% ($n = 10$) aged 6-10, and 7.0% ($n = 5$) over 10 years of age.

In the youngest group of patients, below two years old ($n = 8$), the final diagnoses were: convulsions in five and acute cerebellar ataxia in three. In the biggest group of children aged two to six years, the predominately represented clinical syndrome was acute cerebellar ataxia ($n = 21$), followed by convulsions and acute aseptic meningitis diagnosed in 9 patients each, with acute encephalitis ($n = 5$) and ischaemic stroke ($n = 3$) being least common. In children aged 6-10 years ($n = 10$), diagnoses of convulsions and acute encephalitis were made four times each, and in two children diagnosis of acute cerebellar ataxia. Above the age of ten years, only five patients were in need of hospitalisation due to neurological complications of chickenpox, and the diagnoses made were as fol-

lows: acute cerebellar ataxia in two cases and each of the following once: acute aseptic meningitis, convulsions and acute encephalitis.

Diagnosis of convulsions was present in every age group, predominantly ($n = 14$) in the youngest children up to 60 months. The final diagnosis made in this group was febrile seizures. Among older children over 5 years old ($n = 5$), only one had a diagnosis of epilepsy before a seizure attack during chickenpox. The rest of the patients, hospitalised after the first unprovoked seizure episode and hence who did not meet the criteria for epilepsy, were at discharge referred to specialist neurological care for further observation. As we reported previously [6], from the remaining patients, one child was diagnosed with epilepsy eventually. For the rest of the children, convulsions causing the need for hospitalisation in chickenpox were the only seizure episode in the follow-up.

Neurological complications during VZV infections in children above 10 years of age (7.2%) were less common in proportion to the total number of varicella cases, predominantly presented as cerebellar ataxia and CNS inflammatory diseases. Finally, encephalitis and meningitis were observed with similar incidence throughout older age groups (40% in children aged over 10 years and 6-10 years, 33.3% in children aged 4-6 years) with the less common presentation in younger children (29.7% in the 2-4-year-old group, and no case below that age). Data are presented in Figure 1 B.

Interestingly, our study showed a link between age and the type of neurological complication. Children with a diagnosis of encephalitis were distinctively older than those without any neurological complication, as well as with other types of neurological diagnosis. Table 3 displays the type of neurological complication concerning the age of hospitalised patients.

Taking into account the dominant symptoms in the context of the final diagnosis, we found that headache was most commonly diagnosed with meningitis, followed by cerebellar ataxia and encephalitis (31%, 27.6% and 24.1%, respectively). Emesis was often reported by patients diag-

TABLE 3. Principal diagnosis concerning age in the study and control groups

Main diagnosis	Age			
	Mean \pm SD	Median	IQR	<i>p</i> -value
Study group				
Cerebellar ataxia ($n = 28$)	4.77 \pm 2.5	4.35	3.2-5.6	0.21
Convulsions ($n = 19$)	4.07 \pm 3.0	3.10	1.9-6.0	0.91
Meningitis ($n = 10$)	5.25 \pm 3.9	4.04	3.4-4.8	0.33
Encephalitis ($n = 10$)	6.46 \pm 2.1	5.85	5.2-7.9	0.034
Ischaemic stroke ($n = 3$)	4.11 \pm 1.5	4.30	2.5-5.5	0.75
Facial palsy ($n = 1$)	3.60	-	-	-
Control group				
VZV ($n = 40$)	4.77 \pm 4.6	3.62	1.1-6.6	-

IQR – interquartile range, SD – standard deviation, VZV – varicella-zoster virus

TABLE 4. Results of cerebrospinal fluid (CSF) analysis in the subgroup with confirmed meningitis and encephalitis. (Suspected: patients with clinical signs of meningitis; confirmed: patients with abnormal results of CSF analysis)

Main diagnosis		Meningitis	Encephalitis	p-value
Number tested		Suspected: 8	Suspected: 9	
		Confirmed: 7	Confirmed: 5	
Pleocytosis [cells/ μ l] Normal < 5	Mean \pm SD	172.0 \pm 321.3	55.6 \pm 31.9	0.5
	Median	31.0	60.0	
	IQR	6.0–160.0	25–80	
Protein [mg/dl] Normal: 15–45	Mean \pm SD	26.6 \pm 10.4	28.4 \pm 11.1	0.57
	Median	27.0	32.0	
	IQR	16.0–30.0	18.0–34.0	
Glucose [mg/dl] Normal: 60% serum	Mean \pm SD	57.7 \pm 17.3	56.8 \pm 11.6	0.64
	Median	52.0	52.0	
	IQR	48.0–65.0	50.5–63.0	

nosed with cerebellar ataxia (40.6%), meningitis (21.9%) and encephalitis (18.7%), the rest of the cases being connected with convulsions (12.5%) and ischaemic stroke (6.3%). Dizziness, as a single symptom, predominantly occurred in patients diagnosed with cerebellar ataxia (81.3%) and less commonly with encephalitis (12.5%) and meningitis (6.2%).

Analysing every type of complication in the study group separately, we found that among patients with cerebellar ataxia, the most commonly reported symptoms were: dizziness (100%), broad-based gait (78.6%), vomiting (42.8%), with headache and dysmetria (28.6% each) reported least. In the group diagnosed with meningitis, the single most characteristic sign was nuchal rigidity (100%); 80% of patients presented with a fever above 38.5°C and 70% with vomiting. 9 of 10 children in this group complained of severe headaches. Most patients diagnosed with encephalitis complained of persistent headache (90%) and showed signs of consciousness disturbances at different levels (70%). In 7 of 10 patients, emesis was present, and 50% complained of dizziness. Among uncommon observations, meningeal signs were present in only 4 of 10 children, and fever in 30% of patients. All patients diagnosed with an ischaemic stroke presented with symptoms of consciousness disturbances, while convulsions and emesis were present in 2 of 3 (66.6% each).

Among 71 patients with neurological complications associated with VZV infection, 28 developed symptoms suggestive of CNS infection, which resulted in a lumbar puncture and CSF collection after excluding increased intracranial pressure with computed tomography (CT). Half of this subgroup ($n = 14$) had an abnormal result of the general analysis of cerebrospinal fluid (CSF), with the majority of patients being ultimately diagnosed with either meningitis ($n = 7$; 50%) or encephalitis ($n = 5$; 35.8%), and the remaining case with cerebellar ataxia and convulsions ($n = 1$; 7.1% each). CSF of the patients with

encephalitis showed milder pleocytosis (range 29–92 cells per microliter) compared to the patients diagnosed with meningitis, and the difference was not statistically significant. Levels of protein and glucose in CSF in all those patients were within the normal range with $p = 0.57$ and $p = 0.64$, respectively (Table 4).

Neuroimaging studies in the form of computed tomography (CT) were performed in all patients with suspected neuroinfection, showing no abnormalities in all patients with meningitis and in 3 of 6 (50%) patients with the final diagnosis of encephalitis. Of eight children with encephalitis who underwent magnetic resonance imaging (MRI), six (75%) had abnormal results. Nine patients with acute cerebellar ataxia underwent computed tomography, which in one patient indicated the development of generalised cerebellar oedema. Two more children had magnetic resonance imaging (MRI), with no abnormal results. All three patients diagnosed with stroke underwent MRI, and the results of all tests in this group were anomalous. The images of the MRI of the first patient showed in the sagittal parts of the left temporal lobe at the temporal corner of the lateral ventricle and area of increased signal – a sign typical for acute ischaemic stroke. The MRI neuroimaging of the second patient revealed extensive ischaemic stroke of the right hemisphere in the areas supplied by the middle cerebral artery, including the frontal, temporal, parietal lobes and islet. In the third child diagnosed with ischaemic stroke, we found features of diffusion restriction in diffusion-weighted imaging sequences typical for frontal cerebral artery supply.

Electroencephalographic (EEG) studies had significant value in confirming the diagnosis and monitoring the disease in patients with encephalitis and stroke, showing abnormal brain activity in every patient tested. None of the patients with meningitis and only four with acute cerebellar ataxia underwent EEG, showing a normal result. The detailed results of neuroimaging and electrophysiology studies in the analysed patients were presented in a pre-

TABLE 5. Study and control group clinical and laboratory parameters

Characteristics	Study group			Control group			p-value
	M ±SD	Median	IQR	M ±SD	Median	IQR	
Time: onset of exanthema to hospital admission (day)	10.88 ±17.33	6	3-9	2.60 ±3.76	2.5	1.0-3.0	< 0.0001
Median hospital stay (day)	11.18 ±10.32	10	6-12	5.82 ±2.65	5.5	4.0-7.0	< 0.0001
WBC [10 ³ /μ]	10.13 ±4.63	8.66	3.07-23.59	8.64 ±4.39	7.11	5.74-10.6	0.050
Neutrophils [10 ³ /μ]	5.36 ± 3.85	4.1	2.8-6.7	3.37 ± 2.17	3.17	1.7-4.1	0.0001
Lymphocytes [10 ³ /μ]	3.04 ± 1.6	2.67	1.72-3.8	3.18 ± 1.84	2.45	2.1-4.6	0.294
RBC [10 ⁶ /μ]	4.52 ±0.38	4.53	3.45-5.68	4.34 ±0.44	4.34	4.03-4.72	0.040
HGB [g/dl]	12.25 ±0.92	12.2	11.7-12.8	12.37 ±1.95	12.3	11.3-13.0	0.605
HCT [%]	35.42 ±3.02	35.2	33.8-37.3	35.13 ±3.98	35.55	32.95-37.05	0.762
PLT [10 ³ /μl]	292.36 ±97.28	291.0	221-347	235.42 ± 80.49	220.0	156.5-313.0	0.0019
CRP [mg/dl]	1.52 ±3.62	0.40	0.2-1.13	2.03 ±3.24	0.98	0.41-2.41	0.005
AST [IU/l]	39.36 ±30.62	34.0	28.0-41.0	46.16 ±19.85	42.0	30.0-61.5	0.0152
ALT [IU/l]	22.39 ±22.37	16.0	13.0-24.5	30.64 ±22.43	24.0	18.0-34.0	0.0002

ALT – alanine transaminase, AST – aspartate transaminase, CRP – C-reactive protein, HGB – haemoglobin, HCT – haematocrit, PLT – platelets, RBC – red blood cells, WBC – white blood cells

vious paper [6], where we reported that the most severe anomalies were linked with the diagnosis of encephalitis.

There was a distinctly longer time of hospitalisation in patients forming the study group (11.2 vs. 5.8; $p < 0.001$), which can be correlated with the severity of the disease (Table 5).

Children in the study group were admitted to the hospital after a longer time starting from the onset of symptoms than those in the control group (10.9 vs. 2.6 days; $p < 0.001$). C-reactive protein activity in patients' sera was statistically significantly lower in the study group ($p = 0.005$), with no such difference noted in the white blood cell count.

In blood the differential level of neutrophils was notably higher in the study group than results obtained in the control group (5.4 vs. 3.4; $p < 0.0001$). No such difference was noted concerning lymphocytes.

There was a difference in the platelet level measured at the moment of admission between the two groups. Mean values in both groups were within the reference values for age but distinctively higher in the studied group (292.36 vs. 235.42; $p = 0.024$). Opposite results were obtained concerning ALT and AST activity in patients' sera, with higher levels in the control group (22.4 vs. 30.6; $p < 0.001$ and 39.4 vs. 46.2; $p = 0.015$ respectively).

DISCUSSION

The proportion of children hospitalised due to neurological complications of chickenpox varies significantly among reports, from 7.8% to 25.4% [1-4, 8, 9], and may depend on population sociodemographic structure (age, comorbidities, etc.) and different hospitalisation policies. The prevalence reported in this study (71 of 484; 14.7%) is within values described by other authors. Comparably,

the study period's seasonal incidence is commonly observed [5, 8, 9, 11].

The mean age of 4.8 years in the study group corresponds with reference data. Analogically to other reports and typically for varicella morbidity, most admitted patients were younger than 10 years, with the majority below 6 years [1-4, 8, 10-12]. The wide range of susceptible cells and the level of maturity of immune response correlate with the diversity of clinical manifestations of VZV infection [18]. The explanation for this age-related association with the type of neurological complication may be the hypothesis that an active VZV infection triggers an autoimmune response leading to neurological complications, which occurs more frequently in older, more immunocompetent children [5, 9, 18].

Our study analysed multiple variables to determine differences in chickenpox clinical course and establish a possible prognostic factor. The most significant differences in the analysed groups were noted regarding the duration of symptoms before hospital admission, with a prolonged pre-hospital time of disease in patients with neurological complications. Furthermore, the duration of hospitalisation was significantly longer in this group of children. An explanation of this phenomenon might be that VZV less frequently causes direct neuronal injury. Usually, the virus stimulates the immune system, which triggers neurological symptoms. Therefore, they develop later in the course of infection. Moreover, the patient immune system pathological activity induced by VZV infection leads to more extended and severe clinical presentation and prolonged hospital stay [17, 18].

Despite the statistical difference, no analysed laboratory parameter seems to be a prognostic factor for developing neurological complications. Our data show that the mean CRP values in both groups were significantly

lower in the study group compared to the control group. The control group consisted of children without neurological consequences of chickenpox, yet some developed bacterial infections of skin lesions. In the reviewed reports, the vast majority of authors conclude that no statistically significant correlation was found between severity of VZV infection and intensity of immune response in the form of levels of acute-phase reactants (i.e. WBC, CRP), which is consistent with our results [19–22].

The difference in platelet count between the study and control group is of low clinical significance since both values are within the reference limits.

A mild increase in aminotransferase activity is typical in childhood varicella, even in uncomplicated cases. Nevertheless, increased aminotransferase activity is considered a clinical expression of visceral disseminated VZV infection [23]. This complication is commonly found in immunocompromised patients and is an independent predictive factor of increased mortality rate in infected individuals [14, 15]. In our study, aminotransferase activity was lower in the group with neurological complications but still within reference values in both groups. The difference between the two groups is apparent, but its clinical significance is not unambiguous enough to assume a relationship with the risk of disease complications. This observation requires further research.

The most common forms of CNS involvement observed in the study group were cerebellar ataxia (39.4%) and convulsions (26.8%). The majority of children met the criteria of febrile seizures. One had diagnosed epilepsy before the current hospitalisation and one developed epilepsy in the follow-up. The remaining patients did not meet the criteria for febrile seizures or for epilepsy as they developed the first unprovoked seizure episode. During the follow-up only one child was diagnosed with epilepsy eventually. For the rest of the children, convulsions causing the need for hospitalisation in the course of chickenpox were the only seizure episode.

Neuroimaging was performed in patients with clinical indications confirming the diagnosis. The findings included cerebellar oedema in cerebellar ataxia or ischaemic regions in the cases of stroke. The EEG allowed monitoring of the abnormal brain activity in the patients with encephalitis or stroke, being normal in children with cerebellar ataxia. Both types of tests enable proper differential diagnosis and monitoring of the patients with various forms of CNS complications in chickenpox.

It should be stressed that none of the patients was immunised against VZV despite the absence of contraindications to vaccination. It is also noteworthy that most patients in the analysed groups did not suffer from chronic diseases. Hence they were not recognised as potentially at risk of a severe course of illness by their caregivers.

The importance of home and schools as environments of transmission has been highlighted in most studies. The morbidity and hence the number of complicated cases

of VZV infection could be diminished by introducing routine varicella vaccination. The vaccine is still recommended in the Polish vaccination schedule but not compulsory and not supported by the government. The obtained results may be a valid argument for the benefit of that solution.

CONCLUSIONS

Our study confirms that severe neurological complications of VZV infection in children may develop in otherwise healthy patients with possible severe and long-term sequelae. No laboratory parameter was found to be a prognostic factor for the development of neurological consequences. Even though neurological complications of chickenpox may not result in long-term effects, they significantly prolong hospitalisation.

DISCLOSURE

The authors declare no conflict of interest.

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