ISSN 2563-9218

REVIEW ARTICLE

Neurological Complication Caused by Zika Virus: Guillain-Barré Syndrome

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Koyun D. Neurological Complication Caused by Zika Virus: Guillain-Barré Syndrome. Int J Biomed Clin Anal. 2022;2(1):20-28.

Abstract

The Zika virus was given this name because it was first isolated in the Zika forests in Uganda. The Zika virus is a type of virus with the Flavivirus genome belonging to the family Falanridae. This virus has an icosohedral structure, enveloped and positive-polarity single-stranded RNA. The primary vector for the infection is mosquitoes. If it is a tropical region, Aedes is carried by aegypti mosquitoes; in temperate regions, it can also be carried by the Aedes albopictus mosquito. Apart from mosquito bites, it can also be transmitted from person to person, from mother to fetus, sexually, by blood transfusion and in cases of exposure in laboratory environment. The first major outbreak occurred in 2007 on the island of Yap in the southern Pacific Ocean, and during the study of cases it was confused with other viral diseases in diagnosing the Zika virus. Therefore, clinical manifestations need to be carefully determined. Looking at the clinical symptoms of Zika virus, it is fever, headache, retro-orbital pain, joint pain, chronic fatigue, weakness, myalgia, anorexia, rash, edema. The Zika virus has also been associated with neurological complications and has been shown to trigger Guillain-Barré Syndrome.

Guillain-Barré Syndrome is an acute inflammatory polyneuropathy that can be seen at all ages. Those who know the most about its clinical manifestations are symmetrical muscle weakness and loss of deep tendon reflexes. If respiratory failure and autonomic involvement occur, it can be fatal for patients. Guillain-Barré Syndrome is a treatable disease. With advanced treatment methods, a complete recovery can be seen in patients. Due to the fact that it has a progressive clinic, the recovery process for patients in early diagnosis can be fast and positive, and according to the studies conducted, there is a relationship between Zika. Today, with the appearance of Aedes mosquitoes, which affect the transmission of the Zika virus, it is necessary to pay attention to infection and neurological effects. In this review, the relationship between Zika virus and Guillain-Barré Syndrome is tried to be explained..

Key Words: *Zika virus; Guillain-Barré syndrome; Mosquito borne infection; Epidemiology; Polyneuropathy*

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Received: July 13, 2022, Accepted: August 3, 2022, Published: August 12, 2022

Introduction

Viruses; are nucleoprotein molecules that can infect living cells up to many microorganisms in animals, plants, bacteria, archaea and multiply using enzymes inside the host cell. Viruses and living cells have common components, such as DNA or RNA and proteins. The vast majority of viruses have RNA genomes. But; viruses are formed as a result of the self-construction of their organic molecules. Therefore, they are not considered alive. They differ from other pathogens in terms of these characteristics. Unlike other pathogens, they do not have any metabolic activities. However, viruses have the ability to mutate to form new races [1]. As a result of all these, the origin of viruses has been discussed and many different views have been put forward. A few of the views put forward are as follows: The origin of viruses is multicellular organisms and over time they have passed into parasitic form and lost all their organelles. Another opinion is; viruses are pre-celled living in a free state; these forms begin to live as parasites in multicellular organisms. Another opinion is; viruses are descended from neither pre-celled nor multicellular organisms. According to the last view, viruses are formed from the hereditary materials of other organisms. As a result of these thoughts, the origin of viruses has not been clarified [2]. Regardless of the origin of viruses, many studies have begun to be carried out on the effects of microorganisms as the damage they have done to living things increases. Thus, studies have been started to identify, name and classify the viruses that cause disease in living things in accordance with certain criteria. In the studies being developed by the International Virus Taxonomy Committee, a general taxonomic structure has been established according to the characteristics of viruses [3]. Thus, he contributed to the investigation of the Zika virus, which causes many neurological diseases and epidemics from past to present.

Zika virus (ZIKV)

The Zika Virus (ZIKV) is a virus in the flavivirus genus from the family flaviviridae. It is a single-stranded ribonucleic acid (RNA) with a diameter of approximately 50 nm, with an icosahedral capsid structure, and a positive polarity and a virus variety of approximately 11-12 kilobases (kb) in size [4,5]. Flaviviruses are a member of the arbovirus family. Arboviruses are a term used to describe the various virus families carried by arthropods, and arthropods are known as viruses that can be transmitted from animals to humans [6].

Epidemiology

The Zika virus was first identified in 1947 by Dick et al., who first studied yellow fever, by inoculating serum samples taken from one of the observation monkeys of the Asian species Rhesus Macaques (Macaca Mulatta) into the mouse brain and then obtaining a filterable virus (ZikaV 766 strain) in the mouse. Thus it got its name from the Ugandan forest from which it was isolated [7,8]. In 1948, Dick et al. succeeded in isolating the virus from mosquitoes of the species aedes africanus and found antibody positivity in the Entebbe region of Uganda [7]. MacNamara detected antibody positivity in the Laro region and Kontagora region of Nigeria [9]. Smithburn et al. showed in 1952 that the Zika virus can also infect humans by demonstrating neutralizing antibodies [10]. In 1954, the virus was detected in a 10-year-old girl in the Western Nigeria region [11]. In 1958, two different types of Zika virus infection were observed from mosquitoes of the genus aedes africanus [12]. Reagan et al. published electron microscope images in 1955 in infected erythrocytes of albino-type mice of the Zika virus [13]. Boorman et al. proved in 1956 that the Zika virus can be transmitted to a. aegypti species other than a. africanus and to cause major outbreaks [14]. In 1964, a researcher observed some symptoms occurring

in certain parts of his body during his studies on the existence of new Zika species [15]. In 1969, infection was observed in a person outside Africa for the first time. The Zika virus has been isolated from a.aegypti mosquitoes in Malaysia and has been detected in Indonesia [16,17].

Regional surveys conducted between 1960 and 1980 show that the Zika virus continues to exist in mosquitoes and rhesus monkeys in countries neighboring the equatorial region of Africa. Zika virus has been found in about 20 species of mosquitoes. Human cases have also been identified, albeit rarely, mostly by serological studies [18-20].

Today, the first significant outbreak of the Zika virus emerged in 2007 on the Yap islands of Micronesia. According to the data of this epidemic, 70% of people have been infected and more than 5000 of the population has been infected [21]. As time progressed, the Zika virus continued to spread rapidly to other regions. It was spotted on Chile's Easter Island in the western hemisphere in February 2014. Later, in May 2015, Zika virus infection was also observed in the Brazilian country [22]. In 2016, Zika virus infection was detected in many states of the United States by being transmitted by different means [23,24].

In our country, due to the visit to South America caused by increasing international trade and travel, diseases caused by Zika virus infection began to spread in October 2017 [25].

Ways of transmission

Zika virus infection can be transmitted to humans in many ways. These paths are as follows [24,26]:

- Infected mosquito bite
- Transplacental
- Sexually transmitted
- Transfusion of blood and blood products
- Organ transplantation
- Laboratory exposure

The primary route of transmission , vectors of which are mosquitoes, and the transmission of infection through mosquito bites is achieved. The Zika virus is carried by Aedes aegypti mosquitoes that live in tropical regions. However, it can also be carried by the Aedes albopictus mosquito, which lives in temperate regions. In addition, Zika virus RNA can be detected in blood, urine, semen, saliva, female genital secretions, cerebrospinal fluid (CSF), amniotic fluid and breast milk [27-29].

Clinical symptoms

The symptoms of Zika virus infection are fever, headache, chronic fatigue, joint pain, itching that spreads to the hands and arms starting from the face of the skin, edema, anorexia and conjunctivitis (eye inflammation). Among these symptoms, conjunctivity is most common; Symptoms of headache and weakness are observed minimally [30-32].

The period of Zika virus infection from the onset of clinical manifestations after infecting an individual with a mosquito tool is from 2 to 14 days. The infection is usually mild and lasts between 2-7 days. While 20% of people infected with the Zika virus get sick, other infected individuals pass the infection in a mild form without showing signs of the disease or carrier. Therefore, case fatality rates are low [31-33]. But the Zika virus has a neurotropic character. This has been proven by conducting studies in both in vivo and in vitro environments [34]. For this reason, Zika virus has also been associated with neurological complications [35]. These complications are listed as follows:

- Guillain-Barré syndrome
- Encephalitis
- Transverse myelitis

- Encephalomyelitis
- Meningoencephalitis
- Chronic inflammatory demyelinating polyneuropathy
- Cerebral ischemia
- Neuropsychiatric and cognitive symptoms

There has been an unexpected increase in cases of Guillain-Barré syndrome in countries affected by Zika virus infection. The most plausible explanation for the available data from outbreaks of Zika virus infection and Guillain-Barré syndrome is that Zika virus infection is a trigger of Guillain-Barré syndrome.

Guillain-Barré Syndrome (GBS)

Guillain-Barré Syndrome (GBS) is a disease first described by French biologists in 1916. Guillain-Barré syndrome is an autoimmune disease characterized by rapidly progressive symmetrical muscle weakness and loss of deep tendon reflexes, with the body's immune system attacking part of the peripheral nervous systems. Guillain-Barré syndrome can affect the nerves that control muscle movement, as well as the nerves that transmit pain, temperature, and tactile sensations. This can lead to muscle weakness and loss of sensation in the legs or arms. The progression of these symptoms is less than 1 month [36].

Guillain-Barré Syndrome can occur at all ages and is not an inherited disorder [37]. Therefore, it is a disease that can be treated. If advanced medical support and treatment methods are applied, a complete recovery can be observed. Guillain-Barré Syndrome usually occurs as a result of a bacterial or viral infection. Campylobacter jejuni and Helicobacter pylori bacteria in the gastrointestinal tract and Mycoplasma pneumoniae bacteria in the respiratory tract are common agents. In viral infections, the Zika virus affects Guiallain-Barré Syndrome. It can rarely be seen after vaccination. However, it has been accepted that the main underlying cause of the symptoms is autoimmune. Antibodies against neurons cause damage to the myelin sheaths surrounding the nerves (demyelination) or axonal damage [36,38].

Guillain-Barré Syndrome is divided into four main subgroups according to clinical, pathological and electrophysiological features. The subgroups are as follows:

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)

Guillain-Barré Syndrome is the most well-known form. 90% of cases are in this group. It is often a matter of you being preceded by an infection or a triggering condition. The symptoms of the acute inflammatory demyelinating polyradiculoneuropathy (AIDP) form are usually symmetrical and progress can continue for up to 4 weeks, starting from the lower extremities. The first week of progression is rapid, and the cranial nerves are often involved. The initial symptoms are usually numbness (paresthesia) and pain. It is seen in 70-80% of clinical symptoms. Especially in the fingertips, symmetrical sensory loss is observed. Most often the patella reflex disappears. Autonomic findings can be counted as blood pressure irregularity, arrhythmias, tachycardia, urinary retention, urinary and stool incontinence, constipation, abdominal distention. Electromyography (EMG) shows motor and sensory demyelination. As a result of the follow-up, the complete recovery rate of the patient is between 75-95% [39-41].

Acute motor axonal neuropathy (AMAN)

Bacterial gastroenteritis causative agent, enteritis caused by C. jejuni, is the most common cause of Guillain-Barré Syndrome of the AMAN type worldwide. This form is also

most commonly affected by children and young adults. In the AMAN form, Guillain-Barré Syndrome has been shown to be associated with the HS:19 and HS:41 strains of C. jejuni. These strains have often been found to be associated with the development of anti-GM1 and anti-GD1a autoantibodies. In acute motor axonal neuropathy, there are other gangliosides that develop the autoantibody. These are as follows: GM1b, GD1b, GalNAc-GD1a, GD1a/GD1b. In the early period of AMAN form, motor axonal degeneration with severe respiratory involvement is observed and the healing process is rapid [39-41].

Acute motor sensory axonal neuropathy (AMSAN)

Acute motor sensory axonal neuropathy (AMSAN) is a rare form usually seen in adults. As with the AMAN type of Guillain-Barré Syndrome, C. Jejuni also affects the AMSAN type. It shows a rapid and classic clinical course.. Respiratory insufficiency may develop in the early period. Involvement of cranial and autonomic nerves is also a common condition. Electromyelography (EMG) shows axonal degeneration of both motor and sensory nerves. The patient's recovery process can take up to a year [39-41].

Miller-Fisher Syndrome (MFS)

It is the most common variant of Guillain-Barré Syndrome and accounts for 5% of all cases. The average age of occurrence of this variant is 40 years. Miller-Fisher Syndrome usually has an upper respiratory tract infection and sometimes C. jejuni enteritis. The C. jejuni strain seen in Guillain-Barré Syndrome is often HS:2 and HS:4. In all cases, ataxia, ophthalmoplegia and areflexia are observed. Anti-GQ1b type autoantibodies have been detected. In electromyelography (EMG), motor demyelination and axonal sensory involvement occur. The recovery process of patients who have had this variant occurs as a slow and complete recovery within weeks or months [39-41].

Acute autonomic neuropathy

It is a subtype of Guillain-Barré Syndrome in which there are disorders of the sympathetic and parasympathetic systems. While this variant can occur at all ages, it is more common in women than in men. Symptoms in acute autonomic neuropathy are upper respiratory tract infection or enteritis. However, no specific factor has been identified. Herpes simplex virus, Herpes zoster, Rubella, infectious mononucleosis are the causative agents of the disease. Acute autonomic neuropathy also includes autonomic findings such as orthostatic hypotension, hypertension, tachycardia, arrhythmia, pupillary abnormalities, urinary retention, diarrhea, constipation, tears and saliva reduction [39-41].

Pathogenesis of Guillain-Barré Syndrome

In Guillain-Barré Syndrome, the damage to nerve cells is caused by the direct effect of the infection or by interaction with T cells triggered by immunological mediators. As a result, it is mediated by autoantibodies produced by B cells. Patients with Guillain-Barré syndrome had a very high percentage (60%) of antiganglioside antibodies in their blood. These gangliosides are found in peripheral nerve membranes and are involved in maintaining membrane integrity. Autoantibodies that cross the blood-nerve barrier cause inflammatory and cell infiltration in these areas. As a result of infiltration, it causes demyelinization and axonal damage to the anterior and posterior roots, proximal and distal nerve trunks, terminal branches, cranial nerves, sympathetic chain and ganglia. Infectious agents such as Zika virus (ZIKV), Ebstein-Barr virus (EBV), Cytomegalovirus (CMV), Mycoplasmapneumonia and Campylobacter

jejuni, surgical intervention, childbirth cause the formation of these antibodies [37,40]. In GBS forms with axonal involvement and in MFS, antibodies against antigens above infectious agents cross-react with gangliosides in the axons of nerve cells; with the disruption of the axonal sodium channels, slowing or loss of transmission is observed [41,42]. This condition causes them to produce autoantibodies against ganglosids of sub-variants of Guillain-Barré syndrome. Thus, they accelerate the healing process of patients.

Clinical symptoms

Guillain-Barré Syndrome has a clinical picture with signs such as muscle weakness, paralysis and deep tendon reflexes (DTR) that occur symmetrically. This infection begins with symptoms such as numbness, loss of reflexes, drowsiness, tingling and weakness in the nervous system; The disease progresses rapidly within the first two weeks. If the central nervous system (CNS), where the brain and spinal cord are located, is not affected, the clinical manifestations of the patients are different [43-45]. The clinical findings observed in the patients are as follows:

- Tingling, needle-like stinging and numbness sensation in the hands, arms, wrists and fingers on both sides.
- Tingling, needle-like stinging and numbness in the ankles and fingers.
- Low or high blood pressure.
- Disorder in the sensory centers
- Weakness in walking and inability to climb stairs
- Difficulty breathing
- Difficulty swallowing
- Incontinence
- Heart rhythm disturbance
- Speech impairment

In Guillain-Barré Syndrome disease, respiratory failure is observed more in adults with head and back pain; Children also have fewer of these symptoms. Children also have more autonomic symptoms such as vomiting, headache, meningitis and encephalopathy [45].

Zika Virus With Guillain-Barré Syndrome (ZIKV)

Zika virus is a virus belonging to the flavivirus family; It is an infection carried by Aedes mosquitoes. When a systematic examination of Zika virus infection was conducted, it was found to be the trigger of Guillain-Barré Syndrome. The association of the Zika virus with Guillain-Barré Syndrome was first documented with the spread of the Zika virus infection that occurred in French Polynesia in 2014. Approximately 25 days after the patients showed clinical symptoms, ZIKV IgM, IgG and PRNT tests were applied in the serum and antibody positivity was demonstrated. According to the results of these tests, a complicated Zika virus was detected with facial paralysis, encephalitis, myelitis and paresthesia, which are the clinical symptoms of Guillain-Barré syndrome disease [30,46,47]. In addition to the neurological complications of the Zika virus, it has been determined that it has effects such as low birth weight, craniofacial abnormalities and eye abnormalities on the fetus in pregnant women infected with it, and as a result of the findings, it has been proven that the virus provides trasnplacental transmission [48,49].

The relationship between the Zika virus and Guillain-Barré Syndrome has also been observed in outbreaks in other countries. Several countries, including Brazil, Colombia, El Salvador, Suriname, and Venezuela, have reported an unusual increase above the baseline of Guillain-Barré Syndrome, which has come to terms with the Zika virus outbreak. These observations, along with the findings of a recent case-control study from the French Polynesia

outbreak, support the role of Zika virus infection as a triggering event for GBS. However, other infectious diseases common in the Americas and the Caribbean are known to be associated with Guillain-Barré Syndrome [47].

Conclusion

The Zika virus emerged from the first ZIKV outbreak in the state of Yap, and began to show the potential for the emergence of ZIKV. In the second outbreak in French Polynesia, serious neurological diseases were observed for the first time and neurological diseases began to be associated with the Zika virus. One of the neurological diseases is Guillain-Barré Syndrome. It began to spread from French Polynesia to all regions from the Pacific and continued to spread rapidly to several continents [50]. The number of cases gradually increased and when the symptoms were examined, it was revealed that it triggered Guillain-Barré Syndrome. However, the physiopathological mechanisms underlying the Zika virus and Guillain-Barré Syndrome are not yet known [51]. Zika virus infection has shown that it can become a serious global public health in the future.

References

1. Taylor NMI, Leiman PG. Editorial overview: virus structure and expression, current opinion in virology. Curr Opin Virol. 2020;45:iii-v.
2. Uzunoğulları N, Gümüş M. Virüs taksonomisinin tarihsel gelişimi ve son durumu. Bahçe. 2018;46:51-7.
3. Stanway GF, Brown P, Christian T, et al., 2005. Family Picornaviridae. In: Fauquet CM, Mayo MA, Maniloff J, et al. (eds), Virus Taxonomy. Eighth Report of the International Committee on Taxonomy of Viruses. Elsevier/Academic Press, London. 2005;pp:757-78.
4. Kuno G, Chang GJ. Full-length sequencing and genomic characterization of Bagaza, Kedougou, and Zika virüses. Arch Virol. 2007;152:687-96.
5. Pielnaa P, Al-Saadawe M, Saro A, et al. Zika virus-spread, epidemiology, genome, transmission cycle, clinical manifestation, associated challenges, vaccine and antiviral drug development. Virology. 2020;543:34-42.
6. Faye O, Freire CC, Iamarino A, et al. Molecular evolution of Zika virüs during its emergence in the 20(th) century. PLoS Negl Trop Dis. 2014;8:e2636.
7. Medin CL, Rothman AL. Zika virus: the agent and its biology, with relevance to pathology. Arch Pathol Lab Med. 2017;141:33-42.
8. https://www.who.int/news-room/feature-stories/detail/the-history-of-zika-virus
9. MacNamara FN. Annual Report, Virüs Research Institute, Nigeria, 1952.
10. Smithburn KC. Neutralizing antibodies against certain recently isolated virüses in the sera of human beings residing in East Africa. J Immunol. 1952;69:223-34.
11. MacNamara FN. Zika virus: a report on three cases of human infection during an epidemic of jaundice in Nigeria. Trans R Soc Trop Med Hyg. 1954;48:139-45.
12. Musso D, Gubler DJ. Zika virüsü. Clin Mikrobiyol Rev. 2016;29:487-524.
13. Reagan RL, Chang SC, Brueckner AL. Electron micrographs of erythrocytes from Swiss albino mice infected with Zika virüs. Tex Rep Biol Med. 1955;13:934-8.
14. Boorman JP, Porterfield JS. A simple technique for infection of mosquitoes with virüses: transmission of Zika virüs. Trans R Soc Trop Med Hyg. 1956;50:238-42.

15. Simpson DI. Zika virüs infeciton in man. Trans R Soc Trop Med Hyg. 1964;58:335-8.

16. Marchette NJ, Garcia R, Rudnick A. Malezya'daki Aedes aegypti sivrisineklerinden Zika virüsünün izolasyonu. J Trop Med Hyg. 1969;18:411-5.

17. Plourde AR, Bloch EM. Zika Virüsü Literatür Taraması. Emerg Infect Dis. 2016;22:1185-92.

18. Haddow AD, Schuh AJ, Yasuda CY, et al. Genetic characterization of Zika Virüs strains: geographiz expansion of the Asian lineage. PloS Negl Trop Dis. 2012;6:e1477.

19. Himeidan YE, Kweka EJ, Mahgoub MM, et al. Doğu Afrika ve Orta Doğu'da son zamanlarda rift vadisi ateşi salgınları. Ön Halk Sağlığı. 2014;2:169.

20. Duffy MR, Chen TH, Hancock WT, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med. 2009;360:2536-43.

21. Lanciotti RS, Kosoy OL, Laven JJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. Emerg Infect Dis. 2008;14:1232-9.

22. de Oliveira WK, Carmo EH, Henriques CM, et al. Zika virus infection and associated neurologic disorders in Brazil. N Engl J Med. 2017;376:1591-3.

23. http://governor.hawaii.gov/newsroom/doh-news-release-hawaii-department-of-health-receives-confirmation-of-zika-infection-in-baby-born-with-microcephaly

24. Hills SL, Russell K, Hennessey M, et al. Transmission of Zika Virus Through Sexual Contact with Travelers to Areas of Ongoing Transmission - Continental United States, 2016. MMWR Morb Mortal Wkly Rep. 2016;65:215-6.

25. https://hsgm.saglik.gov.tr/tr/zoonotikvektorel-zika/detay.html

26. https://www.cdc.gov/zika/prevention/index.html

27. Gourinat AC, O'Connor O, Calvez E, et al. Detection of Zika virus in urine. Emerg Infect Dis. 2015;21:84-6.

28. Musso D, Roche C, Nhan TX, et al. Detection of Zika virus in saliva. J Clin Virol. 2015;68:53-5.

29. Prisant N, Bujan L, Benichou H, et al. Zika virus in the female genital tract. Lancet Infect Dis. 2016;16:1000-1.

30. Ioos S, Mallet HP, Leparc Goffart I, et al. Current Zika virüs epidemiology and recent epidemics. Med Mal Infect. 2014;44:302-7.

31. https://www.cdc.gov/zika/hc-providers/preparing-for-zika/clinicalevaluationdisease.html

32. Dirlikov E, Ryff KR, Torres-Aponte J, et al. Update: ongoing Zika virus transmission - Puerto Rico, November 1, 2015-April 14, 2016. MMWR Morb Mortal Wkly Rep. 2016;65:451-5.

33. Maharajan MK, Ranjan A, Chu JF, et al. Zika virus infection: current concerns and perspectives. Clin Rev Allergy Immunol. 2016;51:383-94.

34. Garcez PP, Loiola EC, Madeiro da Costa R, et al. Zika virus impairs growth in human neurospheres and brain organoids. Science. 2016;352:816-8.

35. http://apps.who.int/iris/bitstream/10665/204348/1/zikasitrep_5Feb2016_eng.pdf?ua=1

36. Lee JH, Sung IY, Rew IS. Clinical presentation and prognosis of childhood Guillain-Barré syndrome. J Paediatr Child Health. 2008;44:449-54.

37. Agrawal S, Peake D, Whitehouse WP. Management of children with Guillain-Barré Syndrome. Arch Dis Child Educ Pract Ed. 2007;92:161-8.

38. Sarnat HB. Guillain-Barré Syndrome. In: Kliegman RM, Behrman RE, Jenson HB, et al. (Eds) Nelson Textbook of Pediatrics (18thedn), W B Saunders Company, Philadelphia. 2007;pp:2565-6.

39. Ryan MM. Guillain-Barré Syndrome in childhood. J Paediatr Child Health. 2005;41:237-41.

40. Rabie M, Nevo Y. Childhood acute and chronic immune-mediated polyradiculoneuropathies. Eur J Paediatr Neurol. 2009;13:209-18.

41. Hughes RAC, Cornblath DR. Guillain–Barré syndrome. Lancet. 2005;366:1653-66.

42. van den Berg B, Walgaard C, Drenthen J, et al. Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol. 2014;10:469-82.

43. Winer JB. Guillain-Barré syndrome. BMJ. 2008;337:a671

44. Asbury AK. New concepts of Guillain–Barré Syndrome. J Child Neurol. 2000;15:183-91.

45. Zaeem Z, Siddiqi Z, Zochodne DW. Guillain-Barré sendromunda otonomik tutulum: bir güncelleme. Clin Auton Res. 2019;29:289-99.

46. https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-zika-virus-infection-outbreak-french-polynesia

47. Oehler E, Watrin L, Larre P, et al. Zika virus infection complicated by Guillain-Barre syndrome-case report, French Polynesia, December 2013. Euro Surveill. 2014;19:20720.

48. Ventura CV, Maia M, Bravo-Filho V, et al. Zika virus in Brazil and macular atrophy in a child with microcephaly. Lancet. 2016;387:228.

49. Kleber de Oliveira W, Cortez-Escalante J, De Oliveira WT, et al. Increase in Reported Prevalence of Microcephaly in Infants Born to Women Living in Areas with Confirmed Zika Virus Transmission During the First Trimester of Pregnancy - Brazil, 2015. MMWR Morb Mortal Wkly Rep. 2016;65:242-7.

50. Musso D, Cao-Lormeau VM, Gubler DJ. Zika virus: following the path of dengue and chikungunya? Lancet. 2015;386:243-4.

51. Hardy TA, Blum S, McCombe PA, et al. Guillain-Barré Syndrome: Modern Theories of Etiology. Curr Allergy Asthma Rep. 2011;11:197-204.