

## Current Situation of Rabies Prevention and Control in Developing Countries: Ethiopia Perspective

Abebe M Aga\*, Birhanu Hurisa and Kelbessa Urga

Vaccine and Diagnostics Production, Ethiopian Public Health Institute, Ethiopia

\*Corresponding author: Abebe M Aga, Vaccine and Diagnostics Production, Ethiopian Public Health Institute, Ethiopia, Tel: +251112134032; E-mail: [abebeaga.or@gmail.com](mailto:abebeaga.or@gmail.com)

Received date: November 06, 2015, Accepted date: February 15, 2016, Published date: February 22, 2016,

Copyright: © 2016 Aga MA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### Abstract

Rabies is a neglected zoonotic disease which kills up to 60,000 people a year, most of them in Africa and Asia. In the majority of developing countries, the number of patients receiving post exposure prophylaxis has steadily increased over time, particularly in urban areas due to dog related rabies. Studies conducted in sub-Saharan Africa show that most of the rabies cases in animals and humans are caused by canine rabies virus, mostly transmitted by domestic dogs and thus comprehensive and sustained dog vaccination is sufficient intervention in reduction and eventual elimination of human rabies in the region. In many developing countries, progress in preventing human rabies through control of the disease in the dog reservoir were slow due to technical, intersectoral, organizational and financial barriers. For developing countries like Ethiopia, strategy should be developed to prevent and control the disease. Sustainable resources for effective dog vaccination are likely to be available through the development of intersectoral financing schemes involving both medical and veterinary sectors. Prevention of animal rabies through dog vaccination, better public awareness, improved access to cost-effective and high-quality human rabies vaccines, and improved local capacity in rabies surveillance and diagnostics are essential for the elimination of human rabies. Generally, elimination of canine rabies is epidemiologically and practically feasible through mass vaccination of domestic dogs which is cost-effective approach to the prevention and elimination of human rabies deaths. The purpose of this paper is to show the burden of the disease and to give direction for effective prevention and control following developed countries experience.

**Keywords:** Awareness; Elimination; Prevention and control; Vaccination campaign; Rabies; Surveillance

### Introduction

Rabies is viral disease that affects warm blooded mammals. The virus shades in the saliva of clinically ill animals and is transmitted through a bite. Once clinical symptoms appear, it is almost 100% fatal. More than 95% of human rabies cases are due to dog bites and the rest associated with cat, fox and other carnivores. The disease particularly affects developing countries in Asia and Africa. The disease is vaccine preventable and can be controlled through vaccination of exposed humans and source animals, mostly dogs [1].

It has been more than 100 years since the first vaccine was developed for pre-exposure vaccination and post-exposure prophylaxis, yet new patterns and trends of rabies infection present a major challenge. The significance of the disease is evident from the continued existence of traditional specialists in rabies treatment within the community [2]. Deaths due to rabies are responsible for 1.74 million disability associated life years (DALYs) lost each year with 0.04 million DALYs are lost through morbidity and mortality following side-effects of unsafe nerve-tissue vaccines [3]. Accordingly, public awareness, health education, dog vaccination and the availability and accessibility of high quality Post-exposure prophylaxis (PEP) are key for rabies prevention and control.

Modern rabies vaccines produced on cell cultures or embryonated eggs are both safe and efficacious. At present, most of Asian countries have moved towards modern rabies vaccine usage, either through

imports or local production. In Thailand, discontinuation of sheep brain vaccine (Semple vaccine) production in 1989 and of suckling mouse brain (Fuenzalida) vaccine in 1993, and importation of increasing quantities of modern vaccines have played a major role in the drastic reduction in the number of cases of human rabies in the country [4]. Due to the high cost of modern cell culture rabies vaccines, outdated nerve tissue origin rabies vaccines are still administered to most socioeconomically disadvantaged people who are at an increased risk of exposure. Additionally, most modern cell culture rabies vaccines are imported into developing countries and because many countries impose an extra importation tax to them, the cost of treatment is increased [5].

It is clear that human rabies can be successfully prevented through the use of modern highly potent cell culture rabies vaccines. These vaccines were developed over two decades ago and yet nerve tissue based vaccines are still used by a million peoples every year in Asia and Africa, and most human rabies deaths occur as a result of the lack of post exposure treatment or due to the lack of safe and effective vaccines. Post exposure treatment with highly purified cell culture vaccines has been dramatically reducing the burden of the disease through the use of intradermal regimens, proven to be highly efficacious. Although some countries have replaced nerve tissue based vaccines with intradermal regimens, more lives could be saved if the use of these vaccines expanded. The cost of upgrading nerve tissue based vaccine production facilities in order to produce cell culture rabies vaccines is beyond the financial budget of most developing countries. Therefore, banning the use of nerve tissue based vaccines alone will not solve the problem as this would remove access to the

post-exposure treatment (PET) available to many patients unable to afford modern cell culture vaccines. Due to this, nerve tissue based rabies vaccines are still the stronghold of post exposure treatment for low-income countries in Asia and Africa [2].

In Ethiopia alone, more than 32,000 doses of nerve tissue based (Fermi type) vaccine is distributed each year (data from recent documentation). A more realistic approach will be to phase out the use of nerve tissue based vaccines through technology transfer and gradual replacement within a given period of time with safe and effective modern cell culture vaccines. To increase modern rabies biologicals availability, strong consideration should be given to commercial vaccine production technology transfers, joint regional purchases, and tariff reduction for the direct acquisition. In parallel to this, existing old vaccines should be discontinued and as they are gradually phased out. Strategies for the control and elimination of rabies should be facilitated through the purchase of commercial products on the world market or via local production of modern cell culture vaccines. This will facilitate the effort of rabies prevention and control in combination with similar activities to implement the strategy.

The lack of effective health education programmes results in a low degree of awareness of the disease burden and the methods necessary to prevent and control rabies. Low awareness also causes poor community participation in local rabies control programmes. All effective public education programmes must consider cultural, religious, and political factors. One of the most important points in rabies prevention is the level of awareness in both the medical profession and the general public. Programmes that use imaginative information highways like schools, religious and other local organizations and meetings have had major impact in increasing awareness on the disease. However, more emphasis is needed on the development and implementation of national guidelines for rabies prevention and control. These types of documents can be secured based on bench marking experiences from countries with similar guidelines in place as well as from WHO general guidelines. Other methods to increase rabies awareness should include specific rabies information given to medical professionals, utilization of currently existing intersectoral opportunities, and public media spotlights.

In developing countries, rabies control programmes are a low priority by governments compared to economic development. Despite its public health and economic impact, there is no clear responsibility and budgetary allocations for rabies programmes in either Ministries of Health or Ministry of Agriculture. Additionally, the costs of rabies elimination campaigns fall short of similar cost/benefit programmes when compared to food production and human health programmes like TB, malaria, HIV/AIDS and EPI [6]. Therefore, existing political and economic situations in developing countries where rabies poses a significant public health problem usually interfere negatively with rabies control programmes. For this, political support must come from within individual countries accompanied by continuing support and pressure from WHO. However, the most important influence for political change will have to originate from private citizens, medical professionals, and agricultural and health ministers within each country which encourage the success of the program.

### **Strategies for Rabies Control and Elimination**

There is lack of information on rabies treatment and prevention both in humans and animals. People have clear understanding on the danger of the disease but believe to cure with different traditional and

religious treatment rather than seeking effective post exposure prophylaxis. Most people use wide variety of traditional treatment in cases of bite by animals (mostly dogs) believed to be rabid. The significance of the disease is evident from the continued existence of traditional specialists in rabies treatment within the community [3]. This has significant impact on the effort of rabies prevention and control, and need to work on awareness creation about the danger of the disease unless effective PEP given following exposure. Strategies for the prevention of human rabies are aimed at protecting those at highest risk of exposure, post exposure treatment and supportive management for the clinically ill.

As dog is the main source of rabies in humans, principal method of dog rabies control is mass vaccination, and has been successfully used to eliminate human dog-mediated rabies in countries like Malaysia, Philippines, Tunisia, Western Europe and North America among others. According to the World Organization for Animal Health (OIE) and the WHO recommendations, the critical percentage of dogs to be vaccinated to prevent rabies cases should be at least 70% [4]. This target coverage has been supported by empirical evidence and theoretical observations worldwide investigating the relationship between vaccination coverage and reduction in rabies incidence. A study conducted in Tunisia indicates 70% dog vaccination coverage through parenteral vaccination in most regions of the country resulting in elimination of the disease [7]. In areas with high dog turn-over, where large number of births and deaths like many regions in Africa and Asia, high coverage is especially important to maintain the population level immunity. Evidence from work in the Serengeti ecosystem in Tanzania suggests that domestic dogs are the only population essential for rabies maintenance [4]. From experiences in Western Europe and North America, rabies elimination in dogs has been successful despite the presence of wildlife hosts capable of transmission.

Continuous education of health professionals on proper dog bite wound cleaning and management, and administration of PEP is necessary to provide effective prevention of human rabies. On the other hand, effective rabies surveillance in humans and animals enhances early detection and reporting of cases, vital for initiating timely responses and enabling informed decisions about when and where to intensify rabies control efforts. Once rabies interventions are implemented, surveillance is essential in generating data to monitor progress or impact of the control efforts, which is essential for their sustainable implementation. As control efforts progress towards rabies elimination, surveillance becomes even more critical in ascertaining rabies free status. Outbreak response should be coordinated involving both human and animal health personnel towards implementation of the program.

### **Rabies Vaccine Development**

Rabies infection is always fatal unless prompt post exposure treatment is administered before symptoms begin. Until 1885, when Louis Pasteur and Emile Roux developed a vaccine, all human cases of rabies were fatal as the case fatality rate almost 100%. In 1885, Louis Pasteur experimented with rabies vaccination by using the term virus (Latin word for 'poison') to describe the agent. At the time, Pasteur did not discriminate between viruses and other infectious agents but originated the terms virus and vaccination (in honor of Jenner, British scientist) and developed the scientific basis for experimental approach to vaccination and well known historical achievement in the field of vaccination [8]. Through adaptation of street (wild-type) rabies virus

to laboratory animals, he was able to change virus properties which can change virulence and incubation period over several passages. After adaptation to laboratory animals and cell lines, the virus was known to lose its virulence other than intracerebral route of inoculation and increase expression of G-protein to the host cells resulting in high immune responses [9]. During that time, desiccated spinal cords from rabies virus infected rabbits became the first rabies vaccine, which were supposedly safe, although now it is known that the fixed viruses from which these vaccines were derived were not pathogenic but could actually cause the disease. Till the 1980s, Nerve tissue-derived vaccine (NTV) was manufactured using the fixed RABV Beijing strain 3aG, which was isolated in 1931 [8]. The development of safe and effective rabies virus vaccines applied in attractive baits resulted in the first field trials in Switzerland in 1978. Thereafter, technical improvements occurred in vaccine quality and production, including the design of recombinant viruses, as well as in the ease of mass distribution of millions of edible baits over large geographical areas [10].

The heteroploid Vero cell line was introduced in 1982 to the production of inactivated rabies vaccine; which retained all the advantages of the human diploid cell system, while offering the possibility of the large-scale industrial production of Purified vero rabies vaccine (PVRV). In 1988, cell culture rabies vaccines for human use, highly immunogenic and well tolerated, were used for pre-exposure immunization as well as for post-exposure treatment. In 1992, WHO recommended a new inactivated rabies vaccine grown on Vero cells, PVRV with the vaccine cultivated on Human diploid cells vaccine (HDCV), for both pre and post-exposure prophylaxis [11]. In 2001, WHO issued a resolution for the complete replacement of NTVs by 2006 with cell culture rabies vaccines [8]. Similarly, Oral rabies vaccine (ORV) was developed to control rabies in terrestrial reservoir species by distributing vaccine in baits. As an example, the US-licensed ORV consists of a rabies virus glycoprotein gene inserted into the thymidine kinase gene of an attenuated strain of the Copenhagen vaccinia virus [12].

### Countries experience in rabies control and elimination

Long before the recognition of bat and other wildlife rabies and the availability of modern vaccines, rabies in Japan was successfully controlled through mass vaccination of dogs [8]. Large-scale oral vaccination campaigns were first used to fight rabies epidemic successfully in foxes during 1980s [13]. Control of rabies in developing countries can be very successful based on appropriate planning, health education, 70% vaccine coverage for dog populations, and epidemiological surveillance [14]. According to one health definition established by the paraprofessional One Health Task Force, the confluence of environmental, animal, and human interactions can be used as opportunity by working together to fight such diseases like rabies. The paraprofessional health team recognizes that there is no more important disease to begin educating and developing our efforts than rabies.

In America, progressive elimination of rabies in wildlife has been a general strategy and the common campaign tactics are Trap vaccinate release (TVR), Point infection control (PIC), and ORV [15]. These tactics have proven crucial to elimination of raccoon rabies in Canada and to maintain ORV zones for preventing the spread of raccoon rabies [15]. The first successful example of a mass vaccination program in a dog population occurred in the city of Memphis and Shelby County, Tennessee in the United States in 1948 which reduced both animals and humans cases to zero [16].

In 1990, there were 16,464 reported cases of canine rabies in Latin America and reduced to 2,608 in 1998. Human rabies cases were reduced from 252 to 74. Most of the rabies case reduction was in Buenos Aires, Lima, and Sao Paulo, all of which completely eliminated rabies by vaccinating from 60 to 80% of their estimated dog populations during a series of three-month campaigns [14].

In Canada, before rabies control programs were implemented, red foxes accounted for 45% of all rabies cases in Ontario [17]. During 1989-1995, oral rabies vaccine was used in Ontario to progressively eliminate arctic fox-variant rabies that has been transmitted to another species of red foxes and spread southward [15]. To eliminate raccoon variant rabies from the Ontario, a point infection control tactic, which integrated population reduction trap-vaccinated-release, and oral rabies vaccine was implemented resulting elimination of the variant from Ontario [15]. Additionally, to prevent raccoon rabies from reemerging in southern Ontario, oral rabies vaccine baiting for raccoon-variant rabies continues in northern New York [17]. In Mexico, the national rabies control program using mass parenteral vaccination of dogs started in 1990. As a result of the mass dog vaccination campaigns in Mexico, human rabies cases due to dog-mediated rabies decreased from 60 in 1990 to 0 in 2000 and the number of rabies cases in dogs decreased from 3,049 in 1990 to 70 cases in 2007 [18].

In Europe, the elimination of rabies was demonstrated following oral vaccination of foxes in Western, where red foxes are the reservoir host [14]. There have been many changes and accomplishments in rabies control and prevention since the first International Conference on Rabies in Europe [19]. However, empirical evidence indicates that, in regions with less than 70% immunization coverage, rabies has still been eliminated [20]. The immediate challenge for rabies control is to stockpile enough vaccines for mass dog vaccination campaigns [8]. In Europe, primary efforts should be focused on the implementation of effective passive and active surveillance systems for the rabies related virus, EBLVs in bats [20]. Few countries in the Central and Eastern Europe are rabies free, and several others are close to being rabies-free [20]. In Poland, after 13 years of oral rabies vaccination, rabies incidence decreased sharply, from 3,084 cases in 1992 to 82 in 2006 as a result of oral rabies vaccine which indicate 97% decrease in the number of rabies cases [21]. The last endemic case of rabies in Switzerland was diagnosed in 1996 after an adaptation of the vaccination strategy [22]. Twenty people died of rabies in France between 1970 and 2003, 80% on returning from Africa and the last occurrence of animal rabies in French was reported in 1998 as a result of comprehensive prevention and control strategy [23]. In Germany, oral rabies vaccine of foxes using modified-live-virus vaccines offered a new method of rabies control in wildlife [24]. With the enlargement of vaccination areas in West Germany reaching a maximum size of about 215 000 km<sup>2</sup> in 1995, the policy of using oral rabies vaccine became increasingly successful and rabies incidence decreased drastically in subsequent years. As a result of oral rabies vaccination, the rabies incidence drastically decreased during the past 20 years from 10,484 rabies cases in 1983 to 56 in 1999; the lowest number of rabies cases ever reported in Germany at the time [24].

The human rabies burden is highest in Asia, with majority of the deaths occurring in India [25]. This situation reflects the relative lack of systematic control and prevention initiatives, including surveillance and response systems. In Asia, the only country with a steady decline in rabies case is Thailand, where the number of cases has decreased from around 200 to 20 cases per year [26]. In addition, the most

dramatic changes were observed in China with human rabies cases declined from around 5,000 cases per year in the 1980s to 160 in the mid-1990s. During the past 20 years, 15,000 persons received rabies post exposure prophylaxis after dog bites, but no rabies occurred. However, these trends have since been reversed, a steady increase has been reported over the past 10 years with more than 3,200 cases reported in 2006 [27]. Although there are many factors that contribute to the epidemic or endemic nature of rabies in these countries, the single most important factor is the failure to immunize domestic dogs, which transmit rabies to humans [28]. Due to this reemerging rabies in China, the country has set strict pet population control policies [8]. The most recent attempt to quantify the burden of human rabies in India concluded that its incidence was 2 per 100,000 populations, giving an annual total of more than 20,000 deaths [29]. The key priorities in the fight against rabies are enhanced laboratory capabilities, improved access to modern vaccines, enforcement of responsible dog ownership, and enhanced public education and awareness of the disease.

In Japan, no rabies case has been reported for about 50 years. Since 1957, Japan has successfully eradicated human and animal rabies through registration, confinement and compulsory vaccination of family dogs, and elimination of stray dogs [30]. After eradication of rabies from the country, the last recorded case of imported rabies was in 2006 where two cases of human rabies imported into Japan from the Philippines next to the other identified during 1970 when a college student died in Tokyo after a trip to Nepal where he had been bitten by a stray dog.

The true impact of rabies in Africa remains undefined. The virus can be detected sporadically, but canine rabies poses the greatest threat to humans. In rural Africa, households with livestock own significantly more dogs than households without livestock, probably because the dogs are mainly kept for livestock safety. Mass vaccination of domestic dogs has significant result, even in areas such as the Serengeti ecosystem, which comprise a wide diversity of wildlife species indicating that when sufficient domestic dogs vaccinated, rabies also declines in wildlife, and human exposures to the rabies virus are significantly reduced [14,31]. But, dog vaccination is difficult in many African countries because of high dog turnover rates, shortages of funding and workforce, and different competing priorities of public health problems. In South Africa, central-point dog vaccination campaigns in villages in the affected area were intensified after identification of the increased numbers of rabies cases in domestic dogs. A community awareness program related to the hazards of dog bites and the importance of timely visits to the clinic for rabies post exposure prophylaxis and healthcare workers were educated regarding appropriate management of dog bites. In addition, vaccine and immunoglobulin availability was improved by increasing the number of facilities providing the vaccine and by ensuring that patients did not have to pay for treatment with doses of vaccines increased from 3,000 in 2004 to 6,000 in 2005 and 56,000 in 2006 [32]. As a result, the number of human rabies cases in Limpopo Province of South Africa decreased after May 2006 and no further human cases were occurred after June, 2007 [32]. In Africa, high levels of population immunity are rarely achieved due to a number of reasons [33]. Recent initiatives have begun to improve the situation in many areas with the Southern and East African Rabies Group (SEARG), the African Rabies Expert Bureau (AfroREB) and the Rabies in West Africa (RIWA) group being networks dedicated to the fight against rabies.

Even though cats, foxes and other warm blooded animals contribute to rabies transmission in Nigeria, dog bites known to be the main mode of transmission of the disease to man and remains a serious public health hazard. Therefore, cost-effective approach to rabies control was aimed at elimination of stray dogs in addition to single mass immunization in the shortest possible time with at least 80% of the entire dog population [5].

### **The effort of rabies control in Ethiopia**

A number of obstacles prevent a coordinated approach to the global elimination of canine rabies; including a lack of awareness and education of the public health and veterinary sectors, the absence of diagnostic facilities, inadequate surveillance and reporting systems, limited access to modern vaccines and failures of responsible dog ownership [34]. But, still elimination of canine rabies from Africa and Asia is epidemiologically and practically feasible, provided mass vaccination and enforcement of responsible dog ownership [31]. The lack of effective control of canine rabies in developing countries is often attributed to low prioritization, epidemiological and operational constraints and insufficient financial resources.

In Ethiopia, retrospective data registered between 2001 and 2009 at one center (EPHI) showed that fatal human cases were 386 with annual range of 35 to 58 [35]. Study done at North Gonder of Ethiopia indicated an annual estimated rabies incidence of 2.33 cases per 100,000 humans; 412.83 cases per 100,000 dogs; 19.89 cases per 100,000 cattle; 67.68 cases per 100,000 equines, and 14.45 cases per 100,000 goats [36]. Dog bite was the source of infection for almost all fatal rabies cases throughout the country.

There are a number of challenges in the prevention and control of rabies in Ethiopia. One of these is inadequate laboratory capacity and lack of diagnosis centers at different sites for effective surveillance and response. Rabies diagnosis and management is largely dependent on diagnosis of rabid animals at one center, at Ethiopian Public Health Institute. Thus, there is only one laboratory that has the capacity to confirm rabies in humans or animals resulting in poor management of rabies cases. Dog bites are used as a proxy for suspect rabies cases in humans for rabies surveillance and response system. However, dog bites are under-reported in health facilities resulting in missed cases and misclassification of deaths due to rabies. There is also inadequate sharing of surveillance data between human and animal health care sectors at both local and national levels, resulting in loss of opportunities to prevent human rabies, early detection and timely response to rabies outbreak. The national surveillance data is unreliable, meaning that the true burden of the disease in the country or high risk areas remains undefined; making it difficult to target prevention and control measures. There is little coordination and collaboration between the human and animal health sectors and other agencies responsible for rabies control.

There is low awareness among the public, human and animal health workers have no adequate knowledge on management of dog bite wounds, and pre- and post-exposure prophylaxis. Studies showed that, high canine rabies burden and lack of sufficient awareness about the disease and high reliance on traditional treatment that interfere with timely post exposure management account for a major human cases [36]. Most patients who die from rabies are either do not report the case immediately or do not receive timely and appropriate post-exposure treatment after exposure to the virus. In particular, many dog bites in children are not reported and may go completely unrecognized or be discovered by both parents and health care providers late after

disease progression. The other is the challenge of traditionally used medication like root and leaf of medicinal plants, and other religious approaches to treat the case as evil. On the other hand, knowledge of the responsible dog ownership and dog population management among the public is low and there is little understanding among the public of dog vaccination and the value of timely post exposure treatment following animal bite. There is lack of awareness among policy makers on the importance and burden of rabies and the cost-effectiveness of rabies control through dog vaccination. Data on economic benefits of rabies control, dog demographics and ecology, and alternative dog population management methods is lacking.

The Fermi type adult sheep brain nervous tissue vaccine produced at the Ethiopian Public Health Institute (EPHI) since 1940's. The country is still producing and using this long time WHO banned Fermi type anti-rabies vaccine for post exposure treatment. Regardless of its quality, there is limited supply of rabies vaccine and also lack of adequate, safe and effective PET and PEP biologics in public health. Whereas high quality vaccine may be available in some private facilities, the cost is prohibitive and cannot be afforded by public at large. The possibility of producing rabies vaccines locally have been explored during the last five years and currently produced from Pasteur Virus (PV) and Evinyl Rokitnki Abelseth (ERA) rabies virus strains, and pre-clinical trial completed [37].

The current rabies control and prevention activities, particularly dog vaccination, by the concerned body are not in place. According to Rabies Control Strategy prepared by the Ministry of Agriculture and Rural Development in 2010, only vaccination of dogs and cats during outbreak was indicated and no further prevention strategy was mentioned for sustainable prevention and control of the disease. Thus, rabies control activities are not adequate or even not in place resulting in little impact on rabies prevention and control activity. In addition, the country does not have guidelines on rabies control that capture the requisite integrated approach that involves all the stakeholders like Ministry of Agriculture and Ministry of Health. This inadequacy has resulted in uncoordinated and largely ineffective actions.

### **Opportunity for rabies elimination in Ethiopia**

A number of factors have come together to make this an opportunity time to undertake rabies control and elimination strategy. These factors include the establishment of a One Health Office in the country and increased interest in rabies elimination by partners. A pilot project was designed by the joint efforts of the University of Gondar, Ethiopian Public Health Institute, Ohio State University, and the US Centers for Disease Control and Prevention; with the aim to control canine rabies in a northern Gonder of Ethiopia which can be used for further scale up. The other opportunity is the ability for local production of safe and effective modern rabies vaccine for both animal and humans. Modern cell culture anti-rabies vaccine production for animal use has been transferred to National Veterinary Institute from the Ethiopian Public Health Institute for mass production. For human purpose, the effort to replace Fermi type with modern cell culture vaccine is in progress at EPHI and currently preclinical trials were finalized. In the coming two years, it is assumed to replace Fermi vaccine which is expected to contribute to the control and elimination of the disease in Ethiopia.

### **Conclusion**

Elimination of human rabies is dependent on the elimination of dog rabies. Although canine rabies has been eliminated from developed countries through registration and vaccination of dogs and responsible dog ownership, infected dogs remain the primary source of human and livestock exposures in Asia, Africa and much of South American countries [38]. Availability of safe and effective vaccine play a major role in fight against the disease, relying on local vaccine production for adequate and timely supply at affordable price. Information, Education and Communication activities for rabies control are insufficient in many developing countries like Ethiopia. Inadequate efforts made to educate the public about the epidemiological features of rabies and simple precautions that can protect individual and bring about a reduction in the overall incidence of rabies [6]. Intersectoral and regional coordination among various agencies like Ministry of Health, Ministry of Agriculture, OIE, WHO and other stakeholders is of key importance. On the other hand, continuous education of medical and health professionals on PEP and passive immunization with RIG in cases of third-degree bites is necessary to provide quality medical services to the bite victims [39]. Surveillance strategies for rabies and other rabies-related viruses in Africa and Asia must be improved to better understand the epidemiology of this virus, roles of vaccines and its implication for global public health. In countries like Ethiopia where rabies is one of the public health problems, control and prevention of the disease should be of priority issue. For this, current local production of modern rabies vaccine for both human and animals should be taken as an opportunity and supported by other intersectoral groups working towards rabies prevention and control. Budget allocation by the government should be improved and continuously strengthening the coordination and collaboration among stakeholders involved in rabies prevention and control is mandatory. To control other lyssaviruses, future vaccination strategies should be made because current evidences are insufficient that current rabies vaccines provide protection against other rabies-related viruses as G-protein similarity less than 64% for rabies related viruses like Mekola and Legos bat [40]. Generally, mass vaccination of dogs, proper post exposure management, appropriate surveillance system, and increasing the awareness of the community about the disease needs special attention for control and elimination of the disease.

### **References**

1. Zinsstag J, Schelling E, Roth F, Bonfoh B, de Savigny D, et al. (2007) Human benefits of animal interventions for zoonosis control. *Emerg Infect Dis* 13: 527-531.
2. Pankhurst R (1970) The history and traditional treatment of rabies in Ethiopia. *Med Hist* 14: 378-389.
3. Knobel DL, Cleaveland S, Coleman PG, Fèvre EM, Meltzer MI, et al. (2005) Re-evaluating the burden of rabies in Africa and Asia. *Bull World Health Organ* 83: 360-368.
4. World Health Organization (2005) WHO Expert Consultation on Rabies, 2004. WHO technical report series 931: 111-121.
5. Awoyomi OJ, Adeyemi IG, Awoyomi FS (2007) Socioeconomic Factors Associated With Non-Vaccination of Dogs against Rabies in Ibadan, Nigeria. *Nig Vet J* 28: 59-63.
6. World Health Organization (2012) Strategic Framework for Elimination of Human Rabies Transmitted by Dogs in the South-East Asia Region. WHO Library.
7. Jibat T, Hogeveen H2, Mourits MC2 (2015) Review on dog rabies vaccination coverage in Africa: a question of dog accessibility or cost recovery? *PLoS Negl Trop Dis* 9: e0003447.

8. Wu X, Franka R, Svoboda P, Pohl J, Rupprecht CE (2009) Development of combined vaccines for rabies and immunocontraception. *Vaccine* 27: 7202-7209.
9. Aga AM, Hurisa B, Tesfaye T, Lemma H, Nigus D, et al. (2014) Adaptation of Local Rabies Virus Isolates to High Growth Titer and Determination of Pathogenicity to Develop Canine Vaccine in Ethiopia. *J Vaccines Vaccin* 5: 245.
10. Rupprecht CE, Hanlon CA, Slate D (2004) Oral vaccination of wildlife against rabies: opportunities and challenges in prevention and control. *Dev Biol (Basel)* 119: 173-184.
11. Nagarajan T, Rupprecht CE, Dessain SK, Rangarajan PN, Thiagarajan D, et al. (2008) Human monoclonal antibody and vaccine approaches to prevent human rabies. *Curr Top Microbiol Immunol* 317: 67-101.
12. Hanlon CA, Niezgodá M, Shankar V, Niu HS, Koprowski H, et al. (1997) A recombinant vaccinia-rabies virus in the immunocompromised host: oral innocuity, progressive parenteral infection, and therapeutics. *Vaccine* 15: 140-148.
13. Eisinger D, Thulke H (2008) Spatial pattern formation facilitates eradication of infectious diseases. *J Appl Ecol* 45: 415-423.
14. Reisner AE, Taheripour F (2007) Reaction of the local public to large-scale swine facilities. *J Anim Sci* 85: 1587-1595.
15. Sterner RT, Meltzer MI, Shwiff SA, Slate D (2009) Tactics and economics of wildlife oral rabies vaccination, Canada and the United States. *Emerg Infect Dis* 15: 1176-1184.
16. Tierkel ES, Graves LM, Tuggle HG, Wadley SL (1950) Effective Control of an Outbreak of Rabies in Memphis and Shelby County, Tennessee. *Am J Public Health Nations Health* 40: 1084-1088.
17. Rosatte R, MacDonald E, Sobey K, Donovan D, Bruce L, et al. (2007) The elimination of raccoon rabies from Wolfe Island, Ontario: animal density and movements. *J Wildl Dis* 43: 242-250.
18. Lucas CH, Pino FV, Baer G, Morales PK, Cedillo VG, et al. (2008) Rabies control in Mexico. *Dev Biol (Basel)* 131: 167-175.
19. Meslin FX, Briggs DJ (2013) Eliminating canine rabies, the principal source of human infection: what will it take? *Antiviral Res* 98: 291-296.
20. van der Poel WH, Lina PH, Kramps JA (2006) Public health awareness of emerging zoonotic viruses of bats: a European perspective. *Vector Borne Zoonotic Dis* 6: 315-324.
21. Smreczak M, Trebas P, Orłowska A, mudziński JF (2008) Rabies surveillance in Poland (1992-2006). *Dev Biol (Basel)* 131: 249-256.
22. Zaroni RG, Kappeler A, Müller UM, Müller C, Wandeler AI, et al. (2000) Rabies-free status of Switzerland following 30 years of rabies in foxes. *Schweiz Arch Tierheilkd* 142: 423-429.
23. Peigue-Lafeuille H, Bourhy H, Abiteboul D, Astoul J, Cliquet F, et al. (2004) Human rabies in France in 2004: update and management. *Med Mal Infect* 34: 551-560.
24. Müller T, Selhorst T, Pötzsch C (2005) Fox rabies in Germany - an update. *Euro Surveill* 10: 229-231.
25. Burki T (2008) The global fight against rabies. *Lancet* 372: 1135-1136.
26. Banyard AC, Horton DL, Freuling C, Müller T, Fooks AR (2013) Control and prevention of canine rabies: The need for building laboratory-based surveillance capacity. *Antiviral Res* 98: 357-364.
27. Zhang YZ, Xiong CL, Xiao DL, Jiang RJ, Wang ZX, et al. (2005) Human rabies in China. *Emerg Infect Dis* 11: 1983-1984.
28. Fu ZF (2008) The rabies situation in Far East Asia. *Dev Biol (Basel)* 131: 55-61.
29. Sudarshan MK (2007) The changing scenario of rabies in India: are we moving towards its prevention and control? *Indian J Public Health* 51: 145-147.
30. Satoshi I (2007) The Rabies Prevention and the Risk Management in Japan. *J Dis Res* 2: 90-91.
31. Lembo T, Hampson K, Kaare MT, Ernest E, Knobel D, et al. (2010) The feasibility of canine rabies elimination in Africa: dispelling doubts with data. *PLoS Negl Trop Dis* 4: e626.
32. Cohen C, Sartorius B, Sabeta C, Zulu G, Paweska J, et al. (2007) Epidemiology and molecular virus characterization of reemerging rabies, South Africa. *Emerg Infect Dis* 13: 1879-1886.
33. Rupprecht CE, Gibbons RV (2004) Clinical practice. Prophylaxis against rabies. *N Engl J Med* 351: 2626-2635.
34. Zhang J, Jin Z, Sun GQ, Zhou T, Ruan S (2011) Analysis of rabies in China: transmission dynamics and control. *PLoS One* 6: e20891.
35. Asefa D, Abraham A, Mekoro B, Bethlehem NS, Eshetu Y, et al. (2010) The status of rabies in Ethiopia: A retrospective record review. *Ethiop J Health Dev* 24: 127-132.
36. Jemberu WT, Molla W, Almaw G, Alemu S (2013) Incidence of rabies in humans and domestic animals and people's awareness in North Gondar Zone, Ethiopia. *PLoS Negl Trop Dis* 7: e2216.
37. Birhanu H, Abebe M, Bethlehem N, Sisay K, Gezahegn K, et al. (2013) Production of Cell Culture Based Anti-rabies Vaccine in Ethiopia. *Procedia Vaccinology* 7: 2-7.
38. Blanton JD, Dyer J, McBrayer J, Rupprecht CE (2012) Rabies surveillance in the United States during 2011. *J Am Vet Med Assoc* 241: 712-722.
39. FAO (2013) Developing a stepwise approach for rabies prevention and control. Proceedings of the FAO/GARC Workshop, November 2012, Rome, Italy. FAO Animal Production and Health Proceedings, No. 18. Rome, Italy.
40. Aga AM, Mekonnen Y, Hurisa B, Tesfaye T, Lemma H, et al. (2014) In Vivo and In Vitro Cross Neutralization Studies of Local Rabies Virus Isolates with ERA Based Cell Culture Anti-Rabies Vaccine Produced In Ethiopia. *J Vaccines Vaccin* 5: 256.