Biological Times

Volume No. 3 | Issue No. 2 | Pages 15-16

Tick-borne Encephalitis Virus

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ABSTRACT

The tick-borne encephalitis virus belongs to the family Flaviviridae. Its composition has three structural proteins and seven non-structural proteins and these all make the genomic structure of TBEV. TBEV also has subtypes that are based on genomic analysis. These subtypes are prevalent in numerous countries. The main reservoirs of the virus include rats, mice, and other rodents. Humans and domesticated animals are accidental hosts. They get the virus by the bite of an infected tick of *Ixodes* spp. or by taking raw milk products. If ticks pass a part of their life cycle on one host and the rest of their life is passed on another host, then chances of pathogen transmission are reduced. The symptoms of TBEV may be monophasic or biphasic. In biphasic disease, mild symptoms appear in the first phase, fatigue, pyrexia, and pain, but in the second phase, neurological symptoms are present. Serological and molecular methods are used for the diagnosis of TBEV in serum and cerebrospinal fluid. For treatment and prevention of TBEV, no antiviral treatment is available. Some countries have made vaccines that are used to produce an immune response for prophylactic control of TBEV.

INTRODUCTION:

Tick-borne encephalitis virus (TBEV) is a member of the genus Flavivirus and belongs to the family Flaviviridae. It consists of a positive-stranded RNA genome. The single open reading frame encodes for one polyprotein which is composed of three structural proteins E(envelope), C(capsid), and M (membrane), and seven non-structural proteins, all these make genomic structures of TBEV [1]. Three subtypes of TBEV have been proposed that are based on genomic structure; 1) TBEV-Sib (Siberia) variants are spreading throughout Russia and reach to eastern parts of Europe. 2) TBEV-Eu (Europe) is prevalent in the mainland of Europe. 3)TBEV-FE (Far East) is present in northern China, Asia, and in the east of Russia [2]. Two other subtypes have been identified: the Baikalian subtype and the Himalayan subtype. Ukraine, some parts of Russia, the Balkans region, the European continent, and many other parts of the world including Pakistan and India [3]. Ticks, rodents, and insectivores are the main hosts of tick-borne encephalitis virus. Humans, domesticated animals, and those animals that are not domesticated but live in TBE-endemic areas are accidental hosts and become infected with the virus. Ticks and small mammals play an important role in the maintenance of a TBE in nature [4]. When infected hard ticks *Ixodes ricinus* bite, then TBEV is transmitted. Direct transmission of TBEV also occurs when the mother feeds their child. Transmission also occurs through the consumption of unpasteurized milk and is also transmitted through food-borne, transplantation of organs, and blood donation [5]. During the first phase of the virus, flu-like symptoms appear, including pyrexia, tiredness, pain, and muscular pain. During this phase, there is no sign of neurological symptoms. But in the second phase, neurological involvement is present, ranging from mild to a severe inflammation of the brain [6].

LIFE CYCLE:

Species of hard ticks (*I. ricinus*) have four stages in their life cycle and need three times feeding of blood for the next stage. The four stages of a tick are larva, nymph, adult, and egg. Larvae feed on small mammals, nymphs feed on birds and reptiles, while adults feed on large mammals. Host of adult ticks are large mammals and birds. Ticks are infected with TBEV when they feed on infected animals. Stages of life cycle are completed in two or three years, and it also depends on environmental conditions. By biting an infected tick or by consumption of raw milk products, humans also become an accidental host of TBEV [7, 8].

TRANSMISSION:

Through the bite of the infected tick, TBEV is transmitted to humans. For transmission of TBEV, ticks act as vectors and hosts are deer and small mammals. Small mammals are the main source of the transmission of TBEV, and large mammals have a very low concentration of the virus. A virus causes the infection after it enters the host's blood when the infected tick bites the host. Viruses are present in tick saliva that enters the host. Within minutes and hours of tick attachment, TBEV is transmitted from the infected tick to the host. If the ticks that are infected with the virus are attached to a host for a long time, then the chances of TBEV transmission are higher. When the infected tick takes its half-blood meal from one host and then moves to the next host, the transmission of TBEV is reduced. Once ticks become infected with a virus, they carry the virus for their entire life and transmit it to other ticks and mammalian hosts. The lifespan of *Ixodes ricinus* tick is up to 8 years [9].

CLINICAL SYMPTOMS:

Initial symptoms of TBEV include fever, feeling tired, anorexia, muscle aches, headache, nausea, and vomiting. After the beginning of the second phase of TBEV, CNS symptoms appear including inflammation of the protective membrane covering the brain and spinal cord [10]. In animals, symptoms are fever, anorexia, depression, and weakness of four limbs. Paralysis of facial nerve, uncontrolled movement of eyes, constriction of pupils, severe neck pain, and stiffness are also included [11]. In TBEV, biphasic and monophasic courses are involved. A biphasic course is one in which symptoms of neurological appear and improve within a day and month. When initial symptoms of the virus are not present, but direct neurological symptoms appear, then this is the monophasic course [12].

DIAGNOSIS:

Serum and cerebrospinal fluid are tested for TBEV by using serological and molecular methods for diagnosis of the virus.

To cite this article: Batool S, RZ Abbas, S Fatima, S Batool, K Tariq & A Hussain. 2024. Tick-borne encephalitis virus. Biological Times, 3(2): 15-16.

In the first phase of the virus, viral RNA is detected in serum by using a polymerase chain reaction (PCR). For diagnosis of the second phase of TBEV, antibodies of TBEV immunoglobulin M (IgM) and immunoglobulin G (IgG) are present in serum. For good sensitivity and specificity, an ELISA kit is used for the detection of IgM antibodies. For the detection of the second phase of TBEV in which neurological symptoms are involved, magnetic resonance and electroencephalogram tools are used [1].

TREATMENT AND PREVENTION:

For TBEV treatment, vaccination effectively reduces the number of patients that suffer from TBEV and death that is because of the virus. Three different pharmaceutical companies, GSK-Encepur (Germany), Pfizer (Austria), and Microgen (Russia) licensed five types of vaccine in Europe and Russia, but Chumakov Institute is licensed only in Russia. For injecting of this vaccine, an intramuscular route is used. European and Russian-made vaccines have different administrations. After the first dose of the vaccine, for immediate immune response second dose of the Pfizer vaccine is given. For TBEV, no specific antiviral treatments is available. Some treatments are given with care and proper ventilation. [1].

CONCLUSION:

Tick-borne encephalitis virus is viral RNA that has subtypes because of its genomic structure, and these subtypes are also prevalent in numerous countries. TBEV is transmitted through the bite of an infected tick, consumption of unpasteurized milk, donation of blood, and from mother to child during feeding. Symptoms of TBEV include muscle weakness, tiredness, pain, and inflammation of the membrane that is around the brain and spinal cord. TBEV is diagnosed by the detection of antibodies IgM and IgG in serum and blood. Some tools are also used for the detection of TBEV. For treatment, no specific vaccine is made but some vaccines are used for boosting of immune system.

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