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REVIEW ARTICLE

Multifactorial Complexity and Zoonotic Aspects of Dog-Mediated Human Rabies in Pakistan

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A B S T R A C T

Rabies, a viral illness classified as a neglected tropical disease by the World Health Organization (WHO), causes thousands of people to die annually, primarily in underprivileged communities of Africa and Asia. In the context of a single health framework, one of the primary objectives of this literature review is to examine the major factors and challenges that maintain the endemic status of dog-mediated human rabies in Pakistan. Rabies-endemic countries have an imperative need to work on preventive strategies to lessen the burden of this terrible disease as per guidelines of World Organization for Animal Health (WOAH) and WHO. Lack of public awareness, free-roaming dogs, and cold chain mismanagement of vaccinations are the 3 most significant factors contributing to the increasing number of dog bite injuries and suspected rabies cases in animals and humans. To control dog-mediated rabies, Pakistan must initiate and strongly support a national One Health project, a subsidized supply of human and animal rabies vaccine in public hospitals, and designated rabies prevention centers at an affordable cost. People should be educated regarding responsible pet ownership and follow-up of basic preventive measures. Empowerment of labs equipped with surveillance systems are also additionally required to strengthen rabies control and prevention activities at least in regional levels. This article gives valuable information for scholars and policymakers who wish to comprehend why this disease remains endemic due to multiplex interplay of zoonotic, medical, and anthropological risk factors and transmission chains in animal and human sectors through viral reservoirs. Achieving the 'Zero By 2030' goal in Pakistan requires joint immediate action from the government, society, and all health departments at regional, provincial, and national level.

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INTRODUCTION

Many underdeveloped countries of Asia and Africa are suffering from multiple outbreaks of dog-mediated human rabies which is a lingering zoonotic disease caused by rabies virus (Rupprecht *et al*., 2019). Annually, 59,000 people die of rabies in 2016, and most of those deaths are mainly concentrated in Asia and Africa (Banyard *et al*., 2018). Dog-mediated human rabies is an endemic disease in Pakistan, but only a little epidemiological data is available because of the absence of a well-structured surveillance system (Iqbal *et al*., 2020; Ahmad *et al*., 2021). Annual rabies incidence in Karachi is between 7 and 9.8 cases per 100,000 people, which translates into between 2000 and 5000 fatalities per year (Salahuddin *et al*., 2016; Ahmad *et al*., 2021). Dog-mediated human rabies is most commonly observed in rural area of Pakistan (Zaidi *et al*., 2013; Ilyas *et al*., 2017; Afridi *et*

al., 2022). Dog bite injuries have surged in Pakistan with every day, 55-60 dogs bite injuries are reported in Karachi (Zaidi *et al*., 2013), while rabies transmission or animal bite injuries data on jackals, foxes, raccoons, and bats are sparse (Naeem *et al*., 2018; Ali *et al*., 2021).

The post exposure prophylaxis (PEP) entails cleaning bite wounds, receiving rabies immunoglobulins (RIG), and doses of vaccinations (Siddiqui *et al*., 2021). The common barriers to get PEP are lack of RIG use and failure to sustain the cold chain, delays in commencing PEP, lack of proper and inappropriate wound treatment, and most importantly the lack of coordinated flow of surveillance network using One Health approach (Guo *et al*., 2019; Siddiqui *et al*., 2021). This approach is the core solution to control and prevent not only rabies, but it also validates the prevention of other viral, bacterial and parasitic zoonoses (Ahmad *et al*., 2021). Furthermore, there are still other constraints that hinder the implementation of One Health approach in Pakistan and resultantly, the cases of dog-mediated human rabies are occasionally observed in Pakistan (Salahuddin *et al*., 2021). Another major obstacle in fighting the disease is the lack of inter-sectoral coordination of major health actors which is caused by rampant lethargy in the government of Pakistan and allied health sectors (Ahmad *et al*., 2021; Ali *et al*., 2021; Salahuddin *et al*., 2021).

Rabies management delays cause complications in Pakistan. Damaged medical facilities limit investigations, monitoring, vaccinations, medical and nursing staff, and veterinary support (Coetzer *et al*., 2019; Ahmad *et al*., 2021). Both veterinarians and human health workers have knowledge gaps, professional habits, and cultural beliefs that hinder efforts to minimize burden of this disease due to prevailing epidemiological constraints (Ahmad *et al*., 2021). Knowledge regarding dog-mediated rabies varies widely in rural areas. Owned and unowned dogs in rural areas rarely get vaccinated, and these dogs also freely roam among the streets unprotected (Zaidi *et al*., 2013). Delaying wound cleansing increases rabies risk by five folds. This delay could reduce rabies risk by increasing wound care awareness. Clinicians disapprove the fact delivered by many Health Care Providers (HCPs) that animal attacks are unnecessary (Siddiqui *et al*., 2021). The HCPs have varied perspectives on how to prevent and control dog-mediated rabies, including cleaning wounds with water and soap and visiting a doctor. Some healthcare experts argue that early medical intervention is more crucial than soap and water wound cleansing (Siddiqui *et al*., 2021; Salahuddin *et al*., 2021). The present literature review investigates all the zoonotic concerns and issues which are preventing Pakistan in attaining the control of this disease at local, regional and national levels.

Transmission of dog-mediated rabies to various animals: The unowned dogs roam freely among the dwelling places in Pakistan. These dogs can be categorized into 2 major sub-categories in developing countries of Asia and Africa (Mansuri *et al*., 2016). One of the categories include unowned dogs that are born as unowned from unowned female dogs, while second category include the dogs which have lost the ownership or the oversee management of its owner that could be the philanthropist, caretaker or the actual owner (Naeem *et al*., 2018; Munibullah *et al*., 2021; Ahmad *et al*., 2021). Hence, the disease is circulating via dogs to other animals and humans erratically (Fig. 1). The transmission of the disease through free-roaming dogs to the humans, food animals, and wildlife could be potentially riskier if the free-roaming dogs or animals have not been previously vaccinated against rabies, while the risk could be low if free-roaming dogs have been vaccinated or shifted to the category of 'owned dogs' under the supervision of sustained ownership (Davlin and Helena, 2012). Here, it is also important to mention that the risk of rabies transmission via animal bite can be lowered using various interventions such as conducting mass dog vaccination (MDV) to attain 70% vaccine coverage of dog population, while responsible pet ownership among animal owners can also minimize the burden of dog-mediated rabies (Rupprecht *et al*., 2019; Ahmad *et al*., 2021).

Prevalence of higher dog bite injuries in animals and humans: Unfortunately, the number of human dog bite injuries are alarming, especially in Sindh and Khyber Pakhtunkhwa provinces of the country (Mughal *et al*., 2018; Mubashar *et al*., 2020), while national or regional burden of dog or animal bite injuries to other animals are also not reportable (Ahmad *et al*., 2021). The number of reported rabies or human dog bite injuries in Baluchistan are the lowest among all regions of Pakistan due to a lower population of free-roaming dogs in the province. Contrary to this, the number of dog bite injuries and suspected cases of dog-mediated human rabies are the worst in Sindh out of all provinces (Ahmad *et al*., 2021). The prevalence of dog bite injuries was 8,565 to 11,992 in public and private hospitals in Karachi and 2,031 to 2,844 in private hospitals (Zaidi *et al*., 2013). For this reason, Karachi also became the hot-spot of thousands of dog bite injuries, and Rabies-Free-Karachi project was launched in 2019 by Indus Hospital in the said city to countercheck the rapid increase of dog bite injuries and suspected cases of human rabies. This project adopted the One Health approaches of WHO and WOAH by conducting MDV in local areas (Acharya *et al*, 2020; Pantha *et al*., 2020). One of the country's highest throughputs is rabies prevention center (RPC) in Karachi, where post-exposure prophylaxis is constantly monitored (Yasmeen *et al*., 2022). According to a study conducted at the Indus Hospital in Karachi, 4998 dog bite victims were registered in 2017, while 5465 dog bite victims were registered in 2018, increasing to 9.3% (467/4998) over 2017 (Salahuddin *et al*., 2021). Between 2011 and 2013, while a total of 150 dog bite injuries were reported in rural district of Rawalpindi (Ilyas *et al*., 2017). Another study found that 2,151 dog bite victims were treated in tertiary health care facilities in Karachi (Naeem *et al*., 2018). In Abbasi Shaheed Hospital Karachi, Pakistan, the estimated annual incidence of dog bite injuries was 7.8 dog bites per 100,000 population (Mansuri *et al*., 2016). The dog bite burden in 4 public sector hospitals of the country reported that the highest number of dog bite injuries (3110) occurred in 2017 (Ahmad *et al*., 2019). Study conducted in rural areas of Lahore showed the lifetime prevalence of dog bite injuries to be 21.3%, while the prevalence of dog bite injuries in urban areas of the city was 2.56% (Ahmed

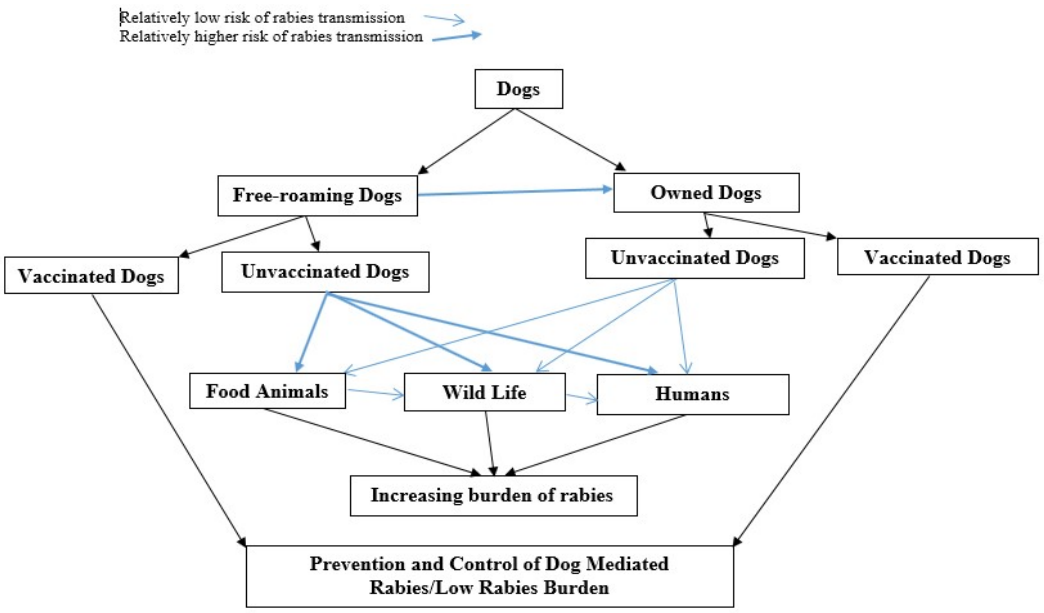

Fig. 1: Dog-mediated rabies transmission chain from unvaccinated dogs to humans and wild life leading to higher burden of the disease in Pakistan.

et al., 2019). National Institute of Health in Islamabad reported that a total of 4,037 dog bite injuries were reported between 2005 and 2010, with the frequency of cases increasing from 313 to 827 (Hussain *et al*., 2017).

Categorical frequency distribution of dog bite injuries in Pakistan: Dog-mediated rabies is prevalent in Pakistan, but most human cases are reported in rural areas (Bajwa *et al*., 2012; Zaidi *et al*., 2013; Ilyas *et al*., 2017; Afridi *et al*., 2022). Each day, 55-60 dog bite injuries occur in Karachi alone. In urban areas, dog bite injuries contribute significantly to the spread of rabies to humans (Zaidi *et al*., 2013). Numerous cases of dog bite injuries have been reported in Karachi, Peshawar, Hyderabad, Rawalpindi, Lahore, and Swat (Bajwa *et al*., 2012; Zaidi *et al*., 2013; Mansuri *et al*., 2016; Naeem *et al*., 2018; Ahmed *et al*., 2018; Salahuddin *et al*., 2021; Ali *et al*., 2021; Afridi *et al*., 2022). Every day, government hospitals receive almost 50 to 70 new cases of dog bite injuries. In Pakistan, Karachi is primarily endemic for human rabies, with a tertiary care hospital managing hundreds of dog bite victims on daily basis (Zaidi *et al*., 2013; Salahuddin *et al*., 2021). Regarding the age wise distribution of dog bite injuries, majority of reported incidents involve males (70-90%), children (10-15 years), and young adults (Bajwa *et al*., 2012; Mansuri *et al*., 2016; Hussain *et al*., 2017; Naeem *et al*., 2018; Salahuddin *et al*., 2018; Ali *et al*., 2021). Dog bite injuries also vary according to seasonal and climate changes in Pakistan. For example, the months with the hottest weather, such as June, July, and August, had the highest number of dog bite injuries in Pakistan (Ahmed *et al*., 2016; Ilyas *et al*., 2017; Ahmed *et al*., 2018). The graphical representation clearly demonstrates the age wise distribution of dog bite injuries among various years (Fig. 2).

Sociocultural risk factors of dog-mediated rabies in Pakistan: The relationship between humans and dogs is complex and is influenced by religious concepts, societal norms, cultural beliefs, and economic issues (Afridi *et al*., 2022). A range of owned and unowned animals (cattle, horses, and donkeys) especially free-roaming dogs roam in the streets of Pakistan and India, hence these animals present a potential risk of animal bite incidents to other animals and humans as shown in Fig. 1 (Ahmad *et al*., 2021). The WHO, WOAH, Food and Agriculture Organization (FAO), and Global Alliance for Rabies Control (GARC) jointly advocate the use of canine rabies blueprint and the Global framework for the elimination of dog-mediated human rabies, which is built on five pillars, the first of which is sociocultural followed by technical, organizational, political, and resources (Nel, 2018; Rupprecht *et al*., 2019; Yasmeen *et al*., 2022). The socio-cultural context affects rabies attitudes (bite prevention, treatment, post-exposure prophylaxis, and so forth) and dog-keeping behaviors such as dog ownership, dog population management, dog vaccination, and other traits of responsible pet ownership (Mansuri *et al*., 2016; Zafar *et al*., 2017). Any plan for the prevention and control of zoonotic diseases must consider the social pathways and drivers of disease transmission within animal or human populations, the variables that influence people's health-seeking behaviors, and the barriers to healthcare (Mubashir *et al*., 2021; Acharya *et al*., 2021). To analyze zoonosis such as rabies, this assessment must consider how people live close to animals and how they approach the animal and interspecies health issues that may create circumstances of pathogen spill-overs (Nel, 2018). Inadequate attention is devoted to the complex and culturally specific network of disease related aspects that bring people into contact with animals and facilitate the spread of rabies virus. Due to these anthropological risk factors of infectious diseases, dog-mediated rabies cannot be controlled merely through biological understanding (Pantha *et al*., 2020; Yasmeen *et al*., 2022). Additionally, only one preventive strategy cannot be expected to solve the multifactorial zoonotic transmission of this disease across all communities, as rabies affects developed and developing countries quite differently.

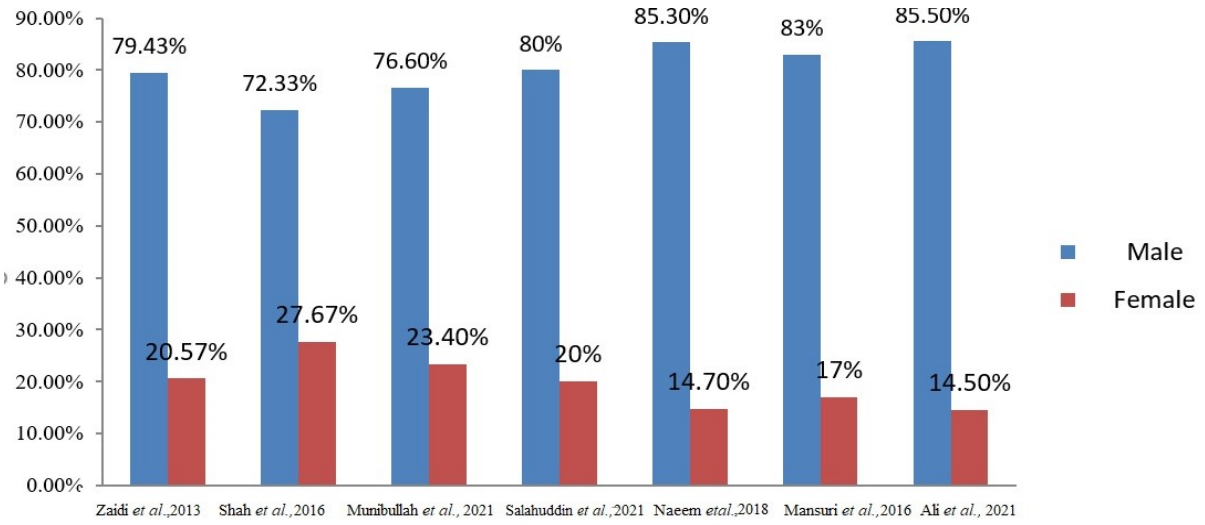

Fig. 2: summarized graph showing gender-wise distribution of dog bite injuries in Pakistan.

Barriers in the control and prevention of dog-mediated rabies in Pakistan

Lack of diagnostics in rabies suspected cases of animals and humans: At present, a range of diagnostic techniques have been well established by WOAH to diagnose rabies at antemortem and postmortem levels, including fluorescent antibody test as the gold standard test (Singh and Ahmad, 2018). Nevertheless, immunohistochemistry also provides actual and precise results with an equal sensitivity and specificity to that of fluorescent antibody test (Stein *et al*., 2010; Faizee *et al*., 2011). Clinical diagnosis can be achieved in biological samples such as skin biopsy, saliva, and cerebrospinal fluid using reverse transcriptase PCR that helps us in virus characterization by detecting specific nucleic acid using gel electrophoresis (Faizee *et al*., 2011). This technique is reliable, quick, and sensitive tool to diagnose rabies in all animal species, even in denatured and decomposed brain samples (Biswal *et al*., 2007; Faizee *et al*., 2011). At necropsy, formalin fixed brain tissue samples are processed by routinely used diagnostic techniques such as histopathology and immunohistochemistry which are being used worldwide in various animals and humans to reveal characteristic lesions and distribution of viral aggregates respectively (Jamadagni *et al*., 2007; Manickam *et al*., 2009; Stein *et al*., 2010; Beigh *et al*., 2014). It is because in developing states, the processing and preservation of fresh brain sample is difficult and burdensome due to mismanagement during sample collection in extreme hot climatic conditions (Beigh *et al*., 2013). Moreover, formalin fixed treated brain samples are not only cost effective and save time, but also preserve the actual form of a sample without rendering further autolysis until processing (Abreu *et al*., 2012). It is unfortunate to mention that such kinds of diagnostic techniques have not been well operated or conducted in animals or humans at local, regional, or national levels of the country (Ahmad *et al*., 2021). Almost all the suspected cases of dog-mediated rabies in animals and humans usually go unnoticed without the diagnosis being made.

One health framework: People's health is linked with the health of animals and the surrounding natural environment. One Health approach functions effectively with a systematic reporting system that allows monitoring and reporting of real time health related events at animal, human, and science-policy interface to address the advocacy of health for all (Pantha *et al*., 2020; Acharya *et al*., 2021; Ahmad *et al*., 2021). Managing rabies outbreaks in both human and animal is a primary focus of the One Health approach (Yasmeen *et al*., 2022). In addition to decreasing the need for post-exposure vaccination in humans, reducing the transmission of dog-mediated human rabies to human also minimizes the economic strain on the public healthcare systems because of the vaccine. One Health strategy is an affordable approach to manage dog-mediated human rabies for economically disadvantaged countries like Pakistan (Acharya *et al*., 2020; Yasmeen *et al*., 2021). There are both Government and Private facilities in urban regions of Pakistan that provide pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (Ahmad *et al*., 2021). Despite the basic knowledge of One Health approach in medical and veterinary professionals, PrEP and PEP are difficult to obtain in rural locations. So far, most HCPs are concentrated in major cities, making it difficult for those dog or animal bite victims of rural areas who have been bitten by animals to get medical attention (Ahmed *et al*., 2020; Iqbal *et al*., 2020). The designated facilities for rabies prevention, availability of vaccine, and other medication are also scarce in rural regions. However, new programs addressing the accessibility, availability, affordability of vaccines and awareness regarding immediate wound treatment could be improved in these underprivileged regions of Pakistan to lower the burden of dog-mediated human rabies cases (Ahmad *et al*., 2021; Yasmeen *et al*., 2021; Ross *et al*., 2022). Rabies can be effectively controlled in Pakistan by MDV since it's a reliable, well-acclaimed control strategy, and an effective way to control the disease. A vaccination coverage of 70% dog population can break the transmission chain of the disease in any specific population (Salahuddin *et al*., 2016; Nel, 2018; Salahuddin *et al*., 2021). Medical professionals and the government must work together under One Health approach to ensure patient safety. It is

possible for doctors and veterinarians to educate their patients about rabies prevention through brief trainings courses, workshops, and seminars at public events, field areas, and public functions or gatherings (Mubashir *et al*., 2021). Doctors, paramedics, and paravets are also needed to be educated in the use of standard diagnostic methods in order to make them skillful pertaining to the patient management (Khan *et al*., 2019; Ahmad *et al*., 2021; Ahmed *et al*., 2020). Their skills should also include the thematic and technical expertise of One Health approach which comprise of developing differential diagnoses of clinical rabies, establishing case definitions, and exposure assessments for dog bite incidents (Khan *et al*., 2019; Yasmeen *et al*., 2022). Both public and private sector health experts and those working in designated rabies centers need systematic planning to acquire, store and report actual information at regional, national, and international databases to identify bold areas (Guo *et al*., 2019; Ahmad *et al*., 2021; Beasley *et al*., 2022). Inadequate pre-hospital care and inter-hospital transfer facilities can prolong the 'golden hour' because traffic delays emergency treatment in Pakistan. Dog-mediated rabies cases will be reported to medical centers more frequently if basic infrastructures like roads, electricity, transportation are improved (Mughal *et al*., 2018; Ali *et al*., 2021). Increased involvement from the general population can be achieved through enhanced public education and outreach programs that focus on low-income and underserved populations (Hussain *et al*., 2017; Iqbal *et al*., 2020). More funds can be allocated for the improvement of diagnostic services via well-equipped labs, screening through rapid test kits that would reduce the work load and availability of reliable yet affordable diagnostic tests to animal and human sectors (Ahmad *et al*., 2021; Ross *et al*., 2022). Surveillance systems must be operational in order to safeguard vulnerable animal populations and prevent further transmission. Such kinds of data are crucial for the development of national plans and control initiatives (Ahmad *et al*., 2021; Salahuddin *et al*., 2021).

Lack of training among health workers: The HCPs lack training in dealing with dog bite cases of animals and humans respectively (Khan *et al*., 2019; Ahmad *et al*., 2021). The lack of awareness about management and treatment of a suspected animal or rabid animal is essential for a practicing veterinarian who is addressing all the animal health concerns in a local community. Healthcare workers in designated rabies facilities experience scarcity of funds, training opportunities, and an overwhelming workload in the form of overburdened patient counseling, management, and medication (Ahmed *et al*., 2020). Basic hygienic wound cleaning, and follow-up of vaccination schedule are also not well comprehended by the patients and few HCPs (Ahmad *et al*., 2021; Afridi *et al*., 2022). Low performance was attributed to a high workload, lack of enforced rules from the medical institutions, inexperience, non-seriousness attitude, and a lack of financial or other compensatory benefits (Khan *et al*., 2019; Ahmad *et al*., 2021; Siddiqui *et al*., 2021).

Shortage and Cost of Animal and Human Vaccines: In rural regions of Pakistan, many people have died from rabies because of a lack of PrEP and PEPs (Siddiqui *et al*., 2021; Afridi *et al*., 2022). The need for vaccines or RIG is a widespread national health concern, especially in public sector hospitals. Only a small number of hospitals in public and commercial sectors had access to these vaccines (Siddiqui *et al*., 2021). As cost of 4 or 5-dose regimen of PEP is relatively higher and every person cannot have the capacity to purchase full dose regimen, therefore, people either forego vaccine shots or seek government-run health care facilities that cannot afford to provide free of cost and thereby unable to treat ever-increasing patient load at once (Salahuddin *et al*., 2016; Salahuddin *et al*., 2021). A somewhat similar scenarios have been observed for animals as animal owners do not get their animal vaccinated against rabies considering the importance of rabies vaccine as negligible or non-significant (Mughal *et al*., 2018). Vaccination against rabies is relatively also expensive due to lack of subsidized availability at public hospitals, and overall shortage at national level (Siddiqui *et al*., 2021). The government may sponsor rabies vaccination to human dog bite victims for free only to a selected group of patients (Hussain *et al*., 2017). Similarly, the rabies vaccination for owned canines (cats, dogs) of private or individual pet owners also exhibit lack of motivation by showing low level of knowledge, attitude, and healthy practice to maintain their animals (Khan *et al*., 2019).

Veterinarian-Client-Patient Relationship (VCPR) mismanagement: Uncertainty about management and handling of suspected or rabid animals and rabies treatment in animals is another issue. The animal HCP should inculcate sense of responsible pet ownership among animal or dog owners, and they should also convey him/her the best possible explanation to treat or manage his/her animal health concern or wound to build sustained, impactful, and dependable VCPR. This VCPR ensures consistency, hope, and sense of accurate judgement and personal satisfaction for veterinarians and animal owners (Nel, 2018; Coetzer *et al*., 2019). Similar example can be quoted for the human dog bite victims, where HCP should accurately administer RIG and rabies vaccinations in a right way. Many clinics do not deliver adequate PEP owing to staff training or the belief that vaccination and RIG are unsafe or unaffordable (Salahuddin *et al*., 2016; Salahuddin *et al*., 2021). Doctors and nurses are unprepared for wound care, vaccines, and RIG administration (Illyas *et al*., 2017). Wound severity is not effectively assessed even in large hospitals, vaccines and RIGs are misused that raise budgetary concerns for HCPs (Salahuddin *et al*., 2016; Ahmad *et al*., 2021). When the animal bite injury is not obvious, rabies PEP can be difficult to assess. When low-or no-risk individuals receive rabies PEP, expenses rise up. Prioritization of high-risk patients must be done whenever RIG is scarce in the clinics. Intradermal immunization is safe and effective, but some doctors are hesitant to use it off-label (Salahuddin *et al*., 2016).

Traditional healers and quacks: Rabies infection can be prevented following an animal bite when appropriate anti-rabies treatment is administered within 24 hours of the animal bite (Sohi *et al*., 2020), but majority of dog bite

victims do not follow this treatment (Ahmed *et al*., 2020). Rather than visiting hospitals, people seek out traditional remedies and spiritual healers to treat dog bite wounds or terrifying symptoms of rabies mostly in India and Pakistan (Dabuma *et al*., 2017; Ahmad *et al*., 2021). Traditional healers are preferred in rural regions for immediate wound treatment in animals and humans because of low accessibility to the nearest health center, high cost or even absence of the vaccine, the inability to skip work, and faith in traditional healing (Ahmad *et al*., 2021; Siddiqui *et al*., 2021). Consequently, rural people commonly search out faith medicine, especially those living in poor areas, as these methods or tactics are more approachable than contemporary medical techniques and significantly less expensive than the latter (Ahmad *et al*., 2021). Chili pepper powder and oils in many rural households are trendy home medicines (Beasley *et al*., 2022).

Awareness among animal and human healthcare workers: Pakistan is a country with a mixed health system. The public and private sectors are working simultaneously to provide healthcare services to the animals and humans. The medical private sector forms the more significant chunk and caters to approximately 70% population (Hussain *et al*., 2017; Blum *et al*., 2018). People's lack of knowledge regarding the importance of seeking immediate treatment following animal bite, poor traditional practices following animal bite, and delay in seeking anti-rabies treatment due to low socioeconomic status, are some risk factors identified in various studies (Bajwa *et al*., 2012; Zafar *et al*., 2017; Naeem *et al*., 2018; Mughal *et al*., 2018; Blum *et al*., 2018; Siddiqui *et al*., 2021; Salahuddin *et al*., 2021). Urbanization exposes families and children to possible rabies reservoirs as wildlife habitat changes to human use (Pantha *et al*., 2020). People know about immunization, but just a few had immunized dogs in Pakistan (Khan *et al*., 2019). Intrusion with dogs resulted in bite injuries in 50.9% of patients. Most patients reported within 24 hours of the dog bite incident, although 17% of patients came to the healthcare facility after 24 hours (Iqbal *et al*., 2019; Khan *et al*., 2019). These results reveal a lack of knowledge about PEP and dog bite sequelae. In Pakistan, attention to educate patients and HCPs on dog bite management is required (Iqbal *et al*., 2019). Mobile phone technologies can help to fill monitoring gaps in low-resource environments. Large-scale health-based infectious disease surveillance systems in underdeveloped countries are needed to support sustainability (Davlin and Helena, 2012; Lopes *et al*., 2018).

Canine rabies blueprint: The blueprint for rabies prevention and control has been produced by the partners for rabies prevention which are international organizations such as WOAH and GARC. Among other aspects, this print version has produced a control strategy through the implementation of dog population control measures using MDV programs (Nel, 2018). There are problems associated with the control of dog-mediated rabies that include widespread varieties of other rabies reservoirs, cross-species disease transmission, the increasing population of free-roaming dogs, insufficient resources for disease surveillance, and public apathy (Ahmad *et al*., 2021). Currently, the world may be divided into three broad rabies zones: areas where enzootic canine rabies is present; locations where enzootic canine rabies is controlled, but wildlife rabies is present; and finally, rabies-free countries and areas (Bannazadeh *et al*., 2018).

Zero by 30 goal to control dog-mediated human rabies: In Pakistan, rabies is still endemic, and we need to come up with answers that might be used in a countrywide ‘Zero By 30’ campaign to eradicate this old and horrifying illness (Ahmad *et al*., 2021). Asian nations' pledge to 'Zero By 30' should be reaffirmed by national stakeholders in the health sector through administrative and legislative measures (Rahman and Isloor, 2018).

The Punjab Animal Health Act 2019 mandates mandatory vaccinations and other preventive measures for all animals in a regulated region in the occurrence of any infectious diseases (Iqbal *et al*., 2020). In Pakistan, a similar law may be adopted for people who mistreat animals or free-roaming dogs, such as torturing and humiliating them to death. Animal welfare organizations, business agreements, academics, and researchers may benefit from these legislative efforts, which aim to strengthen the integration between the veterinary and medical sectors (Zaidi *et al*., 2013; Rupprecht *et al*., 2019). In order to keep track of dog bite injuries, both the public health centers and clinics should keep a log of all incidents, including demographic and animal information (Ahmad *et al*., 2021). Depending on the availability of finances, these laws and regulations may also inspire local funding agencies and national health officials of Pakistan to employ other methods such as the Step-Wise Approach towards Rabies Elimination (SARE), rabies surveillance blueprint, and Global Dog Rabies Elimination Pathway (Nel, 2018; Rupprecht *et al*, 2019).

Pakistani focal persons calculated a SARE-score of 0.5 that shows essentially negligible progress in fighting dog-mediated rabies (Coetzer *et al*., 2019). This low score may reflect a lack of interest from health professionals and a preference for other health issues (Salahuddin *et al*., 2016). A higher SARE score would show Pakistan's progress in countering this zoonotic crisis. In order to improve animal welfare and population control, Pakistan's medical and veterinary health professionals may place an emphasis on MDV and other dog population control methods (Coetzer *et al*., 2019; Rupprecht *et al*., 2019). To begin, collaborative teams of One Health officials should study dog population density and ecological behaviors, empower vaccination of owned dog population in the country through door-to-door method with the help of GPS-enabled cell phones. The ‘Trap-Neuter-Vaccinate-Release (TNVR) in Pakistan necessitates a trained team of animal behaviorists, funds, stringent political support, and support from local and regional communities. In order to prevent dog-mediated rabies, it is necessary to vaccine at least 70% of the dog population (Davlin and Helena, 2012; Rupprecht *et al*., 2019).

Government officials in Pakistan should be informed of the economic means and the precise budget for human and animal prophylactic measures to ensure that required prophylactic measures are available in every medical and veterinary hospital (Ahmad *et al*., 2021). A specified

budget for MDV programs may remove the risk of cash needed for procuring PEP solutions and related patient's treatment expenditures in public health facilities of the country. The MDV campaign's accessibility, affordability, dependability, and effectiveness may all be maintained while using cost-saving public health measures (Coetzer *et al*., 2019). According to Pakistan's rabies focus person, the rabies elimination measures outlined in this evaluation should be quickly reproduced. The MDV pilot projects in Karachi, Pakistan, should be replicated in other regions of the country to accelerate the global vision of 'Zero By 30'. As long as Pakistan adheres to the mission and recommendations set by WOAH and WHO, it will be possible to envisage the control of dog-mediated rabies at national level.

Conclusions: Rural and urban communities alike should have access to rabies vaccines, and the authorities should ensure their safe storage. The Government of Pakistan should realize the importance of One Health concept, MDV programs, and global motive to end dog-mediated human rabies with full passion, dedication, and commitment. Government of Pakistan should also increase the number of healthcare facilities that provide PEP and RIG in order to lower the incidence of dog bite injuries and rabies in Pakistan. Developing a cost-effective rabies vaccine is need of the hour. Rabies prevention is a public good and the government's responsibility. Donations of the investors should be catalytic for program establishment, and a well-planned donor exit strategy should prevent prolonged donor dependence. Health officials, program administrators, scientific personals, and all should involve to adopt informed decisions and efficiently combat this disease. The WOAH-recommended procedures for the management of free-roaming dogs, and consistent supply of PEP and RIG infiltration are not correctly followed due to a lack of national health actors and inadequate training of HCP at designated veterinary and medical health care units. In Pakistan, the lack of fundings for joint ventures of One Health projects make 'Zero By 30' mission more cumbersome. Disease control usually requires global, regional, and national policies and alliances.

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