

A Review on Viral Encephalitis

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Yasmeen J. Al-bayaa * BSc, MSc Microbiology
Shaymaa J. Kadhim * BSc, MSc Microbiology
Zainab A. Hamid * PhD Microbiology



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Abstract

Background: Inflammation of the brain parenchyma brought on by a virus is known as viral encephalitis. It coexists frequently with viral meningitis and is the most prevalent kind of encephalitis.

Objectives: To throw light on viral encephalitis, its types, epidemiology, symptoms and complications.

Results: Although it can affect people of all ages, viral infections are the most prevalent cause of viral encephalitis, which is typically seen in young children and old people. Arboviruses, rhabdoviruses, enteroviruses, herpesviruses, retroviruses, orthomyxoviruses, orthopneumoviruses, and coronaviruses are just a few of the viruses that have been known to cause encephalitis.

Conclusion: As new viruses emerge, diagnostic techniques advance, or we learn more about the pathophysiology of the disease, viral encephalitis has become a more serious public health concern.

Keywords: Encephalitis, Inflammation, Central nervous system, Viral infection.

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Introduction:

A virus causes viral encephalitis, an inflammation of the brain parenchyma. It is the most common type of encephalitis and often appears in the presence of viral meningitis. Viruses can infect a host outside of the CNS and then spread hematogenously or retrograde to the brain and the spinal cord through nerve terminals (1,2). More severe symptoms of encephalitis include seizures, weakness, hallucinations, and coma, among others. Fever, headache, nausea, vomiting, dizziness, altered mental status, including personality changes, are among the symptoms of encephalitis (3) All ages can be affected by encephalitis, However children and the elderly are more frequently affected. It is brought on by autoimmune responses or pathogenic infections, frequently viral infections (4, 5) Primary and secondary viral encephalitis are the two varieties. A pathogen directly infecting the brain and infecting one or more portions of this tissue is referred to as primary encephalitis secondary encephalitis happens When a pathogen spreads from the primary site of infection (such the lungs or kidneys) to the central nervous system (CNS) (6).

Types of Viral Encephalitis:

1- Herpes simplex encephalitis is a virus that infects the central nervous system of humans. Herpes simplex virus-1 (HSV-1) causes the majority of instances of

2- herpes encephalitis. This is the same virus that causes cold sores. Encephalitis is caused by HSV-2, which is primarily spread through sexual contact and spreads by droplets and casual contact (7).

3- California encephalitis is a mosquito-borne disease that affects the central nervous system (CNS) in children and is reported. The majority of infections are asymptomatic, and those who do develop symptoms usually recover fully(8).

4- Equine encephalitis is a disease that affects both horses and humans.

- Eastern Equine Encephalitis is a zoonotic (animal to human) disease also referred to as Triple E or sleeping sickness (9).

- Venezuelan Equine Encephalitis: Is an acute viral illness that causes fever, chills, headache, nausea, vomiting, lumbosacral pain, and myalgia with a chance of developing into encephalitis. It is a serious illness in the Americas that is brought on by the Venezuelan equine encephalitis virus (10).

One of the many viral diseases carried by mosquitoes and capable of causing acute inflammation of the brain parenchyma and meninges is Western Equine Encephalitis (11).

5- Japanese encephalitis: The Japanese encephalitis virus (JEV) causes a brain infection While most infections cause minimal or no symptoms, brain inflammation does occur on occasions (11).

6- St. Louis encephalitis is a virus that is transmitted to humans through the bite of an infected mosquito. Symptoms include headache and fever. Confusion and disorientation, tremors, convulsions, and coma may develop in more severe cases (12).

*College of Medicine/University of Baghdad/
Department of Microbiology.
yasmeenalbayaa@comed.uobaghdad.edu.iq
shaimaajwad@gmail.com
zainaba.hamid@comed.uobaghdad.edu.iq

6-West Nile encephalitis: Encephalitis, meningitis, or sudden flaccid paralysis are all symptoms of West Nile encephalitis. It is normally transmitted by a bite from an infected mosquito, but can also occur following transplantation of an infected organ or contaminated blood or blood products transfusions (13).

7-Cytomegalovirus encephalitis is one of various infections of the central and peripheral nervous systems seen in late-stage HIV infection. Encephalitis, ventriculitis, myelitis, retinitis, and peripheral neuropathies are some of the neurologic symptoms of the infection. Patients with severe immunodeficiency are more likely to contract these infections, as their CD4+ lymphocyte counts are often less than 50/L. (14).

Epidemiology:

Encephalitis is one of the most prevalent neuropathologies that significantly increases morbidity and mortality worldwide. It is an inflammation of the brain parenchyma that produces neurological abnormalities (15). The prevalence of encephalitis varies by nation and ranges from 7 to 15 cases per 100,000 persons. Every year, around 7 encephalitis patients per 100,000 individuals are hospitalized in the United States. In 20 to 50% of the time, viruses are to blame. Varicella-zoster virus (VZV), enteroviruses, and arboviruses make up the majority of the remaining viruses, with herpes simplex virus (HSV) responsible for 50 to 75% of viral infections. The risk of viral encephalitis is greater in children and the elderly (16). Relevant epidemiological factors include the season, location, and interaction with animals or insects. For instance, arboviruses are contagious during the summer, when mosquitoes are prevalent (e.g., eastern equine, western equine, St. Louis, Venezuelan equine, Zika, and West Nile). While tick-borne encephalitis is primarily found in the north central United States (17, 18).

SYMPTOMS:

There have been reports of behavioral issues, tic disorders, persistent headaches, sleeping problems, and motor deficits as viral encephalitis sequel. The effects of viral encephalitis have also been linked to a number of neurocognitive symptoms, including attention-deficit/hyperactivity disorder (ADHD), speech difficulties, memory disorders, and learning disabilities (19).

Specific neurological symptoms including seizures and altered awareness, which can range from lethargy to disorientation, stupor, and coma, are also present in patients with viral encephalitis. Behavior and speech irregularities are common. It is possible to see strange movements, although they are not common. When the hypothalamic/pituitary axis is implicated, hyperthermia can happen. Sometimes encephalitis can have a significant impact on the brain. Global cerebral edema could also start to develop, which would worsen

cerebral perfusion and increase intracranial pressure (ICP) (20). Cranial neuropathies can make it harder to swallow and speak, which raises the possibility of aspiration. Mechanical ventilation is therefore frequently needed (21). Other, more virus-specific symptoms that patients may experience are possible. For instance, whilst the Epstein-Barr virus produces lymphadenopathy and splenomegaly, the Herpes zoster encephalitis results in a rash and skin vesicles. Herpes simplex virus encephalitis typically includes psychiatric symptoms, memory loss, and aphasia because it affects the temporal and frontal lobes. On the other hand, some arboviruses cause parkinsonian movements and choreoathetosis because they primarily assault the basal ganglia (20).

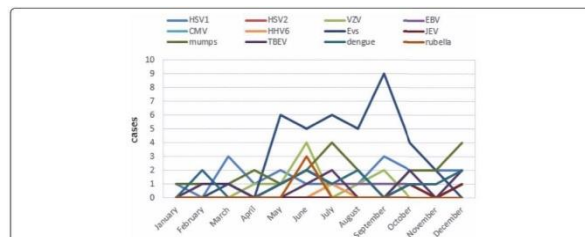


Figure 1.; Seasonal distribution of viral encephalitis cases with a known cause. Human enteroviruses are also known as "EVs," "human herpes virus 6," "mumps virus," "tick-borne encephalitis virus," "Japanese encephalitis virus," "herpes simplex virus 1," "herpes simplex virus 2," "varicella zoster virus," "EBV," "Epstein-Barr virus," and "cytomegalovirus." (22).

Diagnosis:

Tests recommended include the following:

Blood and skin culture

Blood cultures should be performed on all encephalitis patients to rule out bacterial and fungal diseases. Because viremia in the majority of arboviral infections is often mild and transient, blood viral cultures are typically low yield tests.

Skin biopsies, for instance, can be used to diagnose Rocky Mountain spotted fever, while sensory axon staining and a full-thickness skin biopsy from the neck can be used to diagnose rabies. Stool samples, throat viral cultures, and antigen testing for respiratory and herpes viruses are also recommended (23).

Serological tests

Serum IgM antibodies can be used to identify specific encephalitis types (varicella and arboviruses). The most effective and popular approaches for diagnosing arboviral encephalitis at the moment are immunoglobulin M (IgM) and immunoglobulin G (IgG) capture enzyme linked immunosorbent assays (ELISAs) (24).

Imaging and Cerebrospinal fluid analysis:

- A brain imaging test, such as a CT scan or magnetic resonance imaging, is routinely performed (MRI). If

herpes encephalitis is suspected, an MRI is indicated(24).

Once the CSF has been obtained, it should be sent in for standard tests such the WBC count and differential, as well as assessments of the protein and glucose levels. Furthermore, appropriate molecular tests for relevant viruses, like PCR, should be done on CSF (25).

Brain biopsy

The gold standard for diagnosing Herpes simplex encephalitis was traditionally thought to be the isolation of Herpes simplex virus from brain tissue collected during a biopsy. All of the main Herpes simplex encephalitis therapy trials included a brain biopsy (23,26)

Complications:

•Memory issues, personality and behavioral abnormalities are the most prevalent sequelae that develop after encephalitis. Aphasia - issues with speech and language, epilepsy changes in emotions, attention problems, weariness (extreme tiredness) and Intelligence impairment

Changes in mood and behavior extrapyramidal symptoms (particularly dystonia and, on rare occasions, Parkinsonism), weakness, and seizure abnormalities are all common in Japanese encephalitis.

(21, 27).

Discussion:

Clinical history, physical exam results, and epidemiological data can all point to viral encephalitis. Travel history may provide further information about the viral or alternative etiology, such as subacute and chronic clinical evolution for mycobacteria and fungus, animal interaction for fungi and bacteria, suspected diet for bacteria and parasites, and geographic location for endemic diseases (28). General CSF and blood laboratory findings (such as neutrophilic CSF predominance in bacterial, positive blood cultures) and the particular detection of viral particles by type specific primers may be used to distinguish them from other infectious encephalitides during the diagnosis workup. Enzyme-linked immunosorbent assay, or PCR (29),(30). The reported annual incidence of encephalitis is roughly 16/100,000 child-years up until the age of two. When they are ten years old, it remains high, and when they are fifteen, it reduces to roughly 1/100,000 child-years. The most frequent etiology is viral, with different agents occurring more frequently or less frequently depending on the environment, the season, the patient's immune system, and viral genetic changes throughout time. After hematogenic viral propagation into the central nervous system, viral encephalitides typically develop (CNS). Herpes viruses including the lyssavirus that causes rabies, however, can propagate along nerve pathways and cause neurologic disease. The virus claims that they have the potential to cause neurologic irreversible sequel, substantial rates of morbidity, and potentially considerable mortality rates. In order to ensure prevention by immunization and

provide antiviral treatment when accessible, every effort must be made (31,32).

Conclusion:

Encephalitis, an important neuropathology that produces neurological abnormalities by inflaming the brain parenchyma, is one of the leading causes of morbidity and mortality in the world. Pathogenic infections, primarily viral infections, or autoimmune reactions are to blame. In addition to more severe symptoms like seizures, weakness, hallucinations, and coma, encephalitis is marked by minor clinical symptoms such fever, headache, nausea, vomiting, disorientation, and altered mental status (including personality changes). Everyone can get encephalitis, but children and the elderly are more likely to get it than other age groups. It is usually caused by pathogenic infections.

Author's Contributions:

Each of the mentioned authors contributed significantly, directly, and intellectually to the work, and they all gave their consent for it to be published.

References:

- 1-Im JH, Baek J, Durey A, Kwon HY, Chung MH, Lee JS. Current Status of Tick-Borne Diseases in South Korea. *Vector Borne Zoonotic Dis.* 2019 Apr;19(4):225-233.
- 2-Kadambari S, Harvala H, Simmonds P, Pollard AJ, Sadarangani M. Strategies to improve detection and management of human parechovirus infection in young infants. *Lancet Infect Dis.* 2019 Feb;19 (2):e51-e58.
- 3- De Blauw D., Bruning A. H. L., Busch C. B. E., Kolodziej L. M., Jansen N. J. G., Van Woensel J. B. M., et al. (2020). *Epidemiology and Etiology of Severe Childhood Encephalitis in the Netherlands. Pediatr. Infect. Dis. J.* 39 267–272. 10.1097/INF.
- 4-Dubey D., Pittock S. J., Kelly C. R., McKeon A., Lopez-Chiriboga A. S., Lennon V. A., et al. (2018). *Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann. Neurol.* 83 166–177. 10.1002/ana.25131
- 5-Perlejewski K., Pawelczyk A., Bukowska-Oško I., Rydzanicz M., Dzieciatkowski T., Paciorek M., et al. (2020). *Search for Viral Infections in Cerebrospinal Fluid from Patients with Autoimmune Encephalitis. Open Forum Infect. Dis.* 7 ofaa468. 10.1093/ofid/ofaa468
- 6-Jayaraman K., Rangasami R., Chandrasekharan A. (2018). *Magnetic Resonance Imaging Findings in Viral Encephalitis: A Pictorial Essay. J. Neurosci. Rural Pract.* 9 556. 10.4103/JNRP.JNRP_120_18
- 7-Zhang SY, Abel L, Casanova JL. Mendelian predisposition to herpes simplex encephalitis. *Handb Clin Neurol.* 2013. 112:1091-7.
- 8FowlkesAL,HonarmandS,GlaserC, YagiS, SchnurrD, StevenM, etal. *Enterovirus- associated encephalitis in*

- the California Encephalitis Project, 1998-2005. *Clin Infect Dis* 2008;198:1685–91.
- 9- Guilar PV, obich M, urell MJ, O'Guinn ML, Klein , Huaman A, et al. Endemic eastern equine encephalitis in the Amazon region of Peru. *Am J Trop Med Hyg* 2007;76(2):293-8.
- 10- Lundberg L, Carey B, Kehn-Hall K. Venezuelan Equine Encephalitis Virus Capsid-The Clever Caper. *Viruses*. 2017 Sep 29;9(10).
- 11-Sherman, M. B.; Weaver, S. C. (2010). "Structure of the Recombinant Alphavirus Western Equine Encephalitis Virus Revealed by Cryoelectron Microscopy". *Journal of Virology*. 84 (19): 9775–9782.
- 12- The National Institute of Neurological Disorders and Stroke Meningitis and encephalitis fact sheet.. <https://www.ninds.nih.gov/disorders/patient-caregiver-education/fact-sheets/meningitis-and-encephalitis-fact-sheet>. accessed Feb. 1, 2017.
- 13- Patel H, Sander B, Mark P Nelder. Long-term sequelae of West Nile virus-related illness: A systematic review. *The Lancet Infectious Diseases*. 2015;15:951.
- 14-Griffiths P. Cytomegalovirus infection of the central nervous system. *Herpes*. 2004 Jun. 11 Suppl 2:95A-104A.
- 15- Venkatesan A. (2015). Epidemiology and outcomes of acute encephalitis. *Curr. Opin. Neurol*. 28 277–282. 10.1097/WCO.0000000000000199
- 16- Ferreira J. E., Ferreira S. C., Almeida-Neto C., Nishiya A. S., Alencar C. S., Gouveia G. R., et al. (2019). Molecular characterization of viruses associated with encephalitis in São Paulo, Brazil. *PLoS One* 14:e0209993. 10.1371/JOURNAL.PONE.0209993
- 17- George BP, Schneider EB, Venkatesan A. Encephalitis hospitalization rates and inpatient mortality in the United States, 2000-2010. *PLoS One* 2014;9(9):e104169.
- 18- Vora NM, Holman RC, Mehal JM, Steiner CA, Blanton J, Sejvar J. Burden of encephalitis-associated hospitalizations in the United States, 1998-2010. *Neurology* 2014;82:443-51.
- 19- Pöyhönen H., Setänen S., Isaksson N., Nyman M., Nyman A., Peltola V., et al. (2021). Neurological and Cognitive Performance After Childhood Encephalitis. *Front. Pediatr*. 9:251. 10.3389/fped.2021.646684
- 20- Misra UK, Tan CT, Kalita J. Viral encephalitis and epilepsy. *Epilepsia*. 2008 Aug. 49 Suppl 6:13-8.
- 21- Kramer A. Viral Encephalitis in ICU. *Critical Care Clinics*. 2013;29(3):621-649.
- 22- Ai J. , Xie Z, Liu G, Chen Z, Yang Y, Li Y, Chen J. Etiology and prognosis of acute viral encephalitis and meningitis in Chinese children: a multicentre prospective study *Open Access Ai et al. BMC Infectious Diseases* (2017) 17:494.
- 23- Steiner I, Budka H, Chaudhuri A, Koskiniemi M, Sainio K, Salonen O, et al. Viral meningoencephalitis: a review of diagnostic methods and guidelines for management. *Eur J Neurol*. 2010 Aug. 17(8):999-e57
- 24-Jayaraman K, Rangasami R, Chandrasekharan A. Magnetic Resonance Imaging Findings in Viral Encephalitis: A Pictorial Essay. *J Neurosci Rural Pract*. 2018 Oct-Dec;9(4):556-560.
- 25- Solomon T, Michael BD, Smith PE, Sanderson F, Davies N W S, Hart I J, et al. Management of suspected viral encephalitis in adults — Association of British Neurologists and British Infection Association National Guidelines. *J Infect* 2012; 64:347-73.
- 26- Beattie GC, Glaser CA, Sheriff H, Messenger S, Preas C P, Shahkarami M, et al. Encephalitis with thalamic and basal ganglia abnormalities: etiologies, neuroimaging, and potential role of respiratory viruses. *Clin Infect Dis* 2013;56:825-32.
- 27- University of Illinois-Chicago, S. (n.d.). Encephalitis: Types, symptoms, causes, and treatment. [online] *Medical News Today*. Available at: <https://www.medicalnewstoday.com/articles/168997.php> [Accessed 7 Dec. 2017].
- 28- J. Dalmau, C. Geis, F. Graus. Autoantibodies to synaptic receptors and neuronal cell surface proteins in autoimmune diseases of the central nervous system. *Physiol Rev*, 97 (2017), pp. 839-887
- 29- Naito H, Havashi S, Abe, K. Rapid and specific genotyping of hepatitis B virus corresponding to six major genotypes by PCR using type-specific primers. *J Clin Microbiol* 2001; 39:1686.
- 30- Miyakawa, M. Serological detection of hepatitis B virus genotypes by ELISA with monoclonal antibodies to type specific epitopes in the preS2-region product. *J Virol Methods* 1999; 80:97-112.
- 31- Glaser CA, Honarmand S, Anderson LJ, Schnurr DP, Forghani B, Cossen CK, et al. Beyond viruses: Clinical profiles and etiologies associated with encephalitis. *Clin Infect Dis*, 43 (2006), pp. 1565-1577
- 32- Johnson RT. Viral infections of the nervous system. *Viral Infect Nerv Syst*, (1998), <https://www.cabdirect.org/cabdirect/abstract/20002006583>

مراجعته حول التهاب الدماغ الفيروسي

أ.م. ياسمين جواد البياع
أ.م. شيماء جواد كاظم
أ.م. زينب عبد الحسن حامد

الخلاصة

الخلفية: - يُعرف التهاب حمة الدماغ الناجم عن الفيروس باسم التهاب الدماغ الفيروسي الذي يتعايش بشكل متكرر مع التهاب السحايا الفيروسي وهو أكثر أنواع التهاب الدماغ انتشاراً

الأهداف: - إلقاء الضوء على التهاب الدماغ الفيروسي وأنواعه ووبائياته وأعراضه ومضاعفاته.

النتائج: - على الرغم من أنه يمكن أن يصيب الأشخاص من جميع الأعمار ، إلا أن العدوى الفيروسية هي السبب الأكثر انتشاراً لالتهاب الدماغ الفيروسي ، والذي يظهر عادةً عند الأطفال الصغار وكبار السن. الفيروسات المنقولة جنسياً ، والفيروسات اليرقان ، والفيروسات المعوية ، وفيروسات الهربس ، والفيروسات القهقرية ، والفيروسات القهقرية ، والفيروسات الرئوية ، والفيروسات التاجية ليست سوى عدد قليل من الفيروسات المعروفة بأنها تسبب التهاب الدماغ.

اخيراً مع ظهور فيروسات جديدة ، وتطور تقنيات التشخيص ، أو تعلمنا المزيد عن الفيزيولوجيا المرضية للمرض ، أصبح التهاب الدماغ الفيروسي مصدر قلق أكثر خطورة للصحة العامة.