

MINI REVIEW



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<http://www.lifesciencejournal.pk>**Rabies virus: A mini review**Eman Ahmad¹, Muhammad Shaheen Iqbal¹, Muhammad Qasim¹¹Pakistan Council of Scientific and Industrial Research (PCSIR) Labs complex, Ferozepur road, Lahore, Pakistan***Corresponding Author**Muhammad Shaheen Iqbal (shaheen.microbiologist@gmail.com)

Pakistan Council of Scientific and Industrial Research (PCSIR) Labs complex, Ferozepur road, Lahore, Pakistan

Abstract

Deadly rabies virus belongs to the Rhabdoviridae family of viruses. Rabies is a bullet-shaped enveloped negative-sense RNA genome virus. It causes diseases mostly in animal and humans. It is transmitted to human by bites of dogs and bats mostly and causes hydrophobia and eventual death. The virus uses nerve cells for their multiplication and produces mutations in the nervous system. Each year 59 thousand people die due to the rabies virus, the ratio in China is much more. There is no treatment for rabies. Although vaccination for dogs is available. We can't cure this but we can avoid this by taking preventive measures. The purpose of this mini-review is to summarize the rabies virus and its medical importance.

Keywords: rabies virus, Rhabdoviridae, dogs bites, rabies vaccination, bats, replication*Life Sci J Pak 2019; 1(01):40-43. doi:10*

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Copyright © 2019 Ahmed *et al*. This is an open-access article distributed under the **Creative Commons Attribution License**, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.**Introduction**

Rabies is the dreadful disease which causes infection both in human and animals. The causative agent is rabies or lyssavirus which is usually found in the saliva of infected animals and is the most lethal of all the infectious diseases. There is no cure for rabies however it can be prevented by vaccination of affected person (1). The word rabies comes from the 'Sanskrit Rajas' that means 'to do violence'. It is said that rabies is derived from the word 'Rabha' which means violence. Rabies virus is transmitted by bites of sharks, bats, and raccoons but most common is the bite of a dog. (2) The disease shows symptoms in 3 to 5 days and common symptoms are fever, malaise, agitation, irritability, irregular breathing and consequently death (3). Patient exhibits hydrophobia due to inability to swallow which causes paralysis of the throat and facial muscles. Rabies virus belongs to the Rhabdoviridae family which is an enveloped RNA virus having bullet shaped coiled capsid and inside it, a negative sense single-stranded linear genome resides. The virus binds

to acetylcholine receptor cells where it replicates itself and moves along the peripheral nervous system then moves toward central nervous system from where it spreads in other organs of the body and also shows its presence in the salivary glands. It affects CNS and particularly causes inflammation of the brain (4).

History

Rabies disease was first recognized in Egypt in the fourth century by Aristotle who declared that there was something dangerous in a dog bite. Later on, it was discovered by the physician Girolamo Fracastoro in the 16th century and he called it the incurable wound. Eventually, in 1912, it was confirmed in Kenya (5) and in these days the veterinary cases were reported more than human cases. Many emerging microbial threats of rabies disease were seen in Kenya in the year 1996 (6). However, it also posed a major public health issue in 2009 in the United States and Canada. Bat-related rabies cases have also been seen in persons without

being contaminated or bite by a bat (7). A recent statistic from China shows that about 108,412 persons have died due to this disease from 1950 to 2004 (8). Other than dog and bat, fox related cases of rabies virus have also been reported in Asia and Europe. The vaccination against this virus was first prepared by Louis Pasteur in 1885 (9).

Prevalence in the world

According to the World Health Organization (WHO), in the year 2016, 59 thousand people died due to rabies in which 95% of cases were from Africa and Asia. Among these 99% cases were dog-mediated rabies. Every year approximately 30,000 to 70,000 people die from this disease predominating the number of children as compared to adults (10).

Virus structure and features

Rabies is a bullet-shaped virus with 180nm length. It consists of five proteins, an envelope, and a negative sense RNA genome inside the capsid. The five proteins are N nucleoprotein, M matrix protein, P phosphorous protein, G glycoprotein, and L polymerase protein. The G protein is present in the shape of spikes on the outer surface of the envelope, inside this M protein make inner membrane in which N, P, L protein and RNA in inner linked in the chain structure (11). The virus belongs to Rhabdoviridae family and its genus is lyssavirus and it consists of six other viruses which cause diseases in different species like foxes, raccoons, bats, and dogs. Rabies is the enzootic disease which also affects the humans (1). There are two types of rabies which are urban and sylvatic. It is an encephalitis virus and causes acute highly contagious fatal disease. It has the ability to affect peripheral nerves and transfer to CNS and consequently cause inflammation of the brain and responsible for the neurological disease (4, 12). In response to invasion by the virus, the host initially recognizes RNA viruses by cellular sensors and recognition receptors that send an impulse to produce type I IFN (alpha and beta IFN family). Interferon is the signaling protein that is made or released when the body realizes the presence of a foreign pathogen (13). Although the virus is destroyed by simple environmental factors, including temperature, UV light, sunlight, 70% alcohol, ether, deoxycholate, and trypsin. Rabies is transmitted by the bite of an animal without bite there are the very rare cases (14).

Genome structure

Rabies virus is the negative sense RNA virus with 12000 nucleotides that code for the five proteins named nucleoproteins, matrix protein, phosphorous protein, glycoprotein, and polymerase protein. These

all protein have a direct and indirect role in pathogenicity. Lyssavirus genus has 6 different rabies-related viruses. Virus RABV is a member of genotype 1, these five genes code for five protein (7). Gene N (nt 59 to 1483), gene P (nt 1486 to 2475), gene M (nt 2481 to 3283), gene G (nt 3289 to 5355) and gene L (nt 5380 to 11853) (15).

Nucleotide protein is directly bound to viral genomic RNA. N protein is responsible for the encapsulation of anti-genomic and genomic RNA. N protein is bind strongly to leader RNA (16).

Phosphorous protein is multifunctional essential for viral replication, in RNA synthesis act as a cofactor for L protein. P protein antagonizes the type 1 interferon IFN mediated antiviral responses by inhibiting signaling pathway for IFN induction and response suppresses activation of interferon regulatory factor 3. It inhibits the nuclear translocation and DNA binding with IFN and inhibits IRF 3 activation (17).

Glycoprotein has a predominant role in pathogenicity. It is organized as trimmer and is a sole protein exposed on the surface of the virion. G protein promotes viral entry from the peripheral to the central nervous system it spreads trans synaptic trigger apoptosis which cause premature state of the host cell (18).

Matrix protein has a clear function in the pathogenicity but has a regulatory role in viral transcription and replication. It lacks pathogenesis however helps in virus budding (19).

Polymerase protein has a cooperative role with the P protein it works as an RNA polymerase in the infected cell (20).

Life cycle

During virus assembly ribonucleotide protein RNP is enclosed in an envelope that contains an inner layer of M protein and G protein. Rabies virus transfer to the host from the host usually through the bite of infected animals or by the saliva. It uses network of nerves cells in peripheral neurons which linked various body parts to the central nervous system. The virus needs to bind to P75 and TR receptor present on the tips of peripheral neurons, in order to move quickly (21). After the entry it attacks on junction of the muscles from where they go to the neural pathway and enter into the cytoplasm of a nerve cell by retrograde and axoplasmic transport. P protein of virus bind to dynein protein which travels in and outside in cytoplasm of nerve cells by retrograde axonal transport. The virus hijacks transport system of neurons and exploits axonal transport machinery. At this place it starts transcribing itself, transcription is in the form of polymerase shuttering that is the process of transcribing nucleotides several times by polymerase enzyme that shuttles on mRNA (22).

Hydrophobia

Actual it is not the fear of water except infected person has a fear of swallowing any liquid that is called dysphagia. Rabies affects the neurons of respiration and swallowing, generally, it effects neural network and CPG's that have the function of swallowing, mastication, and respiration. It has an effect on respiration and swallowing by the brain stem respiratory neurons and DMRC dorsal medullary reticular column. The virus uses our nervous system to avoid water because in case of water intake virus is diluted and it has the chance of diminished transmission and its life cycle stops which is an evolutionary mechanism (23).

Vaccination of dogs

Risk of rabies is more in the unvaccinated dogs, those roaming outside on the roads. There is not any treatment method for this disease after the onset of symptoms. However, the vaccination method before the symptoms appear can save an infected person. The disease can be prevented via the administration of the vaccine to the population at risk. DNA vaccination is injected via intradermal in ear pinnae that protects dogs for one year (24). Recombinant rabies-canine adenovirus type 2 vaccine in the bait is used orally in dogs that give long-term immunity to dogs (25).

Preventive measure

Rabies can be prevented on national level. To prevent and eliminate the brunt of rabies WHO suggest that 70% of the dog in the population should be immunized (26). Human rabies can be prevented by the use of post-exposure prophylaxis (PEP) in an emergency situation to victims of rabid animal bites (27). To avoid rabies firstly vaccinate the pets (dogs and cats) according to the law of your country (28). Stay away from stray dogs they have more risk than vaccinated pets. Don't keep wild animals and avoid their contact with your pet (29).

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