

One-Health Approach to Control Rabies**31**

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ABSTRACT

In this chapter, we had focused to control one of the most important and dangerous zoonotic diseases named rabies through one-health approach. Rabies is a viral disease associated with Lyssavirus including the rabies virus and Australian bat virus. Rabies is a threat continues to impose a significant number of risks and dangers to the population worldwide. Many people become affected from this zoonotic disease every year. Therefore, the implementation of one-health approach is need of the hour for the control of rabies knowing the interface of the virus interconnected with humans, animals, and environmental health. This discussion illuminates the origin of the virus and its transmission routes including both less common and most commonly used transmission routes. To better understand the risks and severity of this disease, it is important to know the pathogenesis of the virus in the body. So, the mechanism by which the virus attacks the body, resides in it, and infects the nervous system of the individual leading to the severity of the disease symptoms and high mortality within days is also discussed. Also, diagnostic tools used globally and prophylactic measurements are highlighted along with the control actions that can be taken to avoid the disease spread and transmission. By implementing the holistic one-health perspective, the aims to reduce the occurrence of rabies in humans as well as animals addresses the socioeconomic and environmental aspects to control the prevalence of the zoonotic viral disease.

Keywords: Rabies, One-Health importance, Transmission, Pathogenesis, Control.

CITATION

Tahir AH, Khan MA, Ahmad MZ, Saeed Z, Ali I, Kamran M, Rahim MF and Zafar MA, 2023. One-health approach to control rabies. In: Aguilar-Marcelino L, Zafar MA, Abbas RZ and Khan A (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 3: 398-406. <https://doi.org/10.47278/book.zoon/2023.111>

CHAPTER HISTORY

Received: 28-Jan-2023 Revised: 10-April-2023 Accepted: 20-June-2023

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1. INTRODUCTION

Rabies is a well-known zoonotic, fatal viral disease that affects humans and animals through scratches, bites, or contamination of mucous membranes or broken skin with the infected saliva of a rabid animal. Rabies virus primarily affect the brain and spinal cord cause acute progressive inflammation (encephalomyelitis/ encephalitis) and tissue damage develops ultimately resulting in death. There are two types of rabies that exist from a clinical standpoint. The first type is known as furious rabies, two third of infected patients, which is characterized by hyperactivity, hallucinations, lack of coordination, aerophobia (fear of fresh air) and hydrophobia (fear of water). In furious form of rabies, death occurs after a few days. The second type is known as paralytic rabies, one third of infected patients, which is characterized by paralysis of various body parts (Makoto and Naoto 2007). Dogs are the most common reservoirs for human infection, accounting for over 99% of cases worldwide. The infected hosts, like bats, jackals, and foxes, can transmit this infection to humans. In Africa, Asia and Europe, it is linked with dog bite while in America it is associated with bats bites (Thiravat et al. 2013). According to CDC 5000 cases of rabies are reported annually from United States. Rabies is one of the neglected zoonotic diseases despite it has enormous public health importance. The effect of rabies is growing by day even though it can be prevented which is an issue in both industrialized and developing countries.

According to reports, annually, over 55000 individuals are estimated to die from rabies worldwide. Every year, an estimated 1000000 Humans undergo post-exposure therapy after they exposed to animals which are suspected to have rabies. All continents and 150 countries, except for Antarctica, have reported cases of Rabies (Riccardi et al. 2021). The majority of rabies cases occur, after being bitten by a dog particularly in the rural region. Children under 15 years of age account for 40% of cases with Asia and Africa reporting the highest rates of the disease. According to a review, Asia bears a disproportionate share of the public health cost associated with rabies, accounting for an estimated 32,000 fatalities and 96.5% of the disease's economic impact in developing nations, with US\$560 million being spent annually mostly on post-exposure prophylaxis (Krishna 2020). There are currently just a few nations that are rabies free, including Singapore, Taiwan, and Japan.

Animals transmit more than 60% of Infectious diseases which are known and 75% of developing infectious illnesses. In terms of public health, Rabies, Because of its lethality, is the most serious of these diseases. The control and management of these zoonotic diseases are complicated because its multifarious nature one-health approach involving multiple sectors could be a superior strategy for dealing with Rabies. Up to date, Rabies prevention and control programs are carried out by mass vaccination of home and communal dogs and cats as well as public awareness campaigns. However, the problem of rabies has not decreased because these techniques failed to integrate animals, humans, and environmental health sectors controlling the disease program (Krishna 2020).

2. ETIOLOGY

The causative agent of rabies disease is a rabies virus. It has a single-stranded RNA genome belonging to the genus *Lyssavirus* and family *Rhabdoviridae* (Rod-shaped viruses). This family is divided into two phylogroups. Rabies lyssa virus (RABV), which is called genotype 1 is included in phylogroup 1. Other genotypes included in phylogroup 1 are: genotype 4 (Duvenhage virus), 5, 6, and 7 (European bat Lyssavirus, EBLV1-2 and Australian bat Lyssavirus). The phylogroup 2 include genotype 2 (Lagos bat virus) and 3 (Mokola virus) (Monroe 2018).

A highly neurotropic virus in the mammalian host, RABV is the cause of the classic form of rabies in both animals and humans. Once the infection is established and has reached the brain, it invariably results in a deadly encephalomyelitis.

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Various carnivore and bat species serve as the specialized mammalian reservoir hosts for RABV around the world. There have been 15 different Lyssaviruses discovered that resemble RABV in terms of morphology and structural features.

Only 6 of the 16 Lyssaviruses in the genus of *Lyssavirus* that are now recognized have been linked to encephalomyelitis like rabies in humans. Of the 16 identified Lyssaviruses, it should be noted that only RABV has numerous host reservoirs, whilst the other Lyssaviruses are only connected to bat reservoirs. All the viruses belonging to phylogroup "I" are disseminated by bats; only RABV has evolved to employ carnivores as its reservoir host and is spread by them. It is unclear how lyssaviruses transmitted by carnivores and bats developed in connection to one another. Many biological and physicochemical characteristics of other Rhabdoviridae family viruses are shared by *Lyssavirus* species. The morphology of the virus, which has a bullet-like form, the helical nucleocapsid (NC), and the overall arrangement of the viral RNA and structural proteins are some examples. The majority of the biologic roles that these viral proteins perform in other rhabdoviruses are also shared by these lyssavirus proteins (Okumura and Harty 2011). Lyssaviruses, on the other hand, are not spread by insect vectors like all other rhabdoviruses and have evolved to direct transmission. Shortly, Genus *Lyssavirus* contains 16 virus species among all of them rabies virus is the most important and concerning its impact on public health.

2.1. INCUBATION PERIOD

The incubation period of rabies depends upon the site in which the virus is inoculated, it means that incubation period will be shorter if the virus is inoculated near brain or in the area having more nerve proliferation, the degree of the bite and/or damage (a shorter incubation period corresponds to a bite or wound that is deeper and more extensive) and the viral genotype. In most cases, it is 2 to 3 months but may vary from 10 days to month or uncommonly years (Charlton et al. 1997).

3. EPIDEMIOLOGY

- For more than 4,000 years, rabies has been known to exist. It is now present throughout the majority of nations, except for those from which it has not been natively documented, such as several Australian islands or regions that have achieved secondary extinction, like the United Kingdom.
- The bite of a rabid animal is the major source of rabies in humans.
- The likelihood of contracting rabies is highest in those world areas where canine rabies is hyperendemic, such as the majority of Latin America, Africa and Asia.
- In the years 1940 to 1950, the domestic rabies animals were mainly controlled by the America and European countries, now less than 10% of all rabies animal cases reported.
- In United States of America, the wildlife rabies mainly affects the terrestrial predators such as foxes, raccoons, skunks, insectivorous bats etc.
- Almost invariably, a bite is the main cause of human rabies.
- Rabies in humans is mainly brought on by non-bite exposures, which include contamination of an open wound or a mucous membrane by scratches, licks, and aerosol inhalation (Binkley and Gebreyes 2023).
- Rabies is one of the most significant zoonotic diseases in the world, according to the WHO. According to estimates, one in two Americans will experience an animal bite at some point in their lives. It makes sense to divide the world's rabies cases into three geographic epidemiologic regions: (1) nations where

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canine rabies is enzootic; (2) nations where wildlife rabies is predominant while canine rabies is under control and (3) Nations where rabies is not an issue (Willoughby 2023).

- Rabies appears to be periodically transmitted in reservoir host populations because of density-dependent transmission. A weak understanding of the ecological elements that increase or decrease rabies' long-term survival in reservoir animals is present.
- It is unknown where terrestrial rabies first emerged. Because the rabies virus kills, most of its infected hosts and lacks any known stages outside of its living host, it defies two of the key principles for effective pathogens. The parameters of the rabies cycle can be affected by human encroachment when reservoir host animals interact near concentrated food sources, such as pet foods, bird feeders, and landfills, and domestic pets are more exposed to wildlife.
- First case of rabies disease is confirmed in domestic fowl in India (Baby et al. 2015). Although solid evidence has only been available for the past 100 years, the Spanish researchers explore the 1st suspect bats as a vector for rabies in South America (Sami and Ennaji 2020).
- There is estimated that the total 10-15 million humans receive rabies post exposure prophylaxis (PEP) a year after being exposed to animals with probable rabies, however, there is no conclusive reporting of these cases (Oertli 2020).
- Serotypes and genotypes of the virus are categorized.
- There are numerous varieties (strains or kinds) of the virus because of genetic evolution, each of which is kept in a distinct reservoir host. The term "viral "strains or variants" refers to viral populations that may be recognized from other strains by their genetic and antigenic properties and are maintained by a specific reservoir host in a specific geographic area.
- The reservoir host is crucial to the virus's ability to spread. For clarification, raccoon rabies in a dog would be used instead of canine rabies to represent rabies in a dog caused by a rabies variety that is still present in raccoons.
- There are so many factors such as natural habitat, home range, the population of the reservoir host, physical barriers, different variants of the rabies virus, other kinds of diseases of the host species, and vaccinated or natural herd immunity status that influence the epidemiology and prevent disease transmission.
- The reservoir host for rabies cases has undergone a significant alteration, except for Africa, Asia, and India. Domestic animals, primarily dogs, used to have the greatest recorded incidence of rabies cases. That would be indicative of the current global scenario, given that dogs have long been thought to be the primary carrier of this zoonosis and continue to be the primary cause of modern-day human fatalities (Streicker and Biek 2020).

3.1. TRANSMISSION

Rabies has two cycles of transmission, one is sylvatic and other is non-sylvatic. The majority of cases of rabies virus transmission happen when an infected animal bites or engraves another vulnerable animal or human. Additionally, people may get rabies if they come into close contact with an infected animal's saliva on their mucosa or skin sores. Although it is very uncommon for the virus to transfer from person to person, but few cases were reported after transplant surgery. Seasons have a major role in the spread of rabies, with late summer and autumn being the seasons with the highest frequency because of the large number of wild animals looking for a mate and food. In emerging nations, it is predicted that it is an urban disease because of the high level of human-domestic animal interaction (Imran 2020).

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3.2. COMMON TRANSMISSION ROUTES

- The rabies virus (RV) has been linked to several carnivorous animal species.
- Domestic dogs are the primary carriers of the rabies virus in Asia and Africa.
- Instead of dogs, other animals such as racoons, foxes, skunks, coyotes, possums, and bats carry the virus in the US through bites.
- There are three phases of canine rabies that have been identified. The prodromal stage is the first stage characterized by behavioral changes exists for 1 to 3 days. The second stage, which lasts 3 to 4 days, is the excitative stage. This stage of the disease is frequently referred to as "furious rabies" because the infected dog has a propensity to bite when it is overly sensitive to environmental stimuli.
- The paralytic stage, which is the third stage, is brought on by motor neuron injury which causes incoordination because of paralysis of the rear limb, Facial, and throat muscles. Paralysis causes difficulty in swallowing and drooling. Respiratory arrest frequently results in death.
- When a human is bitten by an animal that has the rabies virus in its salivary glands, the disease is transmitted.
- After the initial inoculation, the RV is still cell-free, therefore thorough wound cleansing may lessen the risk of infection.
- Retrograde axonal transport enables RV to infect peripheral nerves and subsequently spread to the CNS. (Müller and Freuling 2020).

3.3. LESS COMMON TRANSMISSION ROUTES:

Less frequent methods of spreading the rabies virus include:

- Mucous membrane contamination, such as that of the mouth, nose, and eyes
- Transmission of aerosols
- Transplantation of the cornea and other organs from an infected donor

4. PATHOGENESIS

- In the pathogenesis of rabies, the virus must get beyond the skin's protective barrier, which is typically accomplished by being bitten by an infected or ill animal. Despite being experimentally proved, other transmission pathways, such as the oral route, are irrelevant to rabies epidemiology.
- Interestingly, the bite of an infected animal is not always cause to development of rabies disease due to intermittent shedding and a species-specific resistance. Muscles or peripheral nerves may initially become directly infected by the virus through infectious saliva.
- The *Lyssavirus* enters a peripheral neuron by receptor-mediated entry and then travels retrogradely in the neuron's axon via endosomal transport vesicles to the spinal cord via either the dorsal root (for sensory neurons) or ventral root (for motor neurons) ganglia.
- Strong immune response activation is something that *Lyssaviruses* successfully suppress and control. Further replication and transsynaptic propagation in the brain cause centrifugal dissemination of numerous infected neurons across the CNS. Clinical indications first appear when neuronal dysfunction worsens.
- The variety of incubation periods recorded with different varying times from virus entry to lead disease in naturally and experimentally infected animals. The clinical stage can last up to 10 days, but it typically concludes with the animal's death following a cardiac arrest and coma.

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- Based on experimental results from previous studies, the WHO-recommended 10 days' observation period.
- The biting animal can simply be studied for 10 days if a dog, cat, or ferret exposes a person, or another animal and rabies needs to be ruled in or out. The danger of rabies virus transmission from the prospective exposure to this animal is minimal if it survives these ten days in good health. If there was a chance of viral shedding and transmission, the animal would have displayed clinical rabies symptoms during the monitoring period, perhaps including rapid death.
- Any clinical symptom or unexpected mortality must be verified by laboratory tests. It is interesting to note that before the pathophysiology of the disease was discovered, confinement and observation of questionable animals had already been a veterinary hygiene measure. (Chomel and Sykes 2021).

5. SIGNS AND SYMPTOMS

The majority of rabies' clinical signs are unconditional. The early signs include temperature with pain and tingling and paraesthesia at the site of the bite. Human cases of rabies often present in three stages, prodromal with vague symptoms, acute neurological symptoms, and lastly is coma leading to death. During the acute neurological phase, there are three ways that rabies can manifest clinically i.e., furious, paralytic, and non-classical. When the virus enters the CNS, it greatly causes inflammation in the brain and spinal cord. The rabies virus-affected animals exhibit specific CNS neurotic symptoms that vary minimally between species.

5.1. PRODROMAL STAGE

This is the first stage which lasts usually one to three days. In this stage, small behavioral modifications may occur such as rage in household animals, loss of fear from humans in wild animals, and loss of appetite.

5.2. FURIOUS STAGE

In this stage the following signs are present: roaming, sobbing, agitation, assault on other animals and humans. At this stage, animals start consuming foreign objects like stones and firewood. Unusual alertness in cattle is a sign of this stage.

5.3. PARALYTIC STAGE

The paralytic stage of rabies can be identified by gradual paralysis. The primary muscles responsible for swallowing become paralyzed due to which animal may not swallow anything. The hypersalivation is present in this stage. The voice of animal changes and the animal starts bellowing and barking. Hind limbs become paralyzed and then complete body paralysis occurs after which animal dies.

5.4. HYDROPHOBIA

The term hydrophobia means fear of water. This sign is present in all the rabid mammals in advance stage. The animal may struggle to drink water, but because of the paralysis of gullet muscles, it doesn't happen. There is a release of foamy salivation in which virus is present.

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6. DIAGNOSIS

The primary factors that determine the diagnosis are the clinical signs and symptoms, the history of the afflicted person, mortality, and immunization prophylaxis. A superior premortem technique to identify the viral antigen is the fluorescent antibody test (FAT). The postmortem diagnosis can be made if negri bodies are found in the brain. FAT is approved by the World Health Organization (WHO) which shows up to 99% accuracy in the result after few hours. More ever ELISA (Enzyme-linked immunosorbent assay), and use of monoclonal antibodies for virus diagnosis, Rabies antibody isolation test can be performed for the accurate diagnosis. The RT-PCR assays is also used to for the confirmation of disease.

7. PROPHYLACTIC MEASUREMENTS

- People who are likely to encounter rabid animals are advised to have pre-exposure to prophylactic immunization.
- Animal handlers, lab workers, and veterinarians should all think about getting routine vaccinations.
- Additionally, those who will not have easy access to medical care while going to locations where dog rabies is widespread should think about getting immunized before leaving.
- A previously inoculated person who may have been exposed to rabies should get two intramuscular doses of the vaccine, the first one as soon as possible after the exposure, and the second one three days later. A booster vaccine should not be followed by routine serologic testing due to the consistency of an antibody response (Del et al. 2020).

7.1. POST-EXPOSURE CARE

- To help lower the risk of bacterial illness, the bite site after an animal bites a person should be thoroughly washed with soap and water. Viral transmission from a bite may be decreased by Povidone solutions or 70% alcohol.
- A bite wound should be evaluated for cosmetic restoration, although closing a wound raises the possibility of bacterial infection.
- It is recommended to get a rabies vaccine. Based on an evaluation of the rabies risk in the animal that bit the person, rabies vaccination should be given.
- The rabies vaccine is 100% effective if given early and still has a chance of success if delivery is delayed.
- There are huge economic losses because of vaccine, more than 15 million people get vaccinated after exposure in the world but vaccines save lives.
- In general, unless the animal exhibits aberrant behavior, a bite from a domestic animal that has been reliably inoculated does not provide a significant risk of contracting rabies and does not call for rabies treatment.
- Low-risk rabies-infected animals can be monitored for 10 days for indications of unusual behavior. The animal should be killed if it exhibits odd behavior, since its saliva might be contagious.
- Domestic animal immunization may not be up to date in poor nations. As a result, whether a dog is domestic or wild, all bites should be regarded as possibly rabid, and treatment should begin right once.
- If an unvaccinated or wild animal bites a person and the animal can be killed and tested for rabies, the patient should get immunized right away, and treatment should continue based on the results of the test.
- Unfortunately, it's difficult to keep an observation on wild animals, therefore; every wild animal bite must be treated as rabid (Gilbert and Chipman 2020).

8. CONTROL

- Routinely visit your veterinarian for a checkup of your dogs and cats and keeps rabies vaccine up to date.
- Always maintain the supervision of your dog, cats and ferrets.
- Neutering and spaying should be done to avoid the unwanted pregnancies because there are difficulties to vaccinate all the animals.
- If you found stray dogs in your neighborhood, please complain to the animals control department.
- No need to adopt wild animals, leave wild animals alone.
- According to WHO, vaccination of 70% or more dog population can reduce the chance of rabies through dog bites. So, need to massive vaccination schedule to control rabies in dogs. Ultimately, they reduce the chances of rabies in dogs as well as in humans.
- Public awareness programs should be adopted to control rabies and for other zoonotic diseases.
- Need to strengthen the laboratories for the diagnosis of diseases as soon as possible.
- Epidemiological studies should be carried out for rabies and other diseases for the identification of different factors involved in diseases.

There should be strong coordination and data sharing among animal doctors, Human doctors and environmental experts etc.

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