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STRATEGIES FOR THE PREVENTION AND CONTROL OF RABIES INFECTION IN DEVELOPING WORLD

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Abstract

Rabies is a major public health problem in developing countries with an estimated 59,000 deaths per year. This review article explores advanced strategies for prevention and control of the disease, highlighting human, animal and environmental health under One Health approach. Key strategies include a mass vaccination campaign targeting dogs (the main reservoir of virus) and the use of oral rabies vaccine for wild animals. New discoveries including geographic information systems have increased surveillance and control efforts. Public education and community participation are key to raise awareness and increase participants in vaccination campaigns. This article also focuses on the importance of global cooperation, sustainable solutions, affordability/access to vaccines and incorporating prevention into broader public health initiatives. Key challenges include resource limitations, cultural and social barriers, climate and environmental factors. Addressing these will be useful to achieve rabies elimination.

Keywords: *100% mortality, Control & prevention of rabies, Oral rabies vaccine, Post-exposure prophylaxis, Pre-exposure prophylaxis, Rabies, RABV, Zoonotic disease*

INTRODUCTION

BACKGROUND OF RABIES

Rabies is an infectious zoonotic disease causing significant number of deaths per annum all over the world and having 100% mortality rate. The causing agent of this disease is *Rabies lyssavirus* (RABV) which belong to the genus *Lyssavirus* and family *Rhabdoviridae* (1, 2). The transmission of this virus occurs through the saliva of infected animal transmitted through bites, scratches or direct contact with mucus membrane. Despite being preventable through vaccination, it remains a significant public health issue, especially in developing countries (2) RABV cause encephalitis by attacking the central nervous system leading to death if left untreated. After the infection, it takes one to three months (incubation period) to show its first symptom and it is almost fatal once clinical symptoms appeared (3). The high mortality is primarily due to Blood Brain Barrier (BBB) which prevents the therapeutic agents including antivirals from reaching infected neurons (4).

Rabies remains a public health concern in the major parts of the world, especially where Pre Exposure Prophylaxis (PrEP) and Post Exposure Prophylaxis (PEP) is limited. The struggles to control and prevent this disease is mainly related to dog vaccination as dogs are the primary reservoir and transmitters of almost 99% of the all human rabies cases(5). There are many challenges to eliminate and reduce the number of cases including inadequate infrastructure, lack of awareness, access to vaccine and even vaccine hesitancy (6, 7) The "Zero by 30" initiative by World Health Organization (WHO) seems to be a great step to control this deadly disease which initiates to eliminate the infection percentage to 0% till 2030 (8).

GLOBAL BURDEN OF RABIES

RABV is responsible for almost 59000 deaths annually worldwide including 35000 in Asia, 21000 in Africa, 10 in Europe, 300 in South America, 5 in North America and less than 3 in Oceania (Fig. 1) (9). It shows that this virus is mainly affecting those countries where vaccine supply, education related to health and other health facilities are not sufficient which cause economic burdens. The economic burden of Rabies is substantial with global costs exceeding $8.6 billion annually and an average of $100 per treatment (9).

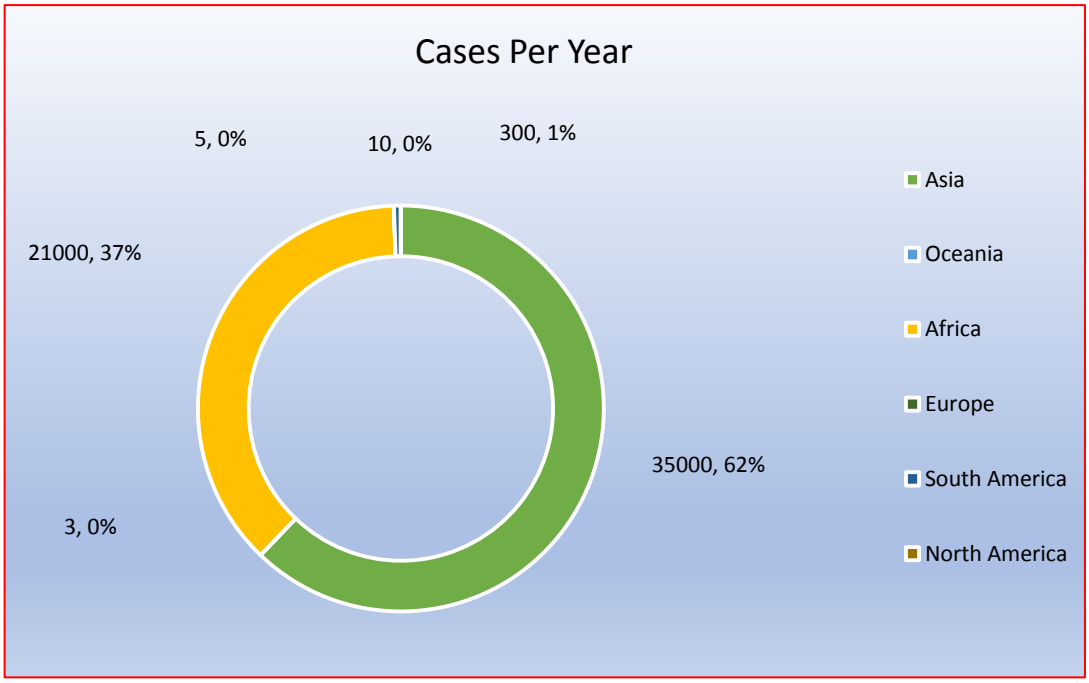

Figure 1: Global distribution of human rabies deaths per year by region. Data from WHO showing higher burden in Asia and Africa as compared to other regions (9)

IMPORTANCE OF CONTROL STRATEGIES

To reduce the number of human deaths, animal deaths and economic burdens, good and effective control strategies are necessary particularly in the more effective regions including Asia and Africa. The WHO's primary goal to control this deadly disease is to prevent human deaths by reducing the transmission from animals to humans (8). Health education to people, easy access to vaccine and the vaccination of domestic animals seems to be the most cost effective strategy to control this zoonosis. It needs a comprehensive approach to stop the spread which include vaccination, public health education and improved access to PrEP (8).

EPIDEMIOLOGY OF RABIES, TRANSMISSION AND SPREAD

Lack of education made a concept in people that this virus can only by transmitted be dogs but as rabies is a virus which can be transmitted from infected animals or person as well. It can transfer from one infected body to another by several ways including, bites, contact with saliva or direct contact with mucosal membrane. The reason behind the fear of dog transmission is that dogs are known to be the primary mode of transmission to humans. Other than dogs, RABV is transmitted through the animals including bats, raccoons, foxes, skunks and even cow (Figure 2). Human to human transmission is very rare and has only been documented in cases of organ transplantation (10). The lack of access to vaccines and PEP contributes to the high burden of the disease in many developing countries. Rural areas are particularly affected due to limited healthcare infrastructure and a higher prevalence of stray dogs. The elimination of this disease is possible as it has been largely eliminated in many developed countries through successful vaccination programs and strict animal control measures (11).

VACCINATION STRATEGIES

HUMAN VACCINE

Human vaccine is crucial to minimize the annual death rate. It is a necessary step especially in the endemic regions. PrEP is recommended for individuals at high risk including veterinarians, animal handlers

Fig. 2. Common transmission route of RABV, including dog to human and bat to human as well

laboratory personnel and travelers. The PEP is crucial for anyone who has been bitten or got starched by any suspected rabid animal. It not only includes the vaccination but it also includes the immediate wound cleaning and even the antibodies or immunoglobulin treatment. It stops the virus to reach the central nervous system to cause symptoms (12). The access to vaccine is limited in many of the developing countries due to high costs and inadequate healthcare infrastructure, which is one of the major causes of the annual deaths by rabies (12) Development of inactivated vaccine is crucial for resource limited countries, as it is composed of 4 basic steps from seed virus development to vaccine purification (Fig. 3).

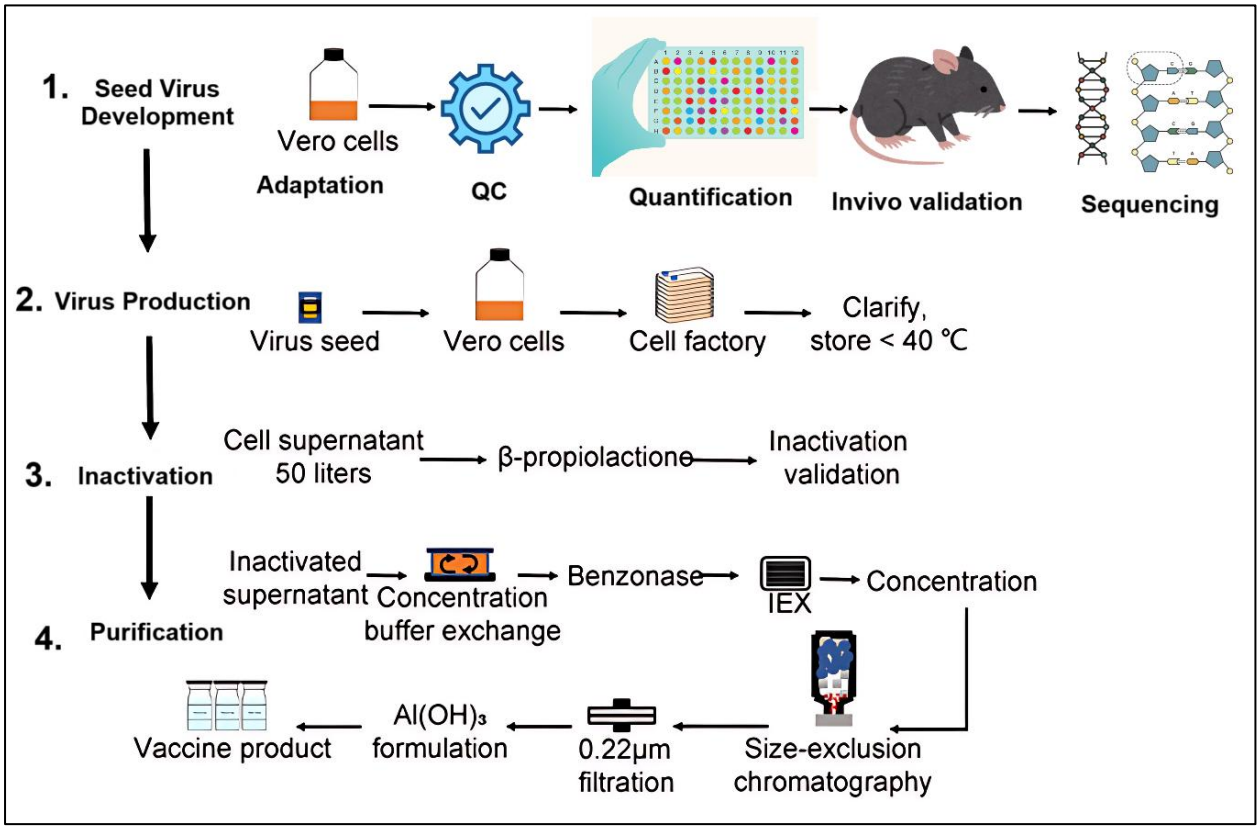

Fig. 3. Workflow for inactivated rabies vaccine production. Steps include seed virus development, propagation in Vero cells, viral inactivation, purification, and formulation

ANIMAL VACCINATION

The vaccination of domestic animals is the most reliable and effective strategy to prevent rabies transmission to humans. Those animals include dogs and the mass dog vaccination campaign seems to be

more effective than any other strategy even a study shown that vaccination of only 70% of the dogs can lead to reduce and eliminate the disease frequently (13, 14) Other than dogs, vaccination of animals including cats, livestock and wildlife can also play an important role in controlling the disease (15) All the strategies are important and can only be applied with the collaboration of Government organization, Non-government organization (NGOs) and the local population and communities. Public education is important to encourage communities to vaccinate their animals, while affordable vaccines and accessible veterinary services are key for success of the program (16).

CHALLENGES IN VACCINATION

There are multiple challenges noted for vaccination program including lack of awareness and education, high cost of vaccine, inadequate healthcare infrastructure and limited access to veterinary services as well. These are the main challenges (primary challenges) to eliminate the deaths by this virus. There are many other challenges (secondary challenges) which are also affecting the programs to end rabies including religious sanctions, vaccine hesitancy, the resistance to not accept the virus's presence, propaganda against vaccines and many more. None of such barriers can be ignored in completing the goal to eliminate RABV from all over the world (16-19). Table I summarizes the main rabies vaccination strategies, its importance and related challenges for humans, domestic and wild animals.

Table I. Vaccination strategies for rabies prevention and control

Target group	Vaccine type	Importance	Challenges
Humans	Inactivated vaccine	Prevents infection and death after exposure	High cost, limited access in low-income areas
Dogs	Mass vaccination	Interrupts 99% of human cases	Requires 70% coverage, logistic challenges
Wildlife	Oral rabies vaccine	Prevents spillover from reservoirs	Distribution, cost

PUBLIC HEALTH INTERVENTIONS

AWARENESS CAMPAIGNS

Awareness campaigns are essential for keeping the disease in check. It's all about educating people about the dangers of rabies and making sure everyone knows that vaccines and quick doctor visits are important to deal with exposures. The main goal of these campaigns is to get people to actually start caring about it and doing multiple things to stay safe (20). These campaigns use a bunch of different ways to get the word out, like television, the internet, and even going into communities to chat with people face to face(21). Sometimes, it's also important to go to schools to teach the young ones because kids are totally the future and they need to know the importance too (22). It is a big team effort with governments, NGOs and the public to work together to spread the awareness (23).

COMMUNITY ENGAGEMENT

Community involvement is another very important step when it comes to dealing with rabies and vaccination campaigns. Local people should be involved in the fight against rabies, it helps build trust and makes sure everyone is on board with getting their pets and domestic animals vaccinated. It's all about making sure the things we do to keep everyone safe from rabies are a good fit for each community's way of life (24). One way that's proven to work well is by using methods where everyone gets to have a role in a campaign, it is known as participatory methods. It is completed by holding meetings with the head of different communities from the neighborhood, chatting in small groups, or even doing some hands on assessments in rural areas. By following this way, the people who actually live in a specific area can help the researchers to figure out the best way to tackle rabies in their area. Training local volunteers, health workers, and community leaders with knowledge about rabies and its prevention is important for safe, good and effective community based control programs. It is an important thing to have some helpful neighbors making sure everyone knows what to do if there's a risk. It's a team effort that makes a huge difference in keeping everyone safe and healthy (24).

SURVEILLANCE AND REPORTING

These two are the fundamental components of rabies control program because they provide the data which is needed to monitor the disease and its spread, evaluate the effectiveness of interventions and guide policy decisions. A good surveillance system includes the systematic collection, its analysis and dissemination of data on the rabies cases from both animals and humans. These surveillance can help in different ways including minimizing the spread of the virus, to identify the high risk area and to detect and enable a good and effective response in case of outbreak (25).

POLICY AND LEGISLATION

Effective policies and laws are critical to rabies control and prevention. National and international policies provide the framework for coordinated efforts to combat the disease. Rabies control policies in many countries are guided by WHO and other international agencies (12, 26). The policy can specify the requirements of PEP for people exposed to rabies, to ensure that Rabies vaccines and immunoglobulins are readily available and inexpensive.

NATIONAL AND INTERNATIONAL POLICIES

WHO provides comprehensive guidelines and recommendations for the prevention and control of the disease which can be used by member states in formulating their national policies (12). International partnerships such as the Global Alliance for Rabies Control (GARC) and the "Zero by 30" initiative aim to eliminate human deaths from dog borne rabies through Coordinate and share resources (9) National policies often include mandatory vaccination of pets especially dogs and the establishment of rabies-free zones through joint vaccination campaigns and animal control measures. The policy may specify the requirements of PEP for person who is exposed to rabies. To ensure that rabies vaccines and antibodies are easily available and affordable. Good policies and regulation to certify a widespread and sustainable rabies control program and international cooperation is needed (27).

IMPLEMENTATION CHALLENGES

Execution of an effective rabies vaccination program faces multiple different challenges mainly in under-developed countries. One of the main and biggest challenges is the high cost of vaccines and PEP, which can be very expensive for individuals in backward areas. The financial burden of these programs also puts some pressure on the resources of governments and NGOs which are working to control the disease (27, 28). The second important challenge is the lack of awareness and education about rabies prevention and control in many communities. Cultural but not religious beliefs and practices may also play a role in obstructing vaccination efforts, For example some people rely on herbalists and faith healers instead of modern medical care. This may delay or prevent effective treatment. The other challenges including poor healthcare infrastructure and poor access to veterinary services which further make difficulties in vaccination efforts. Vaccination campaigns in rural and remote areas may be difficult to access the targeted area with multiple reasons including poor transportation network and low number of trained health care workers and veterinarians. Maintaining vaccine storage and cold chain distribution is also a major challenge in many developing countries (29).

SUCCESS STORIES

Different success stories show the effectiveness of rabies vaccination programs and provide respectable and valuable lessons for other regions. A main example is the Philippines, where the province of Ilocos Norte outfits the One Health project to eradicate the disease which resulted in no rabies deaths for more than two years. This program includes a number of vaccinations for dogs, Public education and community participation which demonstrates the importance of a coordinated approach to rabies control (30). Another success story comes from Tanzania, The large dog vaccination campaign has helped reduce the incidence of Rabies in dogs and humans. The campaign is supported by international organizations and involves extensive community outreach and education (31). In Latin America, the “Pan American Health

Organization" leads a successful rabies control program. This has resulted in the elimination of dog-borne rabies in many countries including Chile and Uruguay. These programs focus on vaccinating large numbers of dogs. Good surveillance and educating people in addition with continuous effort can highlight the importance of international cooperation (32). These stories show that rabies can be controlled and washout by widespread vaccination, education programs and motivation.

ONE HEALTH APPROACH

A One Health approach is a universal strategy that recognizes mutual relations between human, animal and environmental health. This approach emphasizes the importance of cooperation between different regions. To solve the health challenges arising in the interface between humans, animals and the environment. Rabies control is a prime example of how a single health approach can be particularly effective (33). By integrating efforts in human, veterinary and environmental health sectors, a One Health approach aims to create a comprehensive permanent solution for the prevention and control of the disease (34). The foundation stone of this approach is that the health of humans, animals and ecosystems is interdependent. For example, in addition to controlling rabies in domestic dogs, understanding ecological factors that affect the spread of the virus, (wildlife reservoirs and environmental changes) are important for effective development and control strategies (26). Implementation of health guidelines requires strong cooperation and communication between various fields and subjects. This includes joint monitoring, reporting system, coordinated vaccination campaign and integrated public health messages (35).

INTEGRATION OF HUMAN, ANIMAL AND ENVIRONMENTAL HEALTH

Integrating human, animal and environmental health is the cornerstone of a One Health approach. This integration is essential for managing complex health problems and involves many ecosystems as well when considering the interactions between humans, animals, and the environment, Health professionals can develop more comprehensive and effective disease prevention and control strategies (35, 36). For example, a rabies control program that focuses solely on human vaccination may not be sufficient to eradicate the disease. Animal vaccination, on the other side mainly domestic dogs can be combined into human health initiatives to reduce rabies cases. Understanding the role of wildlife and environmental factors in transmission of the disease is crucial for developing targeted goals. This may include living arrangements, Wild animal vaccination project and monitoring environmental changes that may affect the spread of virus (37). Good and reasonable integration requires a strong surveillance system that collects and analyze the data from the human, animal, and environmental health organizations. It is a guideline for allocating resources and support evidence-based policy development. In addition, interdisciplinary research and training programs can help health professionals build capacity to work across disciplines and dealing with multifaceted zoonotic diseases such as rabies (35, 36).

COLLABORATIVE EFFORTS

Cooperative efforts are necessary for successful implementation of a health approach to the control of the virus. This includes teamwork between NGOs, government agencies, educational institutions and many different stakeholders, includes working together in local communities. The stakeholders can generate resources to complete general goals, add expertise and coordinate tasks. One of the big example of successful alliance is the GARC, which combine partners around the world to reduce rabies cases. The GARC initiative includes developing a step wise approach to rabies eradication, which helps the countries to eliminate rabies. This provides a framework for evaluation and identification of areas for improvement. A collaborative approach is important in helping countries develop and implement effective rabies control strategies (13). National allied efforts often involve the formation of interval committees from representatives of public health, veterinary and environmental agencies. These committees facilitate communication and coordination between different areas to make sure that rabies control efforts are rational and balanced. Corporation with educational institutions can support research and training programs that produce health professionals to manage RABV and other diseases as well. Public participation is also a good

component of combine efforts. The participation of local communities in rabies control programs leads to create confidence, stimulate participation and signs that the intervention is culturally suitable and durable (35, 36).

TECHNOLOGICAL INNOVATIONS

Technological innovations have made great advances in the control and prevention of rabies. The most notable innovation is the development of a rapid diagnostic test. These tests, such as the Direct Fluorescent Antibody (DFA) test and the Direct Visual Immunohistochemistry (DRIT) test, have become important diagnostic tools (38, 39). Molecular techniques such as these have improved the sensitivity and specificity of the virus detection. Another important tech evolution is the use of Geographic Information Systems (GIS) and statistical tools for surveillance. These technologies make it possible to map the cases and identify the red areas, facilitate targeted area and resource distribution. The GARC has developed multiple tools, including the Rabies Case Surveillance (RCS) tool, which provides real-time data analysis and visualization (39).

DIAGNOSTIC TOOLS

Clinical equipment is required to detect the disease on time. DFA tests are considered the standard of gold for rabies diagnosis which is highly sensitive and specific that makes it a reliable way to confirm rabies infection in humans and animals (40). Another important clinical device is the DRIT, which uses enzyme-labeled antibodies to detect rabies virus antigens in tissue samples (41). Additionally, molecular techniques such as Real-time Polymerase Chain Reaction (RT-PCR) have brought revolution in rabies diagnosis. (42). Rapid In-field Diagnosis and Epidemiology of Rabies (RAIDER) toolkit is another innovative diagnostic tool developed to improve monitoring (43, 44).

SURVEILLANCE TECHNOLOGIES

Surveillance technology is critical in tracking rabies cases and guiding control efforts. These technologies facilitate analysis of spatial and temporal patterns of rabies transmission. It enables targeted intervention and resource allocation (45). The RCS tool developed by the GARC is a powerful visualization and mapping tool that provides real-time results for human and animal rabies case statistics. This tool has been used successfully in many countries to identify rabies hotspots, track outbreaks, and plan strategic vaccination campaigns (46). Another new surveillance technology is the GARC data platform, which can collect, analyze and visualize rabies data from the community level. It promotes a single health approach to rabies surveillance by providing a centralized database for information on rabies cases. The GARC data platform will increase the accuracy and timeliness of surveillance and supporting evidence based decision making (46).

RESEARCH AND DEVELOPMENT

Research and development plays a significant role for developing strategies on rabies control and prevention. Ongoing research aims to address the limitations of current measures and develop new approaches to rabies control. One area of rabies research and development is the development of new vaccines and methods of vaccine delivery. Research is underway on Genetically Modified Organisms (GMOs) and invasive vaccines which has the potential to increase the efficiency and coverage of vaccination campaigns. Efforts are also underway to develop an inexpensive and scalable rabies immunoglobulin (RIG) production system. More Human vaccines are important for PEP (26). Mathematical and hereditary tree in rabies research are important tools which help to understand the dynamics of infection and the percentage of success of vaccination programs. This participation provides the facility of sharing knowledge, resources and expertise. Promote the development and implementation of innovative control strategies (47, 48).

FUTURE DIRECTIONS

Tackling rabies effectively will demand a combination of multiple innovation, adaptability, and international solidarity. Temperature stable and cost-effective oral vaccines have real power to expand the

approach into hard to reach mobile communities that conventional programs struggle to serve. The deployment of sensitive point-of-care diagnostics, in combination with smart data systems can significantly narrow the window between antigen detection and outbreak response. Implementation of a One Health approach where veterinary, human health, and environmental divisions collaborate and offers a plane way to address challenges from both dogs and wildlife. Coordinated approaches can complement each other to decrease the transmission.

Yet only science isn't enough, strong progress depends on sustained global alignment. This means merging rabies prevention into everyday health services, giving the local clinics and labs the tools they need in combination with training, and maintaining trust through transparent communication. Areas must remain connected through shared policy frameworks and on time information exchange. Only by investing at every single stage from field communication to international coordination we can shift from control efforts toward real long term elimination.

CONCLUSION

Rabies, a disease preventable with a $2 vaccine still claims 59,000 lives each year mostly in children especially in places where health systems are fragile. A child bitten by a rabid dog in rural Kenya today faces the same grim odds as a 19th-century Parisian. That's not a failure of science. It's a failure of collective resolve. Effective elimination requires integration of human, animal and environmental health within a One Health structure. Vaccination of stray dogs, better access to vaccines and community engagement are necessary to reduce the transmission. Achieving the global target of "Zero by 30" depends on international cooperation, policy alignment and investment in monitoring and public health infrastructure. With coordinated efforts, the eradication of dog mediated human rabies deaths is an achievable target.

Recommendations:

To control and eliminate this zoonosis effectively, the following recommendations should be considered.

1) **Mass vaccination campaign:** A mass vaccination program should be carry out targeting domestic dogs. Achieving at least 70% vaccination coverage of dogs is important to stop the spread of the virus and reduce rabies cases.
2) **Public education and community participation:** Local communities should be involved in rabies control projects to promote a sense of belonging and responsibility and promote continued participation and support.
3) **Improve access to PEP:** Ensure the availability and affordability of PEP, including rabies vaccine and RIG which has a true importance in low-income areas. Strengthen healthcare infrastructure and train health professionals to provide effective treatment during exposure to rabies.
4) **Integrate rabies prevention with public health and veterinary services:** Rabies control should be integrated with existing health infrastructure to create a more flexible response system. This includes training veterinary health care professionals and surveillance system improvements.
5) **Technological Innovation:** Advanced diagnostic tools should be used including GIS and digital technology to improve the surveillance and control efforts. Next-generation vaccines and new vaccine delivery methods should be developed to improve coverage and effectiveness.
6) **Global cooperation:** Cooperation should be promoted between international organizations, governments, and NGOs, educational institutions and the private sector to exchange knowledge, information, resources, and expertise as well. The keys should be shared cross boarders to get valuable and equal results throughout the world.
7) **Sustainable solutions:** Everyone should focus on long term plans that ensure affordability and access to vaccines to everyone.

Following these recommendations will help the world make valuable progress in achieving the goal to control rabies virus infection in developing world.

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The contributions of many individuals made this work possible. The main author carried out the research, analyzed data and original draft. The other authors provided important advice and support throughout the research process. They provide expertise and visions that help shape the direction and outcomes of education. Their contributions included reviewing the manuscript, suggestions regarding research design and providing assistance in interpreting data. No funding was received for this study but the author's dedication made this research to be completed by their own.

Conflict of interest:

The authors declare that we have no competing interests.

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