CONGENITAL NEUROLOGICAL DISORDERS IN CHILDREN WITH MICROCEPHALY

[1]Majidova Y. N., [2]Mambetkarimova M. S.
[1,2]Andijan State Medical Institute
https://doi.org/10.5281/zenodo.10612475

Abstract. *Primary microcephaly (PMCF) is a neurodevelopmental disorder characterized by a small brain size, primarily due to a decrease in the cerebral cortex, and varying degrees of mental retardation (Woods et al., 2005;Mahmood et al., 2011;Phan and Holland, 2021;Zaqout and Kaindl, 2021;Gupta, 2023) and several additional neurological problems such as seizures and epilepsy (Shen et al., 2005), with a prevalence of 1/30,000 to 1/250,000. Brain development depends on neurogenesis, the process by which neural stem cells proliferate, migrate, and differentiate to form neurons, and is fundamental to normal brain development (Stiles and Jernigan, 2010;Исаев и др., 2019 ; Zhou et al., 2020). The formation of neurons begins during embryogenesis and continues throughout life. In mammals, the size of the cerebral cortex is determined by the number of neurons it contains (Borrell and Calegari, 2014). In general, an adult consists of about 86 billion neurons (Herculano-Housel, 2012), and the brain size varies from 975 to 1499^{cm3}. Studies have shown that a decrease in the number of neurons leads to primary microcephaly, which is diagnosed when the circumference of the occipital-frontal region is less than two standard deviations below the average value at birth and/or less than three standard deviations below the average after 1 year of life. (Дуринкс и др., 2020).*

Keywords: *head circumference, microcephaly, syndromes, genetic abnormalities, neuroimaging, Zika virus.*

Neurological development is the product of a multi-factorial process that depends on the interaction of genetic and environmental aspects and is influenced by the quality of nutrition of the mother and child, socio-economic level, and stimuli obtained through experience [1]. The period starting from the moment of conception and ending at the age of two is one of the periods of greatest development of the central nervous system (CNS) and at the same time the most vulnerable [2,3]. Various risk factors can disrupt fetal development. Infectious agents can cross the placental barrier and enter the fetal bloodstream, causing direct damage, causing cytotoxic effects, mitotic inhibition, or events leading to vascular damage. Infectious agents can also cause an aggressive reparative reaction, increasing the area of the lesion and causing intracranial calcification [4]. Fetal developmental disorders studied together with congenital malformations in teratology are not always obvious at birth [5].

Viruses*of the Flaviviridae*family are usually not associated with vertical transmission and do not cause severe changes in the fetus [6]. However, after Зикathe 2015 Zika virus outbreak in Brazil, severe cases of congenital infection were reported [7,8,9]. Cugola et al. (2016) demonstrated that the Brazilian Zika virus strain is able to cross the placental barrier, infect human cortical progenitor cells, and promote cell death by inducing apoptosis and autophagy. Consequently, they observed a decrease in the proliferative zones of neurons and a violation of the cortical layers [10]. Microcephaly and severe brain changes such as intracranial calcifications, cortical malformations, decreased white and gray matter volume, and ventriculomegalyare the main markers of this new syndrome [9]. Although the most severe cases

of central nervous system involvement are already well known, the phenotypic spectrum of congenital Zika virus syndrome Зика(CZVS) is not fully defined, and less severe cases have been described. [11 , 12 , 13 , 14]. Knowledge gaps are still being filled for children exposed to Zika virus during the gestational period who do not experience classic outcomes of CZVS at birth. One of these gaps is whether the virus can cause minor disorders observed later, in the first years of life [15,16]. Monitoring of neuropsychomotor development (NPMD) is important so that any damage is quickly identified and directed to early intervention that will help to reach the full potential of the child [17]. Neurological disorders in microcephaly may include: muscular dystonia, spastic paresis, ataxia, convulsions, strabismus, cranial innervation disorders, anisoreflexia, and mild motor coordination disorders. Often, children with microcephaly can suffer from epilepsy and cerebral palsy. Children with microcephaly begin to hold their heads late, sit, crawl, and walk. There is a gross delay in speech development, indistinct articulation, a sharp limitation of vocabulary, and a violation of understanding of addressed speech. In primary microcephaly, the motor sphere is relatively preserved, and neurological symptoms are poorly expressed. With secondary microcephaly, there is usually a significant loss of motor skills, more often by the type of cerebral palsy, convulsions, intelligence suffers the most.

Forecast. Microcephaly is a lifelong condition with no known cure. The prognosis is usually worse for children who have had an intrauterine infection or have chromosomal or metabolic disorders. Depending on the cause and severity, children with microcephaly may experience a number of different problems. These include mental retardation, developmental delay, epilepsy, cerebral palsy, as well as ophthalmic and audiological disorders.

Conclusions. According to these data, children with ICP have a high prevalence of neurological complications associated with ED. These patients require careful follow-up and intensive medical intervention. A longer follow-up will provide data on these chronic neurological complications and how best to intervene.

REFERENCES

1. Bick J., Nelson K. A. Early adverse experience and the developing brain. *Neuropsychopharmacology.* 2016;41:177-196. dpi: 10.1038 / npp. 2015. 252.
2. Fox S. E., Levitt P., III CAN. How time and quality of early experience affect the development of brain architecture. *Detsky Dev.*2010;81: 28-40. doi: 10.1111/j.1467-8624.2009.01380.x.
3. Georgiev M. K., Brunet K. E., Tran P. V. Nutrition at an early age and nervous plasticity. *Dev. Psychopathol.* 2015;27: 411-423. dpi: 10.1017/S0954579415000061.
4. Kalado A.M., Pires M. A. Review of teratology. *Mol Methods. Biol.* 2018 year;L: 3-32. dpi: 10.1007/978-1-4939-7883-0_1
5. Sadler T. V., Sadler T. V. Congenital defects and prenatal diagnostics. In: Sadler T. V., editor. *Медицинская эмбриология Langman Medical Embryology*. 13th ed. Lippincott Williams & Wilkins; Philadelphia, PA, USA: 2015.
6. Coin CB, LaZear HM Zika virus - re-igniting the TORCH. *Nat. Reverend Genet.* 2016;14:707-715.doi: 10.1038/nrmicro.2016.125.
7. De Araujo TVB, Rodriguez L. K., Jimenez R. A., Miranda-Filho DDB, Montarroyos W. R., De Melo APL, Valongeiro S., Albuquerque MFPM, Souza V. V., Braga K. et al. Association between Zika virus infection and microcephaly in Brazil, January-May 2016: preliminary

study report "case-control". *Lancet Infekt.Dis.*2016;16:1356-1363. doi: 10.1016/S1473-3099(16)30318-8.

8. Alves L. V., Paredes K. E., Silva G. K., Mello J. G., Alves J. G.. Neuro-development of 24 children born in Brazil with congenital Zika syndrome in 2015: a case series study. *BMJ Open.* 2018;8: e021304. doi: 10.1136/bmjopen-2017-021304.
9. Del Campo M., Feitosa IML, Ribeiro E. M., Horowitz DDG, Pessoa BAS, Fransa GWA, Garcia-Alix A., Doriki M. J. R., Vanderley HYC, Sanseverino MW, et al. Phenotypic spectrum of congenital Zika syndrome. *I am. J. Med. My wife. Part A.*2017;173:841-857.doi: 10.1002/ajmg.a.38170.
10. Cugola F. R., Fernandez I. R., Russo F. B., Freitas B. K., Diaz H. L. M., Guimaraes K. P., Benazzato K., Almeida N., Pignatari FBRGC, Romero S. et al. The Brazilian Zika virus strain causes birth defects in experimental models. *Nat. Kletochnaya Biol.*2016;534: 267-271. doi: 10.1038/nature18296.
11. Pesanya P. M., Junior SCDSM, Pone S. M., Pone MVDS, Vasconcelos Z., Zin A., Vilibor R. H., Costa R. P., Mayo MDBB, Nielsen-Sainz K. et al. Neuro-development of infants exposed to Zika virus in utero: a series of cases. *PLOS ONE.*2020;15: e0229434. doi: 10.1371/journal.pone.0229434.
12. Faisal A.V., De Oliveira H. K., Oliveira J.V. V., De Almeida B. L., Agra I. A., Alcantara L. K. J., Acosta A. S., De Siqueira I. K. Neural development delay in normocephalic infants exposed to Zika virus in utero.Зика *BMJ Pediatrician. Open.* 2019;3 : e000486. doi: 10.1136/bmjpo-2019-000486.
13. Hertzson L. R., De Almeida K. S., Da Silva J. H., Feitosa MMA, De Oliveira L. N., Shuler-Faccini L. Neurodevelopment of children with non-microcephaly after 18 months of life exposed to Zika virus. *Дж. Чайлдin utero. Нейрол* 2019;35: 278-282. dpi: 10.1177/0883073819892128.
14. Cranston , J.S., Tiene, S. F., Nielsen-Sainz, K., Vasconcelos, Z., Pone, M. V., Pone, S., Zin, A., Salles, T. S., Pereira, J. P., Orofino, D. et al. Relationship between antenatal exposure to Zika virus and anatomical abnormalities and abnormalities in the development of the nervous system in children. children. *JAMA Netw. Open.* 2020; 3 : e209303. doi: 10.1001/jamanetworkopen.2020.9303.
15. Muller V.J., Malki S. B. Lessons of early development of the nervous system in children exposed to ZIKV in utero. *Nat. Med.* 2019;25: 1192-1193. dpi: 10.1038/s41591-019-0540-1.
16. Pansho A., Stoyanov M., Ammerdorfer A., Voga M., Baud D. A new role of Zika virus in adverse fetal and neonatal outcomes. *A wedge. Microbiol. Version*of 2016;29:659-694. dpi: 10.1128/CMR.00014-16.
17. Brazil. Ministry of Saudi Arabia, Atensan Secretariat Атенсанain Saudi Arabia. *Direction of premature stimulation: "Zero cry" for 3 years, associated with neuropsicomotor disorder*. Ministry of Saude do Brasi; Brasilia, Brazil: 2016. p. 184.