Rabies: A Preventable Zoonotic Disease

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ABSTRACT

Rabies is a highly zoonotic viral disease of central nervous system that is caused by genus lyssavirus of family rhabdoviridae .There are several species recognized in this genus all of them affect central nervous system and cause rabies like symptoms .It is characterized by acute progressive encephalomyelitis with case fatality rate of upto 100 %.It is basically transmitted from one animal to other animal through bite of rabid animal via saliva.Almost all mammals are prone to infection by rabies virus and primary reservoir of rabies include foxes ,raccoons ,skunks and dogs .Nervous signs of rabies are exhibited in two forms :furious form and paralytic form.Furious stage also called “mad dog syndrome is presented as nervousness. aggressive behavior and hyperexcitability .Paralytic stage include paralysis of masseter muscle and diaphragmatic muscle and ultimately death.The gold standard test for diagnosis of rabies is Flourescent Antibody Test (FAT)test which is recommended by WHO.Timely diagnosis of rabies is crucial for prompt administration of post exposure prophylaxis to prevent onset of clinical otherwise it has nearly 100% mortality rate .Prevention of rabies is key to lessen the risk of such global public health threat .Mass vaccination of dog , administration of pre exposure and post exposure and oral vaccination of wild animal reservoir is recommended for prevention Major focus is to implement preventative strategies to eliminate rabies globally beacuase it is incurable once clinical signs appear.

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1. INTRODUCTION

Rabies is a preventable zoonotic disease of mammals that is caused by lyssavirus and is characterized by acute progressive encephalomyelitis. According to reports by the World Organization for Animal Health, it is a global public health hazard that is responsible for mortalities of 59,000 people annually with case fatality rate of100% (WHO Expert Consultation on Rabies 2018). It is primarily transmitted to humans by the bite of a rabies infected animal that introduces virus-laden saliva into the host. Its primary reservoir includes dogs, foxes, raccoons, skunks, and bats (Barecha et al. 2017). Dogs serve as important reservoir of rabies and more than 99% of human rabies are caused by dogs (Fitzpatrick et al. 2014). Therefore, combating lethal zoonosis at its animal source is necessary for disease control and elimination. The disease is prevalent worldwide except in Antarctica; most cases are reported in underdeveloped countries of Africa and Asia, with thousands of mortalities reported annually (Wandeler 2012). Clinical signs of rabies are manifested in two forms: classic furious form and paralytic rabies that resembles Guillain-Barré syndrome (Vaish et al. 2011). After exposure to rabies, immediate post-exposure prophylaxis must be followed which includes wound management, rabies immunoglobulin administration, and rabies vaccination course that can prevent the appearance of clinical signs. (Sparrow et al. 2019). It has no pathognomonic clinical signs or gross lesions that can distinguish it from other nervous disorders. The most commonly recommended and gold standard test for rabies diagnosis is the direct fluorescent antibody test. Although it is a preventable disease but it is fatal once clinical signs appear. (Ahmed et al. 2022). An integrated approach consisting of pre-exposure vaccination, control of stray animals, minimizing contact with wildlife, post-exposure prophylaxis, responsible pet ownership, and public awareness rules and regulations regarding animal movements can help control rabies.

2. ETIOLOGY

Rabies is a viral disease caused by the rabies virus of the genus Lyssavirus. It is a single-stranded negative-sense RNA virus that belongs to the genus *Lyssavirus*, family *Rhabdoviridae* and order *Mononegavirales*. (Nigg and Walker 2009). 14 species of genus lyssavirus have been recognized which are categorized based on their genomic sequencing; they are the Rabies virus, Mokola virus, Lagos bat virus, Australian bat lyssavirus, Duvenhage virus, European bat lyssavirus type 1, European bat lyssavirus type 2, Khujand virus, Aravan virus, Irkut virus, West Caucasian bat virus, Bokeloh bat lyssavirus, Shimoni bat virus and Ikoma Lyssavirus (Cifuentes et al. 2017). All these species are genetically related, highly neurotropic, affect the nervous system, and are collectively called rabies-related lyssavirus (Wunner 2007). The majority of these viruses are found in bats, researchers have proved that lyssavirus originated and spilled over from order Chiroptera to Carnivora which led to the emergence of rabies in mammals (Badrane and Tordo 2001).

It is a bullet-shaped virus with a negative sense, single-stranded RNA genome. Rhabdovirus is 180nm in length and 75nm in width. Its structural components include a helical ribonucleoprotein core and an envelope that surrounds the core (Garg and Garg 2014). Its genome encodes five viral proteins that are: matrix protein, nucleoprotein that encapsulates viral RNA phosphoprotein which is required for transcription, the glycoprotein which is a membrane-bound moiety that mediates viral attachment and fusion at cell surfaces. (Zan et al. 2016). In addition, it induces the production of viral neutralizing antibodies and polymerase, which is required for RNA synthesis (Rupprecht et al. 2002). These viruses become inactive outside the host and are quickly deactivated by sunlight, drying and heat Within the host cell rabies virus has a high affinity for nerve cells and replicates also within muscle cells (Nigg and Walker 2009).

3. TRANSMISSION

Since all mammals are vulnerable to rabies this virus is readily transmitted between mammals, whether they are of the same or different species. Most commonly this virus is transmitted by the bite of a rabies infected animal that introduces the virus into the host by saliva (Corstjens et al. 2016). Less often, this virus can also enter the host by abrasion in the skin or mucus membrane. Aerosol transmission of rabies virus has also been reported under laboratory conditions. It has been documented that rabies virus has been transmitted from human to human by organ transplantation. (Lu et al. 2021).

Mammals of order Carnivora and Chiroptera serve as primary vectors of rabies. (Kotait et al. 2019). Whereas, In underdeveloped countries, dog bites are responsible for the majority of cases. Cats are also efficient vectors of disease transmission; however, it appears that neither domesticated nor wild cats act as reservoir hosts. (Rupprecht et al. 2002). In different parts of globe particularly in developed countries, rabies is predominantly transmitted by wildlife, particularly bats. There are two epidemiological cycles for rabies: the urban rabies cycle and the sylvatic rabies cycle (Devleesschauwer et al. 2016). In urban rabies, dogs are the primary reservoir of viruses that transmit disease. In underdeveloped countries of Asia, Africa, and Central America urban rabies cycle predominates where the population of unvaccinated and free-roaming stray dogs is still under control (Barecha et el. 2017).

In developed countries of America and Europe, rabies is transmitted mainly due to contact with wildlife like bats raccoons, foxes and skunks (Nayak et al. 2022). Control of stray animal populations and mass vaccination of dogs have nearly eliminated the urban cycle of rabies transmission. The majority of the cases are caused by contact with wildlife reservoirs of the rabies virus.

The reservoirs of rabies are most important in maintaining the transmission cycle of this disease as shown in Fig. 1. Reservoirs are responsible for the long-term existence, persistence, and transmission of the virus. Canines are considered source for the majority of cases of human rabies in Africa, Asia, and Central America (Ceballos et al. 2014). In more developed countries of the United States and America, bats serve as the primary vector for the transmission of rabies (Finnegan et al. 2002).

4. PATHOGENESIS

Rabies virus is a highly neurotropic virus that infects the central nervous system of the host by traveling within peripheral nerves and ultimately producing fatal encephalitis in the host. The main pathological features of rabies are neuro-invasiveness and neurotropism (Dietzschold et al. 2008). Rabies virus cause dysfunction of the central nervous system unlike other diseases of nervous system that cause marked inflammation and necrosis of the CNS. This feature of rabies is particularly attributed to its ability to avoid the immune system of the host by evading innate and adaptive immune responses and preventing alteration in the permeability of blood-brain barrier that ultimately favors viral propagation in the brain. (Hemachudha et al. 2013). After the entrance of the virus into the host tissue, virus is deposited and remain in the local tissue of muscle for an average of 3 to 6 weeks following preliminary replication in the cytoplasm of the epithelial site (Isloor et al. 2020). Replication of the virus in muscle is very slow that's why the incubation period of the virus is quite prolonged that may extend up to 7 years and immune response is negligible (Hemachudha et al. 2013). Viral infection is initiated after viral attachment to host cell receptors. Viral replication in muscle is facilitated by its binding to nicotinic acetylcholine receptors at the postsynaptic muscle membrane. (Isloor et al. 2020). After replication in striated muscle, it travels to the axons of the motor neuron through the neuromuscular junction. Rabies virus travels towards CNS through retrograde axonal transport at speed of 12-100mm/day (Kelly and Strick 2000). The entry of the virus in neuron is facilitated by its attachment to neural cell adhesion molecules and p75 neurotropic

receptors (Lian et al. 2022). Main mechanism involved in the invasion of CNS is transneuronal spread of virus in brain. At this stage viral infection of the brain leads to an inflammatory response from the host that causes encephalitis by attracting cytokines and chemokines that further attract leukocytes crossing blood-brain barrier. However, rabies induces mild inflammation while producing major neuronal dysfunction supporting the fact that nervous dysfunction is responsible for rabies rather than neuronal degeneration due to the inhibition of synthesis of nerve transmitters in the brain (Jackson 2011).
There is the centrifugal spread of the virus from central nervous system to peripheral nervous system and then highly innervated areas like salivary glands as described in Fig. 2. This virus is secreted from salivary gland into saliva and ultimately infect other animals. (Embregts et al. 2022).

5. CLINICAL SIGNS

Clinical signs and symptoms of rabies progress in five stages: incubation period, prodromal stage, acute neurological phase, coma, and death. (Hemachudha et al. 2013). The incubation period of rabies is highly variable ranging from a few days to several years but the average duration is 1 to 2 months. (Nigg et al. 2009). The incubation period of rabies depends upon various factors including the site of viral infiltration and immunity of the host but the amount of virus inoculated is the primary factor determining the length of the incubation period (Müller and Freuling 2020). It is reported that closer to the inoculation site to the

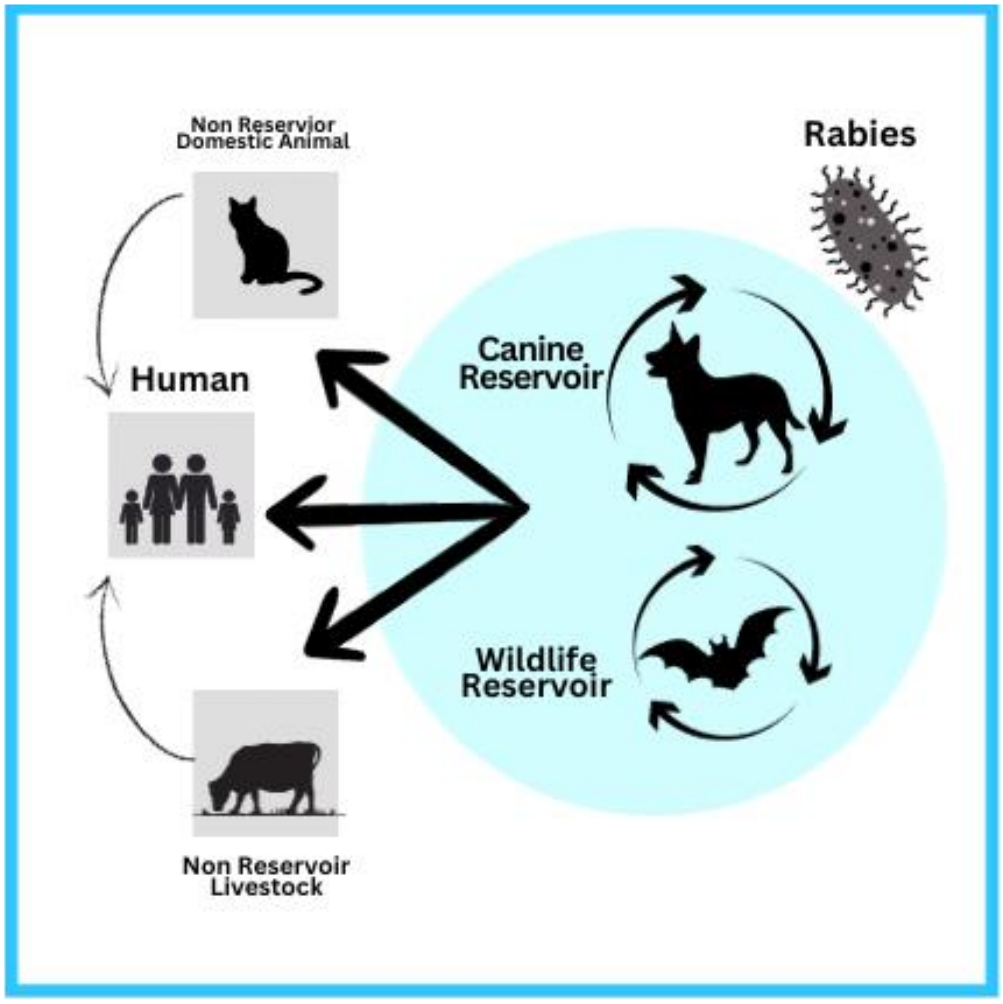

Fig. 1: The transmission cycle of rabies.

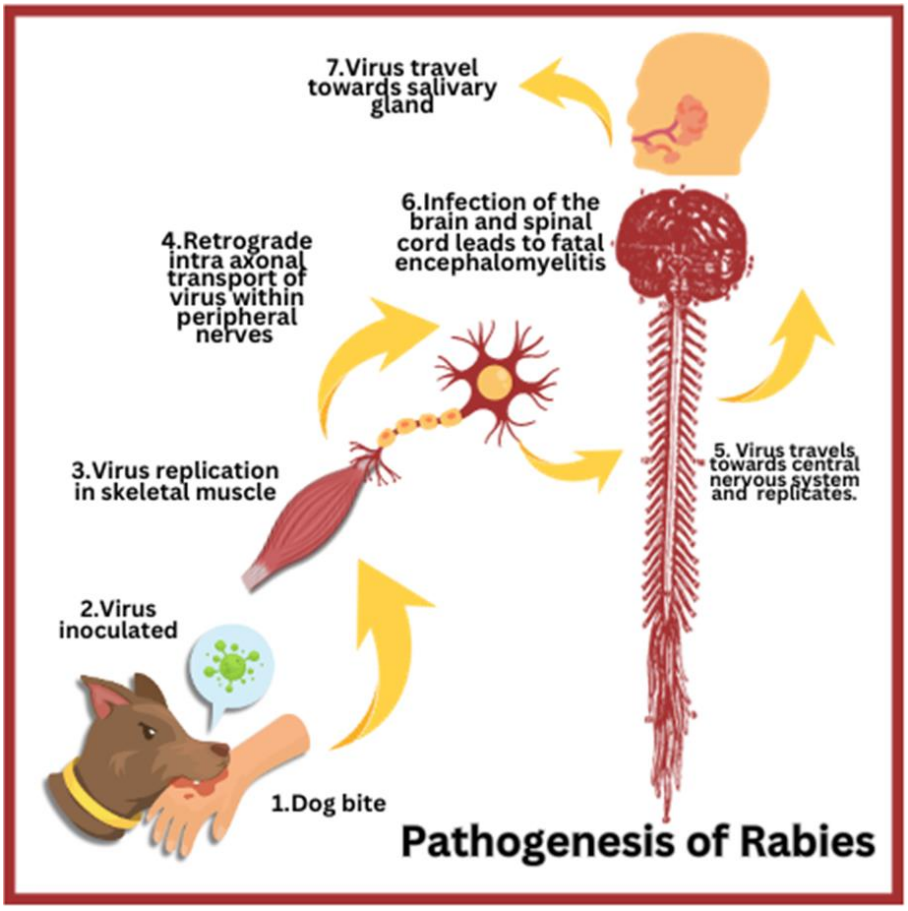

Fig. 2: Pathogenesis of rabies.

central nervous system or highly innervated areas, the incubation period decreases. The incubation period of rabies also decreases with an increase in viral inoculum titer in the host. (Nayak et al. 2022) The immunity of host which primarily depends on vaccination status is a major factor contributing to development of progressive encephalomyelitis in the host.

Initial clinical features of rabies exhibit nonspecific symptoms in the prodromal stage. This stage is initiated 2 to 10 days after exposure (Hankins and Rosekrans 2004). Prodromal stage is characterized by fever, anorexia, and lethargy which progresses to an acute neurological phase both in humans and animals.

Acute neurological phase of rabies is presented in two forms: furious form and paralytic form. Furious form of rabies exhibit severe aggression, hyperexcitability, nystagmus, and hallucinations in humans. In addition to these symptoms in animals, they roam extensively, chew foreign objects, and lose fear of people and this form is rabies is called “mad dog syndrome” (Praveen et al. 2015).

The paralytic form is presented by ataxia, hypersalivation dropped jaw in animals due to paralysis of masseter muscles. This stage further progresses to limb paralysis and ultimately paralysis of the diaphragmatic muscle which causes death. (Rupprecht et al.2002).

The end stage of this disease before death is coma, it is associated with multiorgan failure, myocarditis, cardiac arrhythmias, and death. (Alexander et al. 2022).

6. DIAGNOSIS

Conventionally, rabies was diagnosed on the basis of the history of animal bites accompanied by progressive behavioral changes and laboratory diagnosis which included nonspecific histological evidence

of brain inflammation and detection of eosinophilic intracytoplasmic inclusions bodies known as Negri bodies by seller's staining in neuronal cells (Singh et al. 2017). However, the limitation of this conventional approach is that the presence of acute nervous sign and progressive behavioral change coupled with a history of animal bite cannot be used as foundation for confirmatory diagnosis. Because there are many nervous diseases in which animals exhibit similar signs and in some cases, rabies may be transferred by non-bite route or bite may go unnoticed as in 78% of cases of bat rabies in the United States where a history of animal exposure is not reported. (Willoughby et al. 2015).

Although the presence of eosinophilic intracytoplasmic inclusion bodies is a pathognomonic lesion for rabies these characteristic inclusion bodies may be absent in neurons and often difficult to recognize (Kurup et al.2023).It has very low sensitivity and can only be performed on fresh brain specimens. It is no longer recommended for diagnosis of rabies. (Mani and Madhusudana 2013).

The most widely used and standard diagnostic test for the detection of rabies is the fluorescent antibody test (FAT) of fresh brain samples or preserved brain samples. The sensitivity and specificity of this test is about 99 % (Duong et al. 2016). The organ of choice for the detection of rabies antigen in brain tissue because it is present in neural tissue as opposed to other viruses which are present in the blood (Fooks et al. 2017). Medulla oblongata, thalamus, and pons are those parts of brain that are considered desirable samples for this diagnostic technique (Woldehiwet 2005). The direct fluorescent antibody test is based on the finding that animals infected by rabies virus have rabies virus proteins present in their brain tissue. This test uses fluorescently labeled anti-rabies antibodies and these fluorescently labeled antibodies will illuminate under a fluorescence microscope upon interaction with an antigen that is present in a suspected rabies sample. The labeled antibody will bind to antigen when it is incubated with questionable brain tissue samples for rabies. Unbound antibodies can be removed by washing and antigen-antibody interaction can be visualized as fluorescent green areas using a fluorescence microscope which indicates presence of rabies antigen in the brain sample (Centre for Disease Control). The accuracy of this test is determined by quality of brain tissue, a fresh brain sample is preferable although formalin-fixed brain sample can also be used but the accuracy of test is reduced, it requires high-quality anti-rabies diagnostic conjugates, a fluorescence microscope, and an experienced laboratory technician to yield accurate results. (Wadhwa et al. 2017).

7. IMMUNOCHEMICAL TEST

This test is very similar to the direct fluorescent antibody test. In this test rabies antibody is conjugated to an enzyme such as peroxidase instead of fluorescent isothocyaniate. This conjugated antibody directly measures rabies antigen with the same sensitivity as the fluorescent antibody test. (Shankar 2009).

8. RAPID RABIES ENZYME IMMUNODIAGNOSIS (RREID)

Rapid rabies enzyme immunodiagnosis is a convenient and simple diagnostic technique for the detection of rabies antigens. This test is economical and user-friendly as compared to FAT with the same sensitivity and specificity. It is a specific ELISA technique for rabies that uses monoclonal antibodies that capture rabies nucleoprotein antigen from brain smears. This antigen-antibody interaction is detected by the development of color by streptavidin peroxidase amino-ethyl carbazole and counter-staining with hematoxylin. (Madhusudana et al. 2012.)

9. DOT ELISA

A dot ELISA is also available which can detect the presence of rabies antigen. It is a simple, rapid, and economic test. In addition to postmortem diagnosis which requires a brain specimen as a sample this test

can also be used for antemortem diagnosis utilizing saliva and serum as samples. This test does not require highly skilled laboratory personnel and allows rapid confirmation without compromising sensitivity and specificity at a very early stage of disease when clinical signs are not definitive. All these qualities of dot ELISA make it a good choice not only for diagnostic purposes but also for epidemiological surveys under field conditions. (Singathia et al. 2012). The principle of this test is based upon detection of viral antigen by enzyme immunoassay using an agent blotted on nitrocellulose membrane. (Madhusudana et al. 2004).

10. PAN LYSSAVIRUS REAL TIME PCR

Pan Lyssavirus Real Time PCR offers various advantages over other methods because it enables the detection and differentiation of different species that belong to the genus lyssavirus and cause rabies-like symptoms. Furthermore, these assays offer real-time data and are closed-tube systems that reduce the danger of contamination during setup. (Marston et al. 2019).
This assay has been used by many laboratories that enable rapid and sensitive identification of rabies both in animals and humans. It is beneficial for the detection of viruses in organs with a low viral load like saliva, and eyewash (Wadhwa et al. 2017). It is the best method for early and rapid diagnosis of rabies, for timely provision of post-exposure prophylaxis, and for control of disease.

11. PREVENTION

Once clinical signs appear, it is incurable therefore the primary focus is prevention of disease to avoid the fatal outcome of this disease. The prevention of rabies requires an integrated strategy involving the cooperation of experts in the fields of human, animal, and environmental health as well as a global, strategic, and targeted approach at local, national, and international levels. (Acharya et al.2020.)

12. PRE EXPOSURE IMMUNIZATION

Modern cell culture vaccines can be used for pre-exposure and post-exposure prophylaxis. Veterinarians, lab personnel healthcare workers, and people traveling to endemic areas are more prone to be exposed to rabies must be vaccinated. The use of pre-exposure immunization is very important in areas where rabies is endemic. (Hankins and Rosekrans 2004).
After administration of 1st dose of rabies booster dose is mandatory at day 7, 21 and 28 to maintain a protective antibody titer against rabies (Manning et al. 2008).

13. MASS VACCINATION OF DOGS

In addition to immunizing humans, it is really important to vaccinate dogs as a vast number of cases are caused by dog bites in underdeveloped countries where the urban cycle of rabies is prevalent. According to the World Organization for Animal Health (OIE) and World Health Organization (WHO) vaccine coverage of 70% or more dog population can dramatically reduce the incidence of rabies (Franka et al. 2013). This will ultimately reduce human exposure.Therefore, Investment in canine vaccination, particularly mass vaccination, is beneficial in the long term with higher cost-efficient results **(**Lechenne et al. 2017). Hence, mass immunization of canines is one of the fundamental methods for controlling rabies in both human and animal populations. To maximize the effectiveness of this strategy proper recording, confinement, and mandatory vaccination of stray and domesticated dogs is required. Follow-up booster shots of the vaccine should also be administered to achieve a persistent level of protective antibody titer against the

rabies virus (Acharya et al. 2020). In addition to dogs, cats must also be vaccinated because they effectively transmit rabies to humans although they are not reservoirs.

14. WILDLIFE VACCINATION

In certain states of America and Europe where the sylvatic cycle of rabies is prevalent and rabies is particularly transmitted by wildlife reservoirs, oral vaccination programs for wildlife must be followed to break the sylvatic cycle of transmission. In Europe and Canada, the use of oral vaccines in foxes has successfully controlled fox rabies. This intervention has successfully eliminated the artic fox rabies variant from Canada (Nel and Markotter 2007).US was also declared free of canine rabies in 2007 by eliminating rabies in coyotes through an oral vaccination program (Elmore et al. 2017) For managing the disease, particularly in terrestrial wildlife reservoirs and in populations of free-roaming or feral dogs where parenteral vaccination is not feasible, oral rabies vaccination represents a socially acceptable approach that can be implemented in a wide geographic region (Slate et al. 2009). In short proper vaccination strategies are the foundation for the prevention, control, and elimination of rabies.

15. POST -EXPOSURE PROPHYLAXIS

Post-exposure prophylaxis is a concerted approach to decrease the patient's probability of developing clinical rabies after exposure to the virus (Nigg and Walker 2009). Although there is no treatment for clinical rabies, this disease can be prevented through prompt provision of adequate post-exposure prophylaxis (PEP) (Kessels et al. 2019). Research has shown that proper administration of rabies immunoglobulin along with vaccination after exposure to rabies is 100 % successful in preventing rabies (Kroger et al. 2015.) The long incubation period of the disease offers an advantage to implement this approach successfully. Post-exposure prophylaxis is followed after an animal has been exposed to rabies. Post-exposure prophylaxis regimen consists of washing and flushing the wound, a dose of human rabies immunoglobulin administered intradermally around the wound, rabies immunization administered on the day of exposure then a booster dose of vaccine is administered (Sreenivasan et al. 2019) The recommended dose for human rabies immunoglobulin is 20 IU /kg body weight and for equine rabies immunoglobulin is 40 IU/kg by WHO (Scholand et al. 2022). The fundamental objective of post-exposure prophylaxis is to neutralize or inactivate inoculated virus in the wound before it can invade the nervous system of the patient and initiate acute neurological disease. Therefore, a health care worker must make a quick decision whether to initiate post-exposure prophylaxis based on careful evaluation of risk (Tenzin et al. 2011). Before starting post exposure prophylaxis, it is really important to asses individual critically and determine whether patients should receive this treatment or not based on category of exposures as defined by WHO because resources for contemporary human post exposure prophylaxis are limited in many underdeveloped countries. Exposure to Category II and Category III should immediately receive post-exposure prophylaxis as individuals placed under these two categories of exposure are those who have skin abrasion, laceration, or a major bite from a dog or any other reservoir. WHO category I exposures include contact with a potentially rabid animal, or involve licks on intact skin and do not require intervention (Rupprecht et al. 2002) as presented in Table 1.

Furthermore, animals to which humans were exposed should be observed for at least 10 days by trained health care professionals for the development of any abnormal behavior. If the suspected animal does not develop any sign or symptom related to rabies, then there is no requirement for post-exposure prophylaxis only wound management is needed. (WHO Guide for Rabies Pre and Post Exposure Prophylaxis in Humans Updated 2014). The immune status and behavior of the suspected animal is also a major factor to consider the administration of post -exposure prophylaxis. If the animal is immunized or

Table 1: Represents the requirement of post-exposure prophylaxis according to the category of exposure. (WHO pre- and post-exposure prophylaxis in humans updated 2014).

Category	Description	Type of exposure	Requirement of post-exposure prophylaxis
Category I	Contact with animal or animal lick, skin is intact	No exposure	Not Recommended
Category II	Animal bite, skin is not intact, small skin abrasion	Minor exposure	Recommended
Category III	Major bite	Severe exposure	Recommended

does not exhibit any unusual behavior, then the use of post-exposure is not recommended (Grill 2009). When an animal has been identified as rabies-positive retrospective case assessment should be implied and contact tracing is required to trace potential contacts to timely administer post-exposure prophylaxis. The 1st step of post-exposure-prophylaxis is the management of the wound. The wound should be thoroughly washed at least for 15 min to clear the virus from wound and decrease the risk of bacterial infection. Use of povidone-iodine solution and 20% alcohol or virucidal agent has been reported to reduce viral transmission from wounds (Hankins and Rosekrans 2004).

Human rabies immunoglobulin provides passive immunity against rabies virus by directly neutralizing rabies virus. It should be administered intradermally around the wound immediately after confirmation of exposure. There are two types of rabies immunoglobulin: human rabies immunoglobulin and equine rabies immunoglobulin both are derived from the plasma of humans and equine respectively who have been hyper-immunized by purified cell culture based vaccine against rabies and have very high titer of rabies antibodies against the virus (Haradanhalli et al. 2022).

It is only recommended to use immunoglobulin up to 7 days of vaccine administration because after that time active immunity against rabies has started to activate and the use of immunoglobulin will cause interference of passive immunity with active immunity. If the patient has no history of pre-exposure vaccination then rabies vaccination and immunoglobulin should be administered on day 0 followed by a booster dose of vaccination on days 3,7 and 14. For immunocompromised persons, it is preferable to administer the last dose of vaccination on day 28 rather than day 14 (Center for Disease Control). Patients who have already received either pre-exposure or post-exposure rabies prophylaxis should be administered only two rabies vaccine boosters upon exposure given on Days 0 and 3. Administration of rabies immunoglobulin is prohibited in such patients. This will boost the production of antibodies and cause an anamestic response (Kessels et al. 2019).

16. ONE HEALTH APPROACH FOR PREVENTION

Since rabies is a zoonotic disease, efforts to control rabies must be multidimensional involving veterinary health professionals, human health care workers, and environmentalists. One health program is based on the foundation that the health of humans is associated with the health of animals and our shared ecosystem (Acharya et al. 2020). One health approach emphasizes outbreak management and control of rabies in both humans and animals, preventing animal-to-human dissemination of rabies, it also reduces the cost of post-exposure prophylaxis. Mass immunization of dogs, and control of stray dog population with animal birth control methods like orchiectomy in male dog and ovariohysterectomy in bitch has been implemented in many countries (Acharya et al. 2020.)

Moreover, community awareness and education also play an integral role in the prevention and control of rabies (Barroga et al. 2018). Educating the public about how lethal is rabies for humans, livestock and their companion animals about the importance of vaccination and timely reporting of disease can effectively help in the control of rabies.

In order to efficiently control rabies, surveillance mechanisms must be in place that allow for early case discovery and reporting. Rabies control and eradication depend heavily on an effective surveillance system. Early case detection and reporting made possible by efficient surveillance systems is essential for prompt action and allows for well-informed judgments and decisions regarding when and where to step up control activities. Following the implementation of interventions, monitoring is necessary to gather information on their effectiveness and cost in order to ensure their long-term sustainability. (Townsend et al. 2013).

17. CONCLUSION

To put it briefly, prevention is the only way to avoid the devastating effects of this neglected zoonotic illness that is extremely pathogenic, and lethal, and causes over 1.8 million DALYs (Disability-adjusted life years) every year (Regea 2017). It not only represents a threat to humans but also to companion animals and livestock. As mentioned above, efforts are needed on multiple levels to prevent this disease, including mass vaccination of domestic dogs, which has significantly decreased the burden of rabies in developed countries, oral rabies vaccination of wildlife in the form of bait, reducing contact with wildlife, public education about prevention, prompt reporting of rabies, an efficient surveillance system, and adequate post-exposure and pre-exposure vaccination.

About 95% of human mortalities from rabies are reported from Asian and African countries. (Ling et al. 2023). Several factors are responsible for the heavy burden of rabies in these continents. The majority of countries in these continents lack the infrastructure and resources to implement widespread vaccination programs. Furthermore, there is a significant population of free-roaming stray dogs population that exacerbates the incidence of rabies. In certain areas of Africa, there is a proximity of human and wildlife reservoirs that increase the chances of rabies. Lack of awareness among the public, underreporting, and limited access to healthcare facilities like lack of timely provision of pre-exposure and post-exposure prophylaxis have contributed to this problem. Keeping in view these problems efforts are being made by many organizations to help control this major public health threat. Prospects regarding rabies control is a joint effort by the World Health Organization, World Organization of Animal Health, Food, and Agriculture Organization, and the Global Alliance for Rabies Control whose goal is to end dog-mediated rabies in humans by 2030 (Nel et al. 2017). These organizations are working together to end rabies by 2030. This is only possible if proper prevention strategies are followed to control rabies as discussed above.

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