

## Udary u dzieci Strokes in children

Wiktroria Sielwanowska<sup>1</sup>, Bartłomiej Syzdoł<sup>1</sup>, Monika Żybowska<sup>1</sup>, Anna Rzewuska<sup>1</sup>,  
Magdalena Chrościńska-Krawczyk<sup>2</sup>

**1 Student Scientific Society at the Department of of Paediatric Neurology, Medical  
University of Lublin, Gębali 6, 20-093 Lublin, Poland**

**2 Department of Paediatric Neurology, Medical University of Lublin, Gębali 6, 20-093  
Lublin, Poland**

Wiktroria Sielwanowska: <https://orcid.org/0000-0002-4660-5027>

e-mail: [wiktoria.sielwanowska@gmail.com](mailto:wiktoria.sielwanowska@gmail.com)

Bartłomiej Syzdoł <https://orcid.org/0000-0001-5940-7399>

e-mail: [bartlomiej.syzdol@gmail.com](mailto:bartlomiej.syzdol@gmail.com)

Monika Żybowska: <https://orcid.org/0000-0002-3885-5907> e-mail: [zybowska.m@gmail.com](mailto:zybowska.m@gmail.com)

Anna Rzewuska: <https://orcid.org/0000-0003-4553-0825> e-mail: [aniarzewuska@wp.pl](mailto:aniarzewuska@wp.pl)

Magdalena Chrościńska-Krawczyk: <https://orcid.org/0000-0001-8121-6580> e-mail:  
[magdalenachk@wp.pl](mailto:magdalenachk@wp.pl)

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### Streszczenie

Udar mózgu to zespół objawów neurologicznych, powstałych w wyniku nagłego zatrzymania dopływu krwi do mózgu. W grupie pacjentów pediatrycznych udar mózgu występuje stosunkowo rzadko. Częstość występowania szacuje się na 2,5 przypadki na 100 000 dzieci w ciągu roku. Śmiertelność sięga do ok. 4%. Długotrwałe następstwa i powikłania dotyczą ponad połowy pacjentów.

Etiopatogeneza udaru mózgu u dzieci jest zróżnicowana. Główne czynnikami ryzyka to wrodzone wady serca, uszkodzenia naczyń, choroby metaboliczne i infekcje. Objawy udaru mózgu są zależne od lokalizacji i rozległości zmian niedokrwienych. U dzieci początkowo mogą być niecharakterystyczne. Najczęściej występują bóle głowy, wymioty, drgawki, zaburzenia świadomości, niedowłady połowicze. Złotym standardem w obrazowaniu niedokrwienia mózgu jest angiografia metodą rezonansu magnetycznego mózgu (MRA). W leczeniu istotną rolę odgrywa kontrolowanie podstawowych parametrów życiowych. Leczenie obejmuje leki antyagregacyjne i przeciwzakrzepowe. Możliwe jest przeprowadzenie transfuzji krwi lub leczenie chirurgiczne. Powikłania udaru mózgu u dzieci są zróżnicowane i zależą od wielu czynników. Należą do nich zaburzenia ruchowe, upośledzenie funkcji poznawczych, napięciowe bóle głowy, trudności z ekspresją i płynnością mowy.

Udar mózgu to stan zagrożenia życia, który wymaga wdrożenia natychmiastowego leczenia. U dzieci może dawać niecharakterystyczne objawy. Ostre niedokrwienie mózgu u dzieci niesie za sobą ryzyko wstąpienia długofalowych, ciężkich powikłań. Pacjenci pediatryczni po przebytych ostrym niedokrwieniu mózgu powinni być pod stałą opieką

specjalistycznych ośrodków leczniczych i rehabilitacyjnych, które umożliwią pacjentom samodzielne funkcjonowanie wśród swoich rówieśników.

## **Abstract**

### **Introduction and purpose**

A stroke is a group of neurological symptoms that develops when blood flow to the brain is stopped suddenly. Stroke is relatively rare in the group of pediatric patients. The incidence is estimated at 2.5 cases per 100,000 children per year. Mortality is up to 4%. Long-term consequences and complications concern more than half of the patients.

### **Brief description of the state of knowledge**

The etiopathogenesis of stroke in children is diverse. The main risk factors are congenital heart disease, vascular damage, metabolic diseases and infections. The symptoms of a stroke depend on the location and extent of the ischemic changes. In children they may initially be uncharacteristic. The most common are headaches, vomiting, convulsions, disturbed consciousness, and hemiparesis. The gold standard in cerebral ischemia imaging is brain magnetic resonance angiography (MRA). In treatment controlling vital parameters plays an important role. Treatment includes anti-aggregating and anticoagulant drugs. It is possible to transfuse blood or surgical treatment. Complications of stroke in children are diversify and depend on a lot of factors. These include movement disorders, cognitive functions impairment, tension headaches and difficulty with expression and fluency of speech.

### **Conclusion**

A stroke is a life-threatening condition that requires immediate treatment. It can have uncharacteristic symptoms in children. Acute cerebral ischemia in children carries the risk of developing long-term, severe complications. Pediatric patients with a history of acute cerebral ischemia should be under the constant care of specialized treatment and rehabilitation centers, which will enable patients to function independently among their peers.

### **Introduction**

Stroke is a relatively rare but increasingly recognized disease in children. Over the last twenty years, the number of hospitalizations of children diagnosed with stroke has increased significantly[1]. The first studies conducted in 1965 -1974 by Schoenberg et al. estimated the incidence of strokes among children at 2.5/100,000 per year. The ischemic strokes constituted about 30%, ie 0.63/100,000 per year, and hemorrhagic strokes - about 1.89/100,000 per year [2]. Other studies conducted by Lynch et al. in 1980 -1998 among children from birth to 18 months of age indicate the occurrence of ischemic stroke in children at 7.8/100,000 per year, and hemorrhagic stroke at 2.9/100,000 per year [3]. Mortality is about 4%, while over 50% of children suffer from the long-term consequences of acute cerebral ischemia. These include movement disorders, mental retardation, seizures, psychosomatic symptoms and much more others. [4.5]

## **Reasons and risk factors**

The risk factors and the etiopathogenesis of strokes in children are different and significantly less understood than in adults. Only in 50% of patients it is possible to indicate a certain cause of acute cerebral ischemia. In about 30% patients, despite the complete diagnostics, the cause cannot be identified [6]. The main risk factors are heart disease, most often congenital heart disease, autoimmune vasculitis, hematological disorders, structural vessel abnormalities, systemic vascular disease, vascular damage - injuries, metabolic diseases, and inflammatory diseases -including infections. It is worth paying attention to the possibility of acute cerebral ischemia caused by genetic factors, especially in the case of lipid metabolism disorders, blood coagulation disorders or immune disorders [7]. Contrary to adults, the occurrence of stroke in children is rarely associated with arterial hypertension and diabetes [8]. Heart diseases that significantly increase the risk of stroke in children include congenital defects of the cardiovascular system i.e. ventricular and interatrial septal defects, patent ductus arteriosus, and acquired heart diseases such as rheumatic disease and conduction disorders. The literature emphasizes the importance of immunological factors. High levels of antiphospholipid antibodies, which are present in high concentrations in the course of systemic lupus erythematosus and antiphospholipid syndrome, often lead to vascular incidents in the brain in children [9]. Primary antiphospholipid syndrome is found in 7-9% of children with a history of acute cerebral ischemia [10]. Haematological disorders, which lead to coagulation disorders, play a significant role in the occurrence of strokes in children. They are found in nearly 90% of young patients with venous strokes [6]. Disorders of blood morphotic elements that may contribute to the occurrence of vascular events in the brain include polycythemia vera, thrombocytosis and thrombocytopenia, antithrombin III, protein C and S deficiencies, and Leiden mutations. It is estimated in the literature that as many as 40% of stroke cases in children are caused by coagulopathies [11]. It is very important to perform tests for haemostasis abnormalities. Bonduel et al. emphasize possibility occurrence congenital coagulation disorders at relatives of the patient [12]. Among the metabolic causes of significant importance is the high concentration of homocysteine in the blood, which leads to the development of changes in the wall of blood vessels and the formation of atherosclerosis. Especially in children, a significant relationship has been shown between hyperhomocysteinemia and the risk of acute cerebral ischemia. [13]. Other metabolic causes include Fabry disease - lysosomal storage disease and MELAS syndrome, which includes migraine with aura, deafness, dementia, seizures, retinal degeneration and hypogonadotropic hypogonadism. The number of stroke incidents in children as a result of developing inflammatory diseases has increased significantly in the last two years. The conducted studies showed a relationship with the occurrence of incidents of acute cerebral ischemia in the course of COVID-19. In the study involving 337 pediatric patients during or after COVID-19 infection, eight of them presented signs of acute cerebral ischemia [14,15]. There is little research into the effect of COVID-19 infection in increasing the risk of stroke in children. However, previous studies clearly confirms the relationship with SARS-CoV 2 virus infection and its pro-thrombotic action, by triggering many inflammatory and hemostatic processes [16].

## **Symptoms and diagnosis**

The symptoms of stroke can vary widely. Depending on the location of ischemic lesions, the patient may present only a slight impairment of the functions of one limb. Such

symptoms occur when the lumen of small cerebral vessels is closed or the paresis may affect the entire half of the body. Symptoms may also include Cognitive disorders, epileptic seizures, consciousness and balance disorders, and ataxia. [17]. However, in children, symptoms may be more non-specific. They usually happen suddenly. Sometimes the initial symptoms are seemingly innocent and gradually build up over a period of hours or even days. [18]. In children, the most common symptoms are headaches, vomiting, convulsions, disturbances of consciousness, hemiparesis, as well as symptoms resulting from the palsy of the cranial nerves, including speech disorders. Symptoms may also vary depending on the location of the brain damage and the ability of the collateral circulation. In the course of diagnosis, it is extremely important to analyze the risk factors for stroke occurrence. It is necessary to perform an ECG, heart echo, cerebral flow test, laboratory tests assessing coagulation factors and taking into account hematological disorders, metabolic and autoimmune diseases and inflammation parameters. The basic imaging test is brain magnetic resonance angiography(MRA), which visualizes areas of acute cerebral ischemia and hemorrhagic changes within it. The most useful are the diffusion sequence (DWI) and apparent diffusion coefficient (ADC). When MRI is not available, a computerized tomography (CT) scan can be performed. Unfortunately, it is not as accurate as MRI. The features of acute cerebral ischemia may not be shown. Especially when the CT is performed early (up to 12 hours after the stroke), the ischemic focus is small or is located in the brainstem [19]

## **Treatment**

Treatment of acute cerebral ischemia must be implemented concurrently with the diagnosis. Patients should be hospitalized in specialized centers. The first step is to assess cardiovascular function, including blood pressure, which should not be rapidly lowered. Next, the respiratory system should be assessed. It is recommended to maintain normal body temperature, fluid intake, and avoid hyperglycemia. [20]. When epileptic seizures occur, antiepileptic treatment should be instituted. The occurrence of cerebral edema requires the administration of 20% mannitol 1-2 g / kg / day in 4 doses and furosemide 1-1.5 mg / kg / day in 4 doses. Methods of treating ischemic stroke in children depend on the mechanism of its formation. This may include anti-aggregation and anticoagulant therapy, blood transfusion or surgery [21]. Antithrombotic therapy includes the use of an antiplatelet drug - acetylsalicylic acid at a dose of 3-5 mg / kg / day and anticoagulants (low molecular weight heparin, unfractionated heparin or warfarin). It is recommended to use salicylic acid in a therapeutic dose for 3-5 years after the occurrence of acute cerebral ischemia due to the predisposition to increased platelet aggregation, also due to the antiphospholipid syndrome [19]. In patients with acute cerebral ischemia with sickle cell anemia, one of the treatment options may be blood transfusion [22]. There is insufficient evidence that thrombolytic therapy with tPA tissue plasminogen activator is effective and can be used in pediatric patients [19]. The literature describes single cases of administration of alteplase to young stroke patients, which was associated with a longer duration of treatment and the occurrence of more dangerous and more severe complications [23]. Neurosurgical treatment is not the method of choice for the treatment of acute cerebral ischemia in children. However, hemicraniotomy is considered in pediatric patients with occlusion of the middle cerebral artery [24]. In the case of haemorrhagic stroke, children require urgent neurosurgical intervention to reduce intracranial bleeding and reduce the risk of intussusception [25].

## Complications

The sequelae of acute cerebral ischemia in children are varied and depend on many factors. They are influenced by the location and extent of the ischemic focus, the mechanism of its formation, the age of the child and rate of implementation treatment. Mortality is around 4%. Neurological and neuropsychological complications concern over half of patients [26]. Motor deficits and mild cognitive impairment are the most frequently recognized long-term effects of ischemic stroke in children. Seizures occur in approximately 25% of children. Cortical injuries and the occurrence of epileptic seizures for more than 2 weeks after the onset of acute cerebral ischemia are identified as a risk factor for the development of epilepsy [27]. Other neurological complications of stroke in children include tension headaches, hemiparesis or less severe neurological deficits in the hands and face, difficulties with expression and fluency of speech. In addition to neurological deficits, children after ischemic stroke suffer from attention and concentration disorders, sometimes also from slight cognitive impairment and sleep disorders. Another serious complication is repeated stroke. Its incidence is estimated up to 40%. It is much more common in patients who have several risk factors for stroke, such as congenital thrombophilia and vascular abnormalities. Complete recovery is noted in approximately 40% of patients [28].

## Conclusions

A stroke is a life-threatening condition that requires urgent, detailed diagnosis and immediate treatment. Especially in children, where the mortality rate is relatively high, it should be remembered that it may exhibit initially uncharacteristic symptoms. During diagnostics, one should bear in mind - the risk factors that may predispose children to stroke. Acute cerebral ischemia entails long-term complications in the form of neurological and psychosomatic deficits. Therefore, it is important that a stroke patient should be under the constant care of specialized treatment and rehabilitation centers, which can significantly alleviate the consequences of the disease and enable the child to function among his peers.

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