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Review Article

PROGRESSIVE CONTROL AND MANAGEMENT STRATEGIES IN THE ELIMINATION OF RABIES AMONG THE STRAY DOG *(CANIS FAMILIARIS)* POPULATION IN PAKISTAN

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Abstract *Stray dogs are integrally linked with rabies transmission, and a sizeable unmanaged dog population hinders rabies control program planners. Dog population management (DPM) is one of the best strategies to control rabies transmission, improve health management, and lower the population size of stray dogs. The threat of rabies is very serious due to free-roaming dogs. Foxes, skunks, groundhogs, raccoons, and house bats are rabies vector species and can carry rabies virus without showing any symptoms. Rabies is a life-threatening disease that affects thousands of losses worldwide every year. World Rabies Day is an international awareness campaign coordinated by the Global Alliance for Rabies Control (GARC). In Pakistan, there are reportedly 3 million stray dogs. More than one million dog bite cases are reported annually throughout Pakistan. About 600 dog bite cases are reported daily in the Sindh province, Pakistan. Due to an uncontrolled number of stray dogs, many serious problems arise related to public health, socio-economic, and political issues. The Animal Act of 1890 provides a specific defense against cruelty and establishes its importance in Pakistani culture. Developing long-term and supportable strategies is imperative to overcome the stray animal population worldwide. To overcome the rabies issue in Pakistan, the government should implement projects on breeding control of stray dogs through spaying and neutering surgeries. The government should also provide proper shelters for dogs and rabies vaccines. There is a need to be aware of basic preventive measures such as disinfectants and rabies vaccination. Public awareness, rabies vaccination, and dog sterilization at the national level are crucial factors in preventing rabies and managing the dog population in Pakistan.*

Keywords*:* *Rural; Mental health; Household; Demographic; Variation*

Introduction

Rabies is a Latin word derived from ‘rabere’ that means to rage or rave or madness. Rabies is an acute, progressive, highly fatal, and zoonotic disease (a disease that can be transmitted to humans from animals). Rabies is a life-threatening disorder that affects thousands of losses worldwide every year. Stray rabid dogs are the most common cause of rabies virus. This virus attacks the central nervous system (Balaram *et al*. 2016). The virus is transmitted to humans through bites and scratches from infected animals (Hankins *et al*. 2004).

Rabies is caused by *Lyssa-virus* which is a bullet-shaped, linear negative sense, single RNA virus, and its size is 180 x 75 nm. It belongs to the Mononegavirales order and Rhabdoviridae family. This virus has a lipoprotein envelope carrying knob-like spikes, glycoprotein S, and a non-segmented genome (UNG *et al.* 2021). Rabies infects domestic and wild animals and spreads to people through close contact with infected saliva via bites or scratches (Totton *et al*., 2010). The incubation period of the disease is 6 weeks. Two types of symptoms of rabies

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are documented. One is paralytic or dumb, and the other is furious form. Paralytic rabies has symptoms of ascending weakness that can lead to coma. Furious rabies is characterized by hydrophobia, behavioral changes, aerophobia, salivation, and paresthesias *(Hemachudha et al., 2013).*

The disease is prevalent on almost every continent, but most human deaths, more than 95%, occur in Asia and Africa. Once symptoms of the disease develop, it becomes fatal and causes irreversible damage to the central nervous system (Balaram*et al*. 2016). Rabies causes 2000 to 5000 deaths per year in Pakistan and 55,000 worldwide, of which 31,000 are only from Asia. Out of 97,000 cases of dog bites in Pakistan, 84.2% were from Sindh Province (Kumar and Bakhru, 2022). Diagnosis of rabies virus is confirmed by direct fluorescent antibody test (DFA) of brain tissues recommended by the World Health Organisation (WHO) *(*Soler-Rangel *et al.,* 2020). Rabies can be cured by early vaccination before symptoms develop in the affected patient (Yang *et al*., 2013). Pasteur was the first to diagnose the rabies virus by isolating it from an infected human. In 1885, Louis Pasteur discovered the rabies vaccine and saved 9-year-old Joseph Meister, who was affected by the virus (Davlin*etet al*. 2012). Pakistan is facing a shortage of 80,000 vaccine doses. Most rural areas have no available vaccine (Siddiqui *et al.,* 2021). The current review is compiled on strategies and measurements to control rabies in Pakistan.

Pathogenesis and Transmission

Rabies is transmitted through the bite of a rabid animal, which sheds the virus with their saliva. Lyssavirus enters the body via transdermal inoculation, i.e., wound or direct contact with infectious agents such as cerebrospinal fluid, saliva, or nerve tissues to the mucus membrane of skin lesions. The virus cannot penetrate intact skin. Domestic dogs, cats, and ferrets may shed the virus for several days before the onset of clinical signs (Burrell *et al*., 2017). The incubation period is prolonged and variable. Typically, the virus remains at the inoculation site for a considerable time. Most dog rabies cases develop symptoms within 21–80 days after exposure (Manning *et al*., 2008).

After entering the body, the virus binds to cell receptors and replicates within striated muscles or directly infects nerve cells. The virus travels by axoplasmic transport mechanism via the peripheral nerves to the spinal cord and reaches the brain. Both motor and sensory fibers may play a part in transmission. At CNS, rapid virus replication occurs and causes pathologic effects on nerve cell physiology. After reaching the brain, the virus travels by anterograde axoplasmic flow via peripheral nerves to the salivary glands for shedding (Koyuncu *et al*., 2013).

Hematogenous spread does not occur. Under most circumstances, there is evidence of aerosol transmission of rabies virus. However, aerosol transmission has occurred under very specialized conditions in which the air contained a high concentration of suspended particles or droplets carrying rabies virus (Jackson, 2011). Aerosol infection may occur via direct attachment of the virus to olfactory nerve endings. After replicating in CNS, the virus may be found in almost every innervated organ. Rabies has been transmitted by transplantation of tissues and organs from infected people (Hemachudha *et al*., 2013).

Signs Variations in Different Species

Cattle with furious rabies are dangerous because they attack people and other animals. Milk production terminates abruptly in dairy cattle after rabies. Usual placid expression is replaced by alertness in cattle (Fleming, 1872). Cattle eyes and ears follow sound direction and object movement. A common clinical sign is characteristic abnormal bellowing, which disappears just before death. Horses and mules often show signs of distress, extreme agitation, and body rolling, like colic (Hall *et al*., 2013). Horses may bite or strike people viciously and become unmanageable in a few hours. Similarly, bats rest on the ground, become paralyzed, and unable to fly. They attack people or other animals (Wright *et al*., 2016).

Stray Dog Population Overview

A domesticated dog (*Canis familiaris*) is considered a pet animal. Over 15000 years ago, the dog was the first species to be domesticated before the development of agriculture. The dog is a selective breed due to the adaptability of various behaviors like sensory potentiality, hunting, security, companionship, therapy, and military purpose (Scott *et al*., 1974). In 2013, the estimated population of dogs was between 700 and 987 million globally. In Pakistan, there are reportedly 3 million stray dogs (Salgirli *et al*., 2019). Every year, more than one million dog bite incidents are reported throughout Pakistan, and between 2,000 and 5,000 people pass away from rabies. Most of these dogs live as strays and have no custody status. About 11% of dogs in Pakistan respond aggressively. Due to the uncontrolled number of stray dogs, many severe public health problems and socio-economic and political issues arise. Control of the stray dog population is a challenging issue (Tan *et al*., 2020). Different approaches have been adopted to control the problems of stray dogs. The European Commission contributed a lot to addressing the first global safety principles for controlling the dog population in the

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framework of the World Organisation for Animal Health (OIE) in 2007. Stray dogs are severe threats to humans and animals (Nguyen *et al.*, 2021).

World Rabies Day is an international awareness campaign coordinated by the Global Union for Rabies Control (GURC), a non-profit institute in the United States (US). Rabies Day is celebrated on the 28th of September every year worldwide (Briggs *et al*., 2007). It symbolizes the death anniversary of Louis Pasture, who first introduced the rabies vaccine (Davlin *et al*., 2012). Due to a lack of veterinary care, stray dogs harm the health and welfare of humans and other animals (Root *et al.*, 2003). The population density of stray dogs may vary with different locations. In developing countries, there are large numbers of street dogs. In developed countries, they provide proper shelter and management to the stray dog population. It takes a lot of money to ensure good care and a permanent home (Kartal *et al.*, 2018). One hundred seven stray dogs were recorded in the UK in 2009, and 9000 were devastated. A total of 56,734 stray dog populations were estimated in 2006 in Istanbul, Turkey. There is a need to develop long-term and supportable strategies to overcome the stray animal population worldwide (Alkan, 2016).In Bucharest, the number of stray dogs is between 51,000 and 100,000. Bulgaria's total stray dog population at the end of 2009 was 43,700 (Yousaf *et al.*, 2012). Stray Animal Project is a non-profit association devoted to the education and prevention of cruelty to animals. The purpose is to fund neuter/spay programs and provide education for answerable pet ownership. It is essential to work for a rabies awareness program (Auplish *et al*., 2016).

Death Rate in World

A total of 99%death caused by rabies are due to stray dogs. According to the World Health Organization (WHO), rabies is likely to cause 55000 human deaths annually in over 150 countries, and 95% of cases arise in Africa and Asia (Yousaf *et al*., 2012).

Death Rate in Pakistan

There is no confirmed data on death estimation by rabies because many death cases are unregistered. A vague estimate of 2000-5000 deaths per annum is stated. In 2016, over 97,000 cases of rabies were reported by National Health Management Information System (NHMIS) victims of rabies were registered in which 84.25 of cases were from Karachi (59.7%), Peshawar (13.1%) and Hyderabad (11.4%) (Kumar & Bakhru, 2022).

Rabies Cases in Sindh Province, Pakistan

Most dog bite cases occur in Karachi, the largest city in Sindh Province, Pakistan. Indus Hospital Karachi reported dog bite victims are less than 15 years old. About 600 dog bites are reported daily in the province of Sindh (Afzal *et al*., 2022). Due to the increased population of stray dogs in the Sindh province of Pakistan, dog bite cases have increased since 2019. According to the Sindh health department, in the five months of 2019, a total of 69,453 cases of rabies were reported. About 22,822 people were bitten by stray dogs in Larkana division of Sindh (Rashid *et al.*, 2021).

The 3D pie graph below shows the annual death rate in different cities in the province of Sindh, Pakistan. In Larkana, 22822 cases were reported in 2019. In Hyderabad, 21099 cases were reported in 2019. In rural areas of the province, most cases occur due to the unavailability of vaccines (Figure 1) (Ahmed *et al*., 2020).

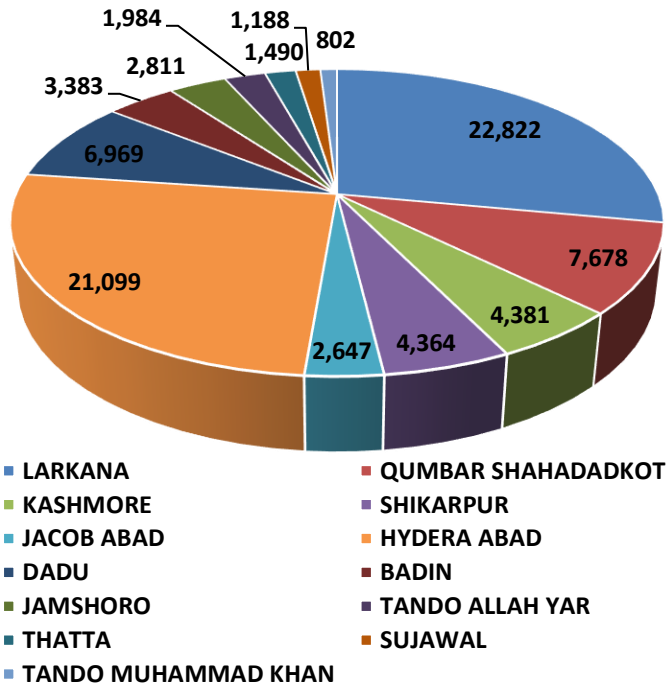

Fig 1: Number of deaths during 2019

Legislations

Legislation is a rule or commandment that parliament approves (Voslarva *et al*., 2012). Pakistan's Prevention of Cruelty to Animals Act of 1890 protects animal welfare. The act provided a specific defense against cruelty and established its importance in Pakistani culture. Pakistan has presented new legislation since the 2014 edition of the animal protection catalog. According to the Halal Authority Act 2015, animals should be slaughtered separately (Voslarva *et al*., 2012). Legislations are imposed at national and municipal levels in different countries **(Table 1).**

Table 1: Legislations Related to the Stray Animal in Different Countries

NA= National MU= Municipal

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Countries	Animal welfare	Stray dogs
Germany	NA	NA
Italy	NA , MU	NA, MU
Greece	NA	NA
Ireland	NA	NA
Switzerland	NA, MU	NA, MU
Sweden	NA	-
Pakistan	NA	MU

NA= National MU= Municipal

Preventive Measures

The Regional Program for Elimination of Rabies (RPER) in Latin America advocates the primary prevention and control activities for rabies. It focuses on providing appropriate treatment for patients who are potentially at risk of acquiring the disease. Treatment includes pre-and post-exposure prophylaxis, mass vaccination of dogs, and epidemiological surveillance (Schneider *et al*., 2007).

Breeding Control of Stray Dog Population

Laws should be implemented to reduce the stray dog population by their breeding control. Breeding should be controlled in the way of neutering and spaying of dogs and bitches, respectively (Jackman *et al*., 2007). The responsible authorities implement the law through community councils, supported by veterinarians and societies of animal welfare departments (Bashandy *et al*., 2015). Another method is to disrupt the transport mechanism of sperms and eggs using spermicides, sponges, intra-uterine devices, and pills via hormonal contraception (Brinster*et al*. 1985). Scientists have used a manufactured protein called monoclonal antibodies that attack sperms before they become zygotes (Lee, 2004).

Euthanasia

Other methods of population management include euthanasia. Many dogs are euthanized for population control. Euthanizing the dog must be done under the supervision of a veterinarian, and recommended drugs should be used. This method is considered inhumane, immoral, and illegal. It is mainly done for research purposes. Barbiturates (pentobarbital sodium, pentobarbitone) are the most commonly used drugs in euthanasia. In other methods, magnesium sulfate, potassium salts, and carbon monoxide are administered orally and cause painful death (Seid*et al*. 2019).

Vaccination

Once symptoms of rabies develop, only palliative treatment is possible. The prognosis of rabies virus is grave. To date, only 6 patients with rabies virus have survived. Pre and post-exposure rabies vaccines are used (Dutta, 2014). Rabies can be controlled using a rabies vaccine as a prophylaxis. In Jinnah Postgraduate Medical Centre (JPMC) Karachi, Pakistan, treatment of 10850 dog bite patients in 2019 was held, and 8000 new cases were registered in 2018 (Gsell *et al.*, 2012). In Karachi, 150 dog bite cases are reported in the city's major hospitals daily (Gayer *et al.*, 2014).

Due to the increased population of stray dogs, it is impossible to control rabies through vaccination and sterilization strategies. Controlling the stray dog population through neutering and vaccination is preferred in such areas (Totton *et al*., 2010). Rabies vaccination can be injected on 0, 3, 7, 14, 30, and 90 days (Gomes, 2021). In this way, Immunity can persist for 5 years. The required dose should mostly be injected through a subcutaneous route. Pre-exposure prophylaxis is given at 0 – 7 – 21 – or 28 – 56 days, and a booster shot should be given after one year. Post-exposure Prophylaxis is given in Six doses at 0 -3 -7-14 – 30 - 90 days. It should be injected via a subcutaneous route. Various brands of vaccines are available in the market, such as Nobivac®, Rabipur®, and Provac® (Strady *et al*., 1998).

Rabies Veterinary Vaccine Market

The global rabies vaccine market was valued at 589.27 Million UDS in 2022 and is expected to grow at a rate of 4.2% during the forecast period. Growing awareness about zoonotic diseases, initiation of government campaigns, and rise in pet ownership risks have boosted the market growth **(Figure 2)** (Polaris et al., 2019-32).

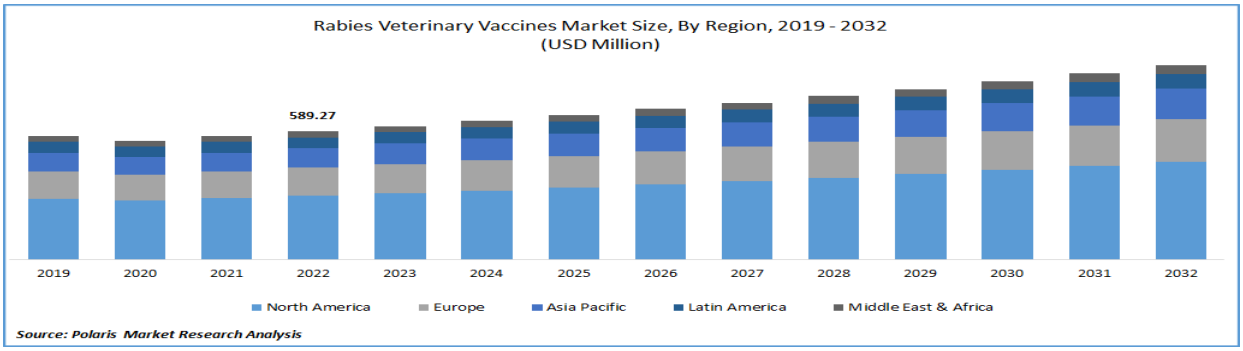

Fig 2: Rabies Vaccine Market Size (Polaris et al. 2019-32)

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Establishment of an Organization

Many organizations are working for stray dog shelters. In Faisalabad, Pakistan, a well-known Tahira animal welfare foundation (TAWF) works in different areas to control the stray dog population. In this way, rabies can be controlled to some extent. Another project, Animal Breeding Control (ABC), is also working in India and Pakistan to control the population. They capture stray dogs and perform spaying and neutering surgeries. After some period, people come for their adoption. Some animals are released in an open environment (Ghassemi *et al*., 1995).

Improved and Active Surveillance System

It has been reported that evidence-based surveillance and diagnostic strategies are required to determine the prevalence and distribution of rabies virus species worldwide. Such measures must include collating animal disease data and transferring data to public health authorities to enable them to make prompt and effective policies. Laboratory-based surveillance and inexpensive vaccine production are crucial to control rabies (Rupprecht *et al.,* 2006).

Dog Population Management (DPM) Approaches

Our community has different kinds of relationships between domestic dogs and people. People rear dogs for different purposes, including security, pet purposes, and, in some countries, as a food source. Due to this connection with humanity, it is essential to control their population through breeding control (Taylor *et al*., 2019).

Dogs may be a family admitted, semi-dependent, in custody status, as a pet, free-roaming, unwanted, in a village or neighborhood in the community (Bogel*et al.* 1990). Two conditions help control disease strategies and dog population management. One condition is that stray dogs in the community are semi-dependent (Smith *et al*., 2019). That population is partially on custody status, in which risk factors for imparting rabies are increased. In this condition, dogs can access different areas and develop the rabies virus differently. Another condition is independent and free-roaming dogs without any custody status. Risk factors for imparting rabies are increased, and access to that population control is easily possible by capturing them and making reproductive control (Table 02) (Kachani *et al*., 2014).

Table 2.Factors Pertinent to Dog Population Management in Different Subgroups of Dogs

Status of holder	Custody status	Depending on humans	Risk factors for imparting rabies (if unvaccinated)	Target for population control
Family Admit (As a pet)	Custody	It depends on humans fully	Decreased	Not in possibility
Family Admit (Community)	Partially in custody/stray	Partially depend on humans	Average	Not in possibility
Family Admit	Stray	Semi dependent	increased	Not in possibility
Stray Dog of Community	Stray	Semi dependent	increased	Might possible
Not Admit	Stray	Independent	increased	Possible

Conclusion

Implementing DPM could break the cycle of rabies transmission through proper awareness programs for human beings. It is essential to eliminate canine rabies. There is a need to overcome rabies in Pakistan to ensure a rabies-free country. Different factors are responsible for rabies transmission, such as the population of stray dogs and the unavailability of vaccines, which were of prime importance. There are lots of issues regarding rabies control. First, we don't have proper data and records of dog population and rabies cases in the country. The second issue is the cost of adaptability programs for rabies. The government should provide stray dog shelters with breeding control programs and mass vaccination of humans and stray dogs nationally. There is a need for mass public awareness, the establishment of small rabies centers in rural areas, mass vaccination, enforcement of laws, development of a surveillance system to monitor dog bite cases, collaboration between government institutions, and development of cost-effective rabies vaccine at the national level.

Declaration

Data Availability Statement

All data generated or analyzed during the study are included in the manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Authors approved the study.

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Not applicable

Conflict of Interest

There is no conflict of interest among the authors regarding this case study.

Authors Contribution

Muhammad Waseem Nazar and Fazal Ur Rehman

Conceptualized the idea and wrote the review paper.

Haseeb Asif, Hammad Ahmad Hashmi, Aiman Rehman, Muhammad Arshad

Assisted in data collection.

Kashif Hussain, Muhammad Shahzad, Zia Ullah, Muhammad Awais

Assisted in final drafting and revised the review paper.

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