

REVIEW ARTICLE

Rabies elimination policy guidelines: Where do we stand?M Swathi Shenoy¹; Archismita Santra²; Anjan Kumar Giri³^{1,3}Department of Community and Family Medicine, All India Institute of Medical sciences, Raipur;²Department of Community Medicine, IQ City Medical College and Hospital, West Bengal

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**Citation**

Shenoy MS, Santra A, Giri AK. Rabies elimination policy guidelines: Where do we stand?. Indian J Comm Health. 2023;35(3):258-263. <https://doi.org/10.47203/IJCH.2023.v35i03.002>

Source of Funding: Nil Conflict of Interest: None declared

Article Cycle

Received: 06/04/2023; Revision: 18/07/2023; Accepted: 24/08/2023; Published: 30/09/2023

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Abstract

Introduction: Rabies is one of the Neglected Tropical diseases. India accounts for 35% of rabies-related human deaths globally. Despite effective preventive and control strategies, India hasn't been able to eliminate rabies. **Methodology:** A narrative review was done by comparing various policies and programmes related to rabies control and elimination in India and other countries, and the gaps persisting in the Indian guidelines and its implementation were assessed. **Results:** There are multiple gaps in the Indian programme implementation ranging from multiple stockouts of vaccines, unavailability of rabies immunoglobulin, and lack of a robust surveillance system to lack of refreshing training of the health staff. **Recommendations:** For effective implementation, the population should have increased awareness, with increased production and an effective supply chain of vaccines and immunoglobulins. There should also be a robust surveillance system with periodic refresher training of the health staff.

Keywords

Humans Rabies; Immunologic Factors; Rabies Vaccines; Rabies Immunoglobulins; India

Introduction

Rabies is a vaccine-preventable viral zoonotic disease caused by the Lyssavirus of the *Rhabdoviridae* family. (1) It is identified as a Neglected Tropical disease by the World Health Organization. (2) It is prevalent in all continents of the world, excluding Antarctica, with 95% of the human deaths occurring in the Asian and African continents. (2,3) India accounts for 59.9% of the rabies deaths in Asia and 35% of rabies-related human deaths globally. (4) 99% of the global cases are due to bites from rabid dogs. (2) (Figure 1) In India, the estimated annual incidence of human rabies was found to be 2 per 1lakh population as per a multicentric survey. (5) Similarly, 95% of the Indian cases are consequences of dog bites, followed by cat bites, and over 3/4th of the cases occur in rural areas. (6) A country is said to be free of dog-mediated rabies if no indigenously acquired cases have been confirmed in humans, dogs, or other animal species for at least two years. (4) Dog-mediated Rabies has been eliminated from Japan, Canada, Western Europe, and Latin American countries. (4) It is a disease of a public health concern as it

is 100% fatal, and as such, there is no treatment strategy currently available. (1) Even though there isn't any effective treatment strategy, vaccines easily prevent the disease. (2) Despite the effective preventive and control strategies and national policies put after that, India hasn't achieved elimination of rabies. Different policy guidelines are developed for rabies prevention across various countries with no uniformity regarding the measures taken.

Aims & Objectives

This review aims to review the policy guidelines for rabies prevention across different countries as well as India and assess the gaps that need to be filled to achieve elimination in our country.

Material & Methods

A search was conducted with the keywords "Rabies," "Rabies Prophylaxis," and "Rabies guidelines" on PubMed and Google Scholar. Twenty-four relevant articles were found, and a collective narrative review was done. The national guidelines of various countries with specific

National programmes related to rabies prevention and management were reviewed. The countries included were Australia, Japan, Canada, Europe, Latin America, South Africa, and Sri Lanka. Various policies and programmes related to rabies prevention and management in India were then reviewed to identify the gaps in the Indian policies, and a comparison of the different strategies employed by the various countries was made to bridge the identified gaps.

National and International, full-text articles and reports stating preventive measures and/or the cost of rabies vaccines and immunoglobulin for rabies were included from all the countries mentioned above from 1988 to 2023. Only articles that were available in English language were included. For India, the review included the national guidelines starting from the introduction of the National Rabies Control Programme from 2012 till 2021.

Results

Methods of Prevention of Rabies followed in various countries:

Most countries followed similar guidelines, such as free vaccination, compulsory dog restriction and dog vaccination and strict surveillance. Few countries had special surveillance programs like the SIRVERA program of Latin America. Rabies stimulus packages providing technical and material support have been provided to some countries for kick-starting the rabies prophylaxis program.(7)(Table 1)

Evolution of rabies prevention and control programme in India and the current scenario: (6-15)

Until the advent of the 11th five-year plan, no specific National Programme related to rabies control and management existed. When the 11th five-year plan was launched (2007-2012), rabies control efforts were first rolled out as a pilot project. This project was launched in 5 cities: Madurai, Bengaluru, Ahmadabad, Pune, and Delhi. It consisted of measures related to controlling animal rabies, generating awareness in the community, manpower training and capacity building, strengthening diagnostic facilities and surveillance system. This strategy was found to be feasible and implementable across the country.

Following the pilot project's success, the Ministry of Health and Family Welfare rolled out the first National Rabies Control Programme in the 12th five-year plan (2012-2017). The program aimed to halve the human rabies deaths by 2017. The programme had human health component rolled out across twenty six states and union territories and animal components initially piloted in Haryana and Chennai. The activities included in the programme consisted of prompt classification of dog bite wounds, post-exposure prophylaxis and pre-exposure prophylaxis to the high-risk groups, which was given very less importance along with awareness generation and capacity building. The provision of free rabies

immunoglobulin for category three wounds was also initiated under this programme.

The veterinary sector also made similar efforts to control animal rabies in the form of "Animal Birth Control Rules 2001" and "Assistance to States for Animal Diseases." The Animal Birth Control Rules 2001 include sterilization of stray dogs to control the dog population. The assistance to states for animal diseases included activities such as vaccinating animals against economically important diseases such as canine rabies.

A national-level survey was conducted in 2005, which concluded that around 12000- 13,000 deaths in humans are caused by rabies in India. No other national-level surveys have been conducted since then. (16) However, a systematic review and meta-analysis conducted in 2021 found an annual burden of 1.3 million DALYs attributed to rabies. (17)

However, gaps persisted; hence, in 2018, the "National Action Plan for dog mediated Rabies Elimination from India by 2030" was conceptualized. It was rolled out in 2021. This programme will follow the one health approach to control dog-mediated rabies in India. One health is a multi-sectoral approach to achieving optimal health by recognizing the interrelationship between animals, humans, and their environment.

What are the gaps in the Indian Policies?

Rabies control activities began in the 11th Five-Year Plan. (4) Very little importance was given to the disease, and the level of awareness regarding pre-exposure and re-exposure prophylaxis in the community was abysmal. Still, significantly less priority is being given to animal vaccinations. There is no National immunization schedule for domestic and stray dogs vaccination. (6). There are limited guidelines related to animal monitoring, restricted mobility, and domestication.

Most cases are seen among the people residing in rural areas belonging to the lower socio-economic class who often lack a) the basic information about rabies, b) diagnostic capacities, and c) pre-exposure prophylaxis and post-exposure prophylaxis. (18–20) There are a few myths and notions that the Semple vaccine is still in use, often leading the bite victims to get treated using alternate medicine. Semple vaccine was a nerve tissue based rabies vaccine which needed multiple administrations over a period of time in the abdominal region which would be painful and also had incidences of adverse effects thus causing vaccine hesitancy.(21)Due to a lack of refresher trainings from time to time among the medical fraternity, a few misclassification of dog bite wounds have led to inadequate treatment. (22)

Even though there are standard diagnostics and management guidelines, there is often a lack of accessibility to these diagnostic facilities. There is a deficit in the supply of vaccines. A study showed about 18.5% stock out at some designated ARV centers. (20)Also, the ID route of immunization needs a longer learning curve;

hence, facilities providing this cost-effective method of vaccination are less or inaccessible to most of the public.(23,24)

The compliance with the IM and ID regimen to complete the vaccine schedule is inadequate. (65.9% (IM) and 85.1%(ID)(19), 60% overall (25), 60%(IM), and 77%(ID)(18)). The most common reasons for non-compliance to the vaccines were the distance of the hospital, forgotten dates, cost of the vaccine, and non-availability. (20,18,19) Volume utilization and wastage were found to be more in the IM regimen, and the ID regimen was found to be more cost-effective. (25,26) Even so, no regimen is considered the regimen of choice. The vaccines aren't freely available at all places, and the cost of Post-exposure prophylaxis estimates up to US\$ 8.6 billion annually. (2) Even with the high death rate, vaccine stockouts exist in many areas of the country. (19,27,28) (Figure 2)

Most commonly, rabies immunoglobulin are unavailable and often associated with high out-of-pocket expenditure. (19,29)

The advent of new monoclonal antibodies for post-exposure rabies prophylaxis is a breakthrough. It is highly effective and is one of the best measures for PEP. However, it hasn't been included in the National Programme for Rabies Elimination by 2030. (30) (Figure 3)

Discussion

Though the rabies control programme in India has evolved since 2012, and many new initiatives have been undertaken, India continues to contribute about one-third of rabies-related deaths globally. (5) Even though the programme exists, various gaps have been identified at the level of policy implementation through this review, and these gaps need to be addressed soon to eliminate rabies in India. According to the gaps, some of the recommendations to achieve rabies elimination lie hereafter.

Way forward to the elimination of Rabies in India:

1. Recommendations for increasing awareness:

Vigorous IEC activities should be implemented with the help of mass media, posters, and local support, including ASHAs. Repeated health education should be done regarding the importance of early initiation and completion of the vaccine regimen. School-going children need to be targeted for providing education and dissemination of information regarding rabies and its prevention.

2. Recommendations for robust disease surveillance:

An effective integrated surveillance system should be implemented to follow up on all dog bite patients in an area, track rabies cases and notify them as early as possible. Follow-up of subjects who have initiated the vaccine schedule should be prompt. It should be made sure that no doses should be missed. An

effective surveillance system should be put in place for the follow-up of those who have initiated vaccination against rabies so that no cases are missed, follow-up loss is minimal, and this system can be digitalized with the help of the health management information system (HMIS) portal. Thus, a surveillance system like SIRVERA in Latin America is the need of the hour.

3. Recommendations for effective pre-exposure and post-exposure prophylaxis:

All animal handlers should be made aware of the need for pre-exposure prophylaxis for rabies, and proper surveillance needs to be done for the vaccination status of animal handlers at the district level. For effective prevention, accessibility and timely availability of the vaccines at a free cost to all bite victims should be ensured. Prompt and timely availability and use of immunoglobulins should be guaranteed. Early identification of dog bite cases and referral for timely vaccination should be made in areas with inadequate supplies.

4. Continue medical education and training among healthcare workers for appropriate classification fo animal bite.

It was found in this review that the Rabies vaccine, when administered intradermally, bears less cost compared to the intramuscular Rabies vaccine. However, administering vaccines by intradermal route requires training. Also, subsequent doses of rabies vaccine need to be administered through the same route as the first vaccine. To ensure that these guidelines are followed, induction and refresher training for the field-level health workers as well as physicians for classification of dog-bite wounds and management, vaccine administration, and adherence to treatment needs to be given.

5. Guidelines for vaccination of stray and domestic dogs

Vaccination of stray dogs, mandatory registration and vaccination of pet dogs, neutering, and population control of stray dogs should be ensured. It is the need of the hour to develop proper vaccination schedules for dogs at the national level.

6. Recommendations for strict and sustained implementation of the national policy:

Even though we have an excellent national programme, we still haven't been able to achieve elimination. Lack of self-sustainability and poor implementation of the programme is the main reason for the failure. Accurate estimation of the monthly stocks, increased vaccine production, and proper allocation of the vaccines to high-risk areas should be done. The implementation strategies related to pre-exposure prophylaxis among high-risk populations should be strengthened. Good intersectoral coordination with the Animal husbandry and

veterinary services department to follow the one-health approach is a must for the sustained implementation of the programme. But all this will not be possible without the capacity building of the human resources and stakeholders involved in the strict implementation of the programme.

7. Forecasting models for vaccine and immunoglobulin requirement should be utilized for effective inventory management and preventing vaccine and Rabies immunoglobulin stock outs.

Conclusion

This review majorly addresses the gaps in implementing the programme across various horizons. It highlights the need for One Health Approach and inter-sectoral coordination to eliminate rabies. Moreover, it can be stated that there is scope for implementation research in this area and proper evaluation of the programme at frequent intervals to ensure it is implemented uniformly across the country in order to achieve the goal set by National Action Plan for Dog-mediated Rabies elimination from India by 2030

Recommendation

Rabies being one of the most fatal diseases, the control programme must be implemented at all levels of the health system with uniformity across the country. To eliminate dog-mediated rabies from India by 2030, a proper surveillance system needs to be established, and programme evaluation needs to be done from time to time to address the gaps and refresher training workshops need to be offered to healthcare workers to ensure proper management of animal-bite cases. Also, the supply chain of rabies vaccines and immunoglobulin needs to be streamlined to ensure affordable rabies vaccines at health facilities. Additionally, importance should be given on pre-exposure prophylaxis against rabies for animal handlers.

Limitation of the study

This being a narrative review, its limitation is that the effectiveness of the various preventive measures undertaken in various countries could not be assessed quantitatively.

Relevance of the study

This study teaches us the lessons learnt from the initiatives taken in countries which have successfully eliminated dog-mediated rabies and also helps us to innovate and implement similar systems in India by addressing gaps in the existing system.

Authors Contribution

All the authors were involved in planning, literature search for the review, preparation of manuscripts and it's proof-reading.

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Tables

TABLE 1 GLOBAL EFFORTS UNDERTAKEN FOR THE ELIMINATION OF RABIES

SN	Country	Methods undertaken	Status of the country
1.	Australia	<ul style="list-style-type: none"> • Strict pre-exposure prophylaxis of high-risk individuals. • Immediate reporting of suspected cases to the local public health unit. • Careful and appropriate handling of bats. • Continuation of rabies prophylaxis for those who have initiated PEP overseas (3) 	Eliminated
2.	Japan	<ul style="list-style-type: none"> • Restricted mobility of all dogs • Capturing of stray dogs followed by close monitoring • Compulsory vaccination of all dogs. (8) • Post-exposure prophylaxis using six dose regimen of subcutaneously injected vaccine (9) 	Eliminated
3.	Canada	<ul style="list-style-type: none"> • Wildlife control and vaccination of the domestic animals • Elimination of strays • Post-exposure prophylaxis to human victims using IM regimen. (10,11) 	Eliminated
4.	Europe	<ul style="list-style-type: none"> • Dog vaccination using oral rabies vaccines • Wildlife control (12) 	Eliminated from Western Europe
5.	South Africa	<ul style="list-style-type: none"> • Dog vaccination banks • Free PEP • Rabies stimulus packages are tool-kits to kick start the rabies elimination program (13)(7) 	Elimination of Human Rabies in KwaZulu-Natal
6.	Latin America	<ul style="list-style-type: none"> • Regional Surveillance System (SIRVERA) • Mass dog vaccinations • PEP provisions (IM/ID)(14) • Health education (13) 	>97% case reduction
7.	Sri Lanka	<ul style="list-style-type: none"> • Notification of human and animal rabies cases nationwide • Mass dog vaccination and sterilization camps • Free PEP to bite victims (13) 	>85% reduction in cases

Figures

FIGURE 1 HUMAN DEATH RATES DUE TO RABIES PER 100,000 POPULATIONS. (4)

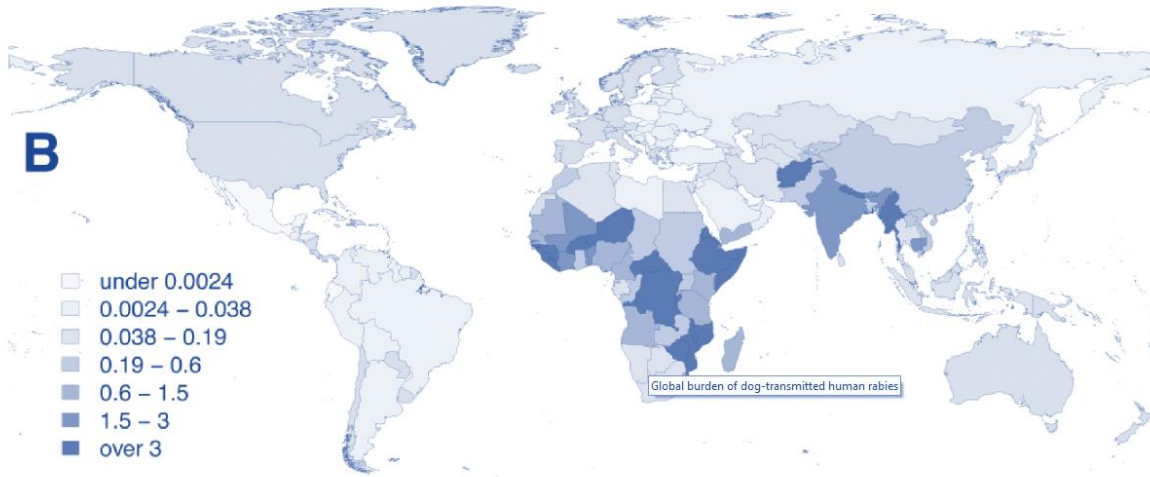


FIGURE 2 VOLUME UTILIZATION, WASTAGE, AND COST OF THE VACCINE (25)

Time and route	Visit of person immunized (A)	Volume (ml) required for i.d. route (B=A×0.2)	Volume (ml) used (C)	Volume (ml) utilized/ person/visit (D=C/A)	Calculated wastage factor* (C/B)	Cost of vaccine/victim/ visit in INR† (D×300)
2013 i.d. route	14,750	2950	3140	0.213	1.065	63.9
2014 i.d. route	17,066	3413.2	3586	0.210	1.050	63.0
2014 intramuscular route	1631	Not calculated	1631	1.000	Not applicable	300

*Wastage factor calculation = volume used/volume required, †Considering 300 INR/1 ml vial of ARV. ARV = Antirabies vaccine, INR = International Normalized Ratio, .d. = Intradermal

FIGURE 3 COST OF RABIES IMMUNOGLOBULIN (29)

Equine rabies Immunoglobulin	0.133/kg	400	Maximum 800	210	83920
Human rabies Immunoglobulin	0.133/kg	2500-6400	Maximum 6400	3	1,06,294
Total cost incurred for post exposure prophylaxis for 1 week = Rs 2,73,614 i.e. \$ 4539.81					