

International Journal of Multidisciplinary Comprehensive Research

Review on control and prevention of human and animal rabies in Africa with emphasis on Ethiopia: Theory and practices

Bayeta Senbata Wakjira

Animal Health Institute, Sebeta, Ethiopia

* Corresponding Author: **Bayeta Senbata Wakjira**

Article Info

ISSN (online): 2583-5289

Volume: 01

Issue: 05

September-October 2022

Received: 29-10-2022

Accepted: 18-10-2022

Page No: 29-39

Abstract

Rabies is a neglected zoonotic disease which kills many 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.

DOI: <https://doi.org/10.54660/IJMCR.2022.1.5.29-39>

Keywords: Awareness, Elimination, Prevention and control, Vaccination campaign, Rabies, Surveillance

1. Introduction

Rabies is a zoonotic disease caused by RNA viruses in the Family Rhabdoviridae, Genus Lyssavirus (Botvinkin *et al.*, 2003) [19]. The name Rhabdo comes from the Greek and identifies the characteristic bullet or rod-shape of the viruses (Moges, 2015) [47]. It is a disease that affects warm blooded mammals. The domestic dog is the most important vector of human exposure (Cleaveland *et al.*, 2002) [14]. Wild animals serve as a large and mainly uncontrollable reservoir of sylvatic rabies, which is an increasing threat to the human population and to domestic animals in many countries (Moges, 2015) [47]. The World Health Organization (WHO) considers rabies to be a neglected disease and declare it to be primarily a problem in areas troubled with poverty and with a lack of economic resources (WHO, 2013a).

Today, no regions or countries in mainland Africa are known to be free of rabies (WHO, 2012). Rabies infection in humans is still a major public health problem all over the world (APHA, 2008). Rabies kills an estimated 35,000 per year, mostly in Africa, Asia and Latin America (Rupprecht *et al.*, 2007) [67]. With over 55 000 human deaths a year (Nilsson, 2014) and signs of it re-emerging (Depani *et al.*, 2012) [19].

The same to other country poor health and productivity of animals due to disease has considerably become the major stumbling block to the potential of livestock industry in Ethiopia (Nejash, 2016) [54]. Rabies is also a common disease that has been recognized as a public health problem for many centuries in Ethiopia (Moges, 2015) [47]. Canine rabies is a completely preventable disease, and over the last decade, programs based on eliminating the source of the disease from dogs have shown success in reducing the public health burden of canine rabies (Taylor *et al.*, 2015) [71].

Due to a massive coordinated canine vaccination program, confirmed rabies cases in dogs across the continent have decreased from approximately 25,000 in 1980 to less than 300 in 2010, and dog-transmitted human rabies deaths decreased from 350 to less than 10 during the same time period (Taylor *et al.*, 2015) [71]. Elimination of human rabies deaths is achievable by eliminating rabies in dogs through mass dog vaccination campaigns, supported by improved access to PEP (WHO, 2013). Rabies control in the region has traditionally been in the hands of the government veterinary authorities, with, in many cases, limited collaboration or communication with the government health authorities. This centralization of implementation responsibility is unlikely to be sustainable for much longer. Public awareness and an increase of knowledge about rabies disease, first aid measures after dog bites, increased knowledge about dog behavior and how to avoid getting bitten by dogs are suggested methods to prevent rabies in humans (Nilsson, 2014).

1.1. Objectives of the paper

- To review the current information available for prevention and control of rabies.
- To discuss on the recent strategies, which is important to implement efficient control and eradication measures against rabies in African countries and status of rabies in Ethiopia

2. Literature Review

2.1. Etiology

The causative agent of rabies is a member of the Lyssavirus genus of the Rhabdoviridae family of bullet shaped viruses, which have a single-stranded RNA genome (Moges, 2015) [47]. The genus includes the classical rabies virus (genotype 1) and six so-called rabies-related viruses, Lagos bat virus (genotype 2), Mokola virus (genotype 3), Duvenhage virus (genotype 4), European bat lyssaviruses 1 and 2 (genotypes 5 and 6), and the recently discovered Australian bat genotype 7 (Warrell, 2001) [77].

2.2. Pathogenesis

Rabies virus replicates in the bitten muscle (local viral proliferation in non-neural tissue) and gains access (viral attachment) to motor endplates and motor axons to reach the central nervous system (Ugolini, 2011) [75]. Virions are carried in transport vesicles (Klingen *et al.*, 2008) [39] and travel to the central nervous system (CNS) exclusively by fast retrograde transport along motor axons, with no uptake by sensory or sympathetic endings (Hemachudha *et al.*, 2013) [33, 34].

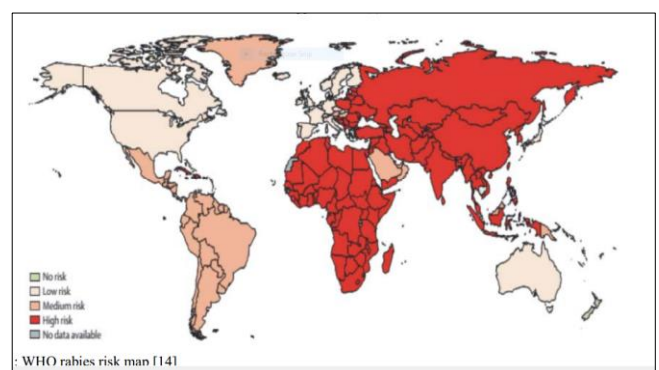
In dogs and cats, the incubation period is 10 days to 6 months; most cases become apparent between 2 weeks and 3 months. In cattle, an incubation period from 25 days to more than 5 months has been reported in vampire bat-transmitted rabies. In humans, the incubation period can be a few days to

several years. Most cases become apparent after 1-3 months (OIE, 2012)

2.3. Epidemiology

2.3.1. Geographic Distribution

In general, it is estimated that 55,000 human deaths are caused by rabies each year, most of which occur in rural areas of Africa and Asia. Rabies is most common in children under 15 years of age (WHO, 2010). With some exceptions (particularly islands), rabies virus is found worldwide. Some countries such as the United Kingdom, Ireland, Sweden, Norway, Iceland, Japan, Australia, New Zealand, and Singapore, most of Malaysia, the Pacific Islands and some Indonesian islands have been free of this virus for many years (OIE, 2008). In Africa, the Ethiopian wolf (*Canis simensis*) and African wild dogs (*Lycaon pictus*) are threatened by this virus; although cases of rabies tend to be sporadic, epizootics are possible (CFSPH, 2012).



2.3.2. Reservoir

Rabies in Wildanimals: In nature, rabies in wildlife is perpetuated in much the same way as with urban rabies. One or two mammalian species in a given ecosystem, typically carnivores and bats, are responsible for maintaining cycle in their respective ecosystem (Murray, 2002). In many countries, wildlife rabies has become of increasing importance as a threat to domestic animals and human (CDC, 2001). In areas where canine rabies has been eradicated, the disease may be reinforced by wild carnivores if the canine population is not adequately immunized (Murray, 2002). In Africa, evidence indicates that the primary rabies virus maintenance cycle is among domestic dogs, although other carnivores may be involved as non-maintenance populations (Haydon *et al.*, 2010). This finding suggests that mass vaccination targeting domestic dogs would have the greatest impact in reducing the risk of infection in all other species including humans, livestock and wildlife (Ernest *et al.*, 2008). All mammals are susceptible to rabies, but only a limited number of species also act as reservoir hosts. They include members of the families Canidae (dogs, jackals, coyotes, wolves, foxes and raccoon dogs), Mustelidae (e.g., skunks), Viverridae (e.g., mongooses), and Procyonidae (raccoons), and the order Chiroptera (bats) (OIE, 2008).

For Humans: Globally, over 98% of all human rabies occurs following exposures to infected dogs (WHO, 2001). Different variants of rabies virus vary by continent and by in developing countries, monkeys are the second most common source of human rabies (Di Quizo and McCarthy, 2008). In developed countries, the animals that most often transmit rabies are foxes, skunks, bats and raccoons (CFIA, 2008). **For Animals:** The most significant vectors are red foxes, bats and striped

skunks (NARMP, 2008).

2.3.3. Transmission

Virus is most often transmitted by the saliva of a rabid animal introduced through a bite or scratch and rarely into a fresh break in the skin or through intact mucous membranes (Heymann, 2008). Human-to-human transmission occurs almost exclusively as a result of organ or tissue transplantation (CDCP, 2008). Most animals can be infected by the virus and can transmit the disease to humans, infected bats (Pawan, 1990) monkeys, raccoons, foxes, skunks, cattle, wolves, coyotes, dogs, mongooses (normally yellow mongoose) (Taylor, 1993). Airborne transmission has been demonstrated in laboratory settings and suggested in caves with heavy bat infestations (Heymann, 2005).

2.3.4. Prevalence and Incidence

Rabies is endemic in developing countries of Africa and Asia, and most human deaths from the disease occur in these endemic countries (WHO, 1998). In Tanzania, it has been predicted that the incidence of human rabies, on the basis of active surveillance is 100 times greater than that of officially recorded (Cleaveland *et al.*, 2002) [14]. Historically, the incidence of human rabies exposure in Ethiopia ranges from 1.3 to 18.6 per 100,000 populations (Yibrah *et al.* 2015).

2.4. Clinical Signs

2.4.1. Clinical Features in Animals

The animal becomes irritable and may viciously and aggressively use its teeth, claws, horns, or hooves to attack humans and other animals, without provocation. Such animals lose caution and fear of humans and other animals (Hemachudha *et al.*, 2013) [33, 34]. Rabid dogs or cats die within 10 days of onset symptoms (Both *et al.*, 2012) [8].

2.4.2. Clinical Features in Humans

The initial symptoms of rabies are fever and often pain or an unusual or unexplained tingling, pricking or burning sensation (Paraesthesia) at the wound site (Johnson, *et al.*, 2010) [36]. Once symptoms of the disease develop, the disease is fatal (Evans *et al.*, 2012) [24].

2.5. Diagnosis

2.5.1. Diagnosis in animals

The diagnosis of rabies in animals can be made by taking any part from the affected brain. But in order to rule out rabies, the test must include tissues from at least two locations in brain, from the brain stem and cerebellum (Swanepoel *et al.*, 2005). The reference method for diagnosing rabies is the fluorescent antibody test (FAT), an immunohistochemistry procedure, which is recommended by the World Health Organization (Dean, *et al.*, 1973) [18].

2.5.2. Diagnosis in humans

In some cases, no signs are observed and rabies virus has been identified as the cause of sudden death (Boonlert, 2005). Diagnosis can only be confirmed by laboratory tests preferably conducted post mortem on central nervous system tissue of animal that bite a person removed from cranium (McElhinney, *et al.*, 2008). When brain tissues were not available for laboratory confirmation, diagnosis of suspected rabies cases was based on history of exposure and clinical evaluation (Tepsumethanon *et al.*, 2005) [73].

2.6. Pathological Lesions

2.6.1. Gross Pathology

There is no visible inflammatory response in the brain of some rabid individuals (Streicker *et al.*, 2012) [70]. There are no pathognomic gross findings. Externally, there may be fresh or healed bite wounds and sometimes gross trauma due to self-mutilation. In the CNS there may be congestion of meningeal vessels, the brain tissue may appear pinker than usual and there may be mild cerebral edema (Fooks *et al.*, 2012) [24].

2.6.2. Histopathology

The general CNS presentation includes perivascular cuffing, vascular congestion, neuronal degeneration and focal to diffuse gliosis. Lesions may be most severe in the brain stem. The presence of Negri bodies is considered pathognomic for rabies, but these are only seen in about 50 - 75% of cases. These are found most commonly in ganglionic cells of the hippocampus and in Purkinje cells of the cerebellum. Spongiform lesions may be found in the grey matter, and in neuronal cell bodies of the thalamus and cerebral cortex. Spinal and cranial nerve ganglia, particularly the Gasserian ganglia, may show an inflammatory response.

2.7. Differential Diagnosis

Can involve many agents and syndromes (e.g. other viral encephalitides, tetanus listeriosis and poisoning) and co-infections, such as malaria, can lead to misdiagnosis (Mallewa *et al.*, 2007) [43].

2.8. Importance of rabies

2.8.1. Economic importance

The economic costs of rabies in country are associated with pet animal vaccinations, animal bite investigations, confinement and quarantine of domestic animals which bite humans or which are suspected of exposure to rabid animals, salaries of animal control officers, laboratory diagnosis and treatment and consultation, public education, staff training and clerical costs (Radostits *et al.*, 2007) [64].

2.8.2. Public health importance

Rabies is an Office International Des Epizooties (OIE) list B disease and currently remains an ongoing threat to human populations infectious diseases in 2000 (Finnegan *et al.*, 2002) [26]. About 98% of the human rabies cases occur in developing countries that possess large number of dogs, many of which are strays. Unfortunately, children share a disproportionately high burden of the disease (WHO, 2004).

2.9. General consideration Of Control and prevention Of Rabies

- **Case Definition:** An animal is determined to be rabid after diagnosis by a qualified laboratory and confirmation either by a positive direct fluorescent antibody test (preferably performed on central nervous system tissue) or Isolation of rabies virus in cell culture or in a laboratory animal (MMWR, 2012) [49].
- **Rabies Exposure Management:** Rabies is transmitted when the virus is introduced into bite wounds, open cuts in skin, or onto mucous membranes from saliva or other potentially infectious material such as neural tissue (CDPH, 2012) [10].
- **Public Health Education:** The majority of animal and human exposures to rabies can be prevented by raising

awareness concerning, rabies transmission routes, and avoiding contact with wildlife. Prompt recognition and reporting of possible exposures to medical professionals and local public health authorities is critical (CDPH, 2012) ^[10].

- **Treatment of Wounds and Vaccination:** Human rabies can be prevented by a) eliminating exposure to rabies virus, b) providing appropriate rabies pre-exposure prophylaxis, and c) prompt local treatment of bite wounds combined with appropriate rabies post-exposure prophylaxis (CDPH, 2012) ^[10].
- **Animal bites reporting:** The local health officer or designee shall be immediately notified of any person or animal bitten by or potentially exposed to a rabid or suspected rabid animal; Potential human rabies exposures are then evaluated and rabies post-exposure prophylaxis (PEP) recommendations made (CDPH, 2012) ^[10].
- **Stray Animals Control:** Strays dogs, cats, and ferrets should be controlled if human exposure has occurred and to give owners sufficient time to reclaim animals (Catherine, 2011) ^[11].
- **Isolation of animals exposed to rabies:** Unvaccinated livestock bitten by or exposed to a rabid or suspect rabid animal should be euthanized (CDPH, 2012) ^[10].
- **Wild Animal Rabies Control:** Immunization of wildlife by widespread distribution of vaccine-impregnated oral baits has shown variable success toward arresting the propagation of rabies in raccoons and coyotes in other states. The use of oral rabies vaccines (ORV) for the mass vaccination of free-ranging wildlife should be considered in selected situations (CDPH, 2012) ^[10].
- **Animal pre-exposure Vaccination:** Following an outbreak in domestic livestock, vaccination of animals without visible bite wounds is strongly recommended (Murray *et al.*, 2009).
- **Animal Post-Exposure Treatment:** If signs suggestive of rabies develop (e.g., paralysis, seizures, etc.), the animal should be euthanized and the head shipped for testing (Hanlon *et al.*, 2002) ^[32].
- **Outbreak Prevention and Control:** The emergence of new rabies virus variants or the introduction of non-indigenous viruses poses a significant risk to humans, domestic animals, and wildlife (Leslie *et al.*, 2006). A rapid and comprehensive response includes the following measures (Rupprecht *et al.*, 2006) ^[67].
 - Characterize the virus at the national reference laboratory.
 - Identify and control the source of the introduction.
 - Enhance laboratory-based surveillance in wild and domestic animals. Increase animal rabies vaccination rates.
 - Restrict the movement of animals.
 - Evaluate the need for vector population reduction.
 - Coordinate a multiagency response.
 - Provide public and professional outreach and education.

2.10. Status of control and prevention of human and animal rabies in African countries

2.10.1. Theoretical Framework

Rabies remains a neglected disease across many developing countries, particularly in Africa and Asia where victims of the

disease come from the poorest sectors of society (Hampson *et al.*, 2015) ^[31].

More than 99% of these deaths occur in developing countries, with about 43% (23 750) occurring in Africa (Knobel, *et al* 2005) ^[40].

In turn, the disease impact is not measured or appreciated, and evidence to support the increased spending required controlling rabies in dog's remains absent. Given this cycle of neglect, it is not surprising that the best available estimates suggest that around 59,000 human deaths and 3.7 million disability-adjusted life years (DALYs) are lost each year due to canine rabies, and the cumulative cost of economic losses estimated to be over US\$8.6 billion every year (Coudeville *et al.*, 2015) ^[31]. Canine rabies is very clearly now a disease that most heavily impacts the poorest sectors of developing countries, yet the scale of the problem is beginning to be appreciated (Morters *et al.*, 2014) ^[50].

With the calculation of economy-wide impacts of premature deaths of humans, livestock losses, and current spending on rabies prevention, there is a realization that the disease affects everyone in these countries, that the global inequality that this represents should not be tolerated, and that freedom from canine rabies should be considered a global public good (Restif *et al.*, 2014). The major international health organizations are uniting to send a clear message that rabies elimination is feasible, and leading by example to ensure that the intersectoral collaboration required for rabies control is achieved (McKinley *et al.*, 2014) ^[50].

The basic elements of canine rabies control are clear (Morters *et al.*, 2014) ^[50]:

1. The maintenance of a population of healthy, vaccinated dogs is the key defense for animals, people and their livestock
2. The protection of humans potentially exposed to rabies needs to be ensured by timely and affordable access to PEP, until such time as the threat is mitigated.

Under limited circumstances, this may require preexposure vaccination of those in high-risk areas at great distances from health services. To achieve these objectives, supporting mechanisms are needed, including: clear intersectoral collaboration to coordinate the provision of animal and human vaccination, public awareness and community engagement to ensure dog vaccination coverage levels are reached and potentially exposed people know how to seek treatment, and adequate surveillance to assess the need for and demonstrate progress in rabies control efforts (Morters *et al.*, 2014) ^[50].

Mass culling of dogs without resort to vaccination is now universally condemned. Instead, vaccinating community dogs creates a population of dogs that can protect their communities from the threat of rabies (Munks, 2012).

2.10.2. Practical Efforts

Africa contributes to 43% of the human deaths due to rabies (Knobel *et al.*, 2005) ^[40]. In addition to human life losses, rabies also a cause of substantial livestock losses (Okell, 2013) a threat to carnivores like the Ethiopian wolf (*Canis simensis*) (Randall *et al.*, 2004) ^[65] and the African wild dog (*Lycaon pictus*) (Alexander *et al.*, 1996). The main cause of transmission of rabies to human in Africa is by bite of a rabid dog (Awoh *et al.*, 2012). Once bitten by a rabid dog, development of the disease in human can be prevented by an

appropriate post-exposure prophylaxis (PEP). However, PEP is relatively expensive and not always available. Moreover, PEP lacks long-term benefits as it will not stop the virus transmission from rabid dogs to other humans or dogs (Meslin *et al.*, 2009) [73]. Dog rabies parenteral vaccination is therefore more cost-effective measure in preventive needs to be vaccinated during an annual rabies mass vaccination campaign in many African countries, (Cleaveland *et al.*, 2013) [83]. The proportion of dogs vaccinated against rabies far below 70% (Coleman *et al.*, 1996). Accessibility of free-roaming dogs for vaccination is often mentioned as an operational constraint (Lembo *et al.*, 2010) [41].

The recent project success stories provide an evidence base that canine rabies can be controlled, not just in theory, but also in practice in countries where this goal was perceived to be the most difficult to achieve. As evidence builds on the feasibility of canine rabies elimination in such countries, the myths that have so long contributed to the lack of progress are being dispelled (Lembo, 2014) [50]. Dogs can be accessed for vaccination in sufficient numbers to allow vaccination targets and the required break in transmission to be achieved (Horton, 2014), rabies transmission in wildlife is not the major barrier it is often assumed (Fitzpatrick, 2012) [27] and even in resource-poor countries, success can be achieved with sustained efforts. Tools such as the Canine Rabies Blueprint (PRP, 2010) and associated stepwise approach towards rabies elimination have been developed as user-friendly online resources that guide countries to the information and support available and allow them to self-assess their progress toward canine rabies elimination.

There is international support and training available from WHO collaborating centers, World Organization for Animal Health (OIE) reference labs, Food and Agriculture Organization of the United Nations, the Pasteur Institute, animal welfare organizations, and many others (WHO, 2013). The recently implemented OIE canine rabies vaccine bank allows donors and countries to purchase high-quality vaccine in bulk at a discounted rate (OIE, 2013). Advocacy and community mobilization through World Rabies Day activities (GARC, 2015) and other initiatives can play a big part to increase community awareness and gain political ground.

The selected articles encompassed research from Southern (South Africa, Madagascar, Zimbabwe, Zambia), Central (Chad), Northern (Tunisia), Eastern (Tanzania, Kenya, Ethiopia) and Western (Nigeria) Africa (Vigilato *et al.*, 2004). The methodological quality of candidate peer review articles was critically assessed by the assessment of multiple systematic reviews measurement tool (Blancou *et al.*, 2013) and supporting information:

Tanzania

Data from the incidence of dog bites in the United Republic of Tanzania, indicate that human rabies cases are between 10 and 100 times higher than officially reported (Cleaveland, *et al.* 2002) [14].

In one study in Musoma District, detailed longitudinal data were collected on the fate of 597 dogs from interviews conducted each month with dog owners in each of the study villages. Over a 12-month period, rabies was reported as the cause of death in 33 of these dogs. Assuming 66.7% accuracy of detection of true cases, the annual incidence of rabies was estimated to be 3.7%. This study demonstrates that

significant improvements in the detection and reporting of rabies cases could be achieved in rural communities with the adoption of relatively simple strategies. With these measures in place, figures obtained for the incidence of dog rabies and the incidence of human bite injuries from suspect rabid animals were higher than previously reported in Tanzania. This suggests that official case incidence data for rabies in Tanzania significantly underestimate the true magnitude of the rabies problem in the country (Cleaveland, *et al.* 2003) [15]. In unrelated experimentation, a mass dog vaccination campaign in the Serengeti district of Tanzania resulted in a significant reduction in dog rabies incidence and a sharp decline in reported bites from suspected rabid dogs compared to control villages without dog vaccination (Kaare *et al.*, 2003) [15]. More respondents (83%) in Tanzania reported they would seek medical attention immediately after dog bite incident (Sambo, 2012) [69]. More recently, three demonstration programs coordinated by WHO and supported by the Bill and Melinda Gates Foundation (Philippines, Tanzania, and South Africa (WHO, 2015)). For the project site in South Eastern Tanzania, the average bite incidence decreased from 26/100,000 in 2011 to 12/100,000 in 2014 (with substantial differences between districts), which directly relates to lower PEP costs incurred by rabies exposures (WHO, 2015).

In yet another study in the country, animal bite injuries were traced and investigated across three districts (Ulanga, Kilombero and Serengeti), from January 2006 to December 2009. Active searching revealed 599 animal bite injuries that met the case definition of being caused by suspect rabid animals as per criteria of the 'six-step' method: 136 in Kilombero district, 248 in Ulanga district and 215 in Serengeti district. Ninety-four percent (391/415) of these suspect bite victims reported to health facilities for PEP. Despite the importance of PEP for saving the lives of bite victims, the study found that shortages of PEP were common at the district hospitals. These shortages together with the expense of PEP created financial difficulties for many poor individuals, particularly those living in rural areas that had to raise money to pay for PEP, transport costs to reach urban areas and subsistence while receiving PEP (Sambo, *et al.* 2013).

Chad

The current policy on rabies control in Chad is restricted to human post-exposure treatment. Public human health authorities in Chad consider rabies a veterinary problem, and the Ministry of Livestock considers the problem to be 'negligible'. Human cases, however, are very underreported (Knobel, *et al.* 2005) [40]. In N'Djame'na, capital of Chad, the annual incidence of canine rabies in 2006 was 1.7/1000 unvaccinated dogs. In 2002 a pilot, free vaccination campaign for dog-owners in N'Djame'na resulted in 64–87% of all dogs being vaccinated. Full-cost recovery concepts will not ensure that enough dogs are vaccinated in Chad (or, most likely, other African countries) to interrupt rabies transmission in dogs in urban areas. Clearly, to have >70% of all dogs vaccinated, public health officials and policy makers must consider methods to substantially subsidize dog rabies vaccinations (Martin *et al.*, 2008) [68].

Kenya

Rabies has existed in Kenya with varying incidence levels since 1912 (Hudson *et al.*, 1994) [35]. Nevertheless, the

magnitude of the problem has remained largely unknown since specimens from rabies-suspect animals in remote locations are rarely sent to the Central Veterinary Investigation Laboratory in Kabete for confirmatory diagnosis (Omemo, 2012) [62]. Customarily, rabies prevention and control in Kenya is the mandate of the Department of Veterinary Services (DVS). The rabies vaccination coverage for this study was below the WHO recommended coverage of 80% required to achieve herd immunity (Samuel *et al.*, 2014). The total in percentage of Vaccinated dogs in the dog owning households interviewed was below the WHO recommended coverage for herd immunity in Machakos District (Kitala *et al.*, 2001) [38].

Rabies control strategies in the country include the traditional mass vaccination of dogs, movement restriction, control of 'stray' dogs and community education. However, the major constraints to the effective control of rabies in the country are inadequate resource allocation, lack of integrated approach, poor infrastructure and lack of proper logistics, rather than a lack of technical competence (Omemo, 2012) [62]. Hospitals and government stores in Kenya have only limited stocks of biological for rabies PEP-rabies vaccine and rabies immunoglobulin (RIG). RIG is virtually unavailable from government facilities, but at least one private hospital (the Nairobi Hospital) has stocks available for patients at a fee. Rabies cases or dog bite injuries are not recorded as such in the current system (Eric Ogola, 2012) [21].

South Africa

In the Republic of South Africa (RSA) two major variants of RABV are distinguished and these circulate in *Canidae* and *Herpestidae* species, respectively (King *et al.*, 1993; Von Teichman *et al.*, 1995; Nel *et al.*, 2005) [37, 76, 55]. The canid RABV variant occurs widespread in the RSA and is mainly associated with the domestic dog (*Canis familiaris*) in the KwaZulu Natal, Eastern Cape, Free State, Mpumalanga and Limpopo Provinces (Coetzee and Nel, 2007, Ngoepe *et al.*, 2009) [16, 57]. A total of 353 laboratory confirmed human rabies cases from the RSA were analysed for the study.

In another project in the province of KwaZulu Natal, a very clear correlation was shown between the falling number of animal and human cases, which have now been brought down to around 2 per month and 0, respectively (WHO, 2015). The disease in domestic dogs in KwaZulu Natal has receded significantly in recent years due to strategic ongoing efforts between the local stakeholders and international support through the Bill and Melinda Gates Foundation project (Shwiff *et al.*, 2014). Likewise, efforts in Mpumalanga have seen a steady decrease in number of dog cases in the past three years (Anderson *et al.*, 2014).

Nigeria

Rabies is endemic in Nigeria and rabies viral antigen has been detected in the brain tissues of apparently healthy Routine vaccination of dogs against rabies in Nigeria and most African countries population is low (Otolorin *et al.*, 2015) [59]. No a national rabies control programmers that is planned and executed jointly by both Veterinarians and human health workers (Aiyedun *et al.*, 2015) [59]. In a study, Result of human deaths due to rabies gotten from 10 States in Nigeria, gave a total of 78 deaths due to rabies. All of which were not confirmed by laboratory techniques only by clinical presentation (Dzikwi *et al.*, 2015) [59]. As under-reporting and misdiagnosis are major factors that contributes to poor

records of the devastating effect of the disease to humans in Nigeria (Ameh *et al.*, 2015) [59].

Rabies in North Africa (Morocco, Algeria, Tunisia, Libia)

Rabies is a serious public health concern in North Africa causing a heavy social and economic burden (Mehdi, 2011) [45]. Despite the substantial committed efforts, rabies is still endemic and not under control in the North African countries and continue to cause human fatalities and hundreds of animal cases (Mehdi, 2011) [45].

Algeria

Average of 22 per year human fatalities, the dog is the main reservoir of the disease (average prevalence of about 50% of reported cases) (Mehdi, 2011) [45]. Rabies presents a public health problem despite the establishment of a national committee rabies control in 1984. It endemic with a seasonal peak in spring 950 cases reported yearly (Mehdi, 2011) [45]. Dogs remain the main reservoir and transmitter of rabies (40 to 70 % of notified cases, 85% cases are from rural areas, Ruminants (19-31-39%) and equines (6-19-8%) are the main victims of rabies among livestock species, 86% unvaccinated, 14% interrupted PET, 89 % due to dog bites with mostly unknown origin Children; major victims of canine rabies (56%). Control (OIE, 2011) [45]. Multiannual program initiated in 1996 mainly based on three actions: Reduction of stray animal population, Vaccination of domestic carnivores; Vaccination of Cattle (since 2003). Data from this program for the year 2007 Number of Dogs and Cats vaccinated 21 and 768 respectively, Cattle vaccinated 802, since the beginning of the operation, Number of animals vaccinated, 1900000, Number of carnivores killed stray, 220000.

Morocco

Rabies is endemic in Morocco, with all provinces being affected, except the southern desert region. The most common lyssavirus present is Genotype 1 (Rabies virus, RABV), with human infections being mostly due to the canine biotype (EL Harrak, 2011) [45]. On average, 22 human fatalities associated with rabies occur annually since 1986 (EL Harrak, 2008). According to the OIE World Animal Health Information System in 2011 Morocco reported 18 cases of rabies in humans, and 19 cases in animal in 2012 (OIE, 2014). A recent global burden of rabies study estimates that around 50 people die from rabies every year (Hampson, 2008) [31].

Rabies has been a notifiable disease in Morocco for more than 10 years. A national case definition for human rabies is given, which includes suspect, probable and confirmed cases. Human rabies surveillance is integrated in the national disease surveillance system (Taylor, 2015) [71]. The main vector for rabies in Morocco is the domestic dog. In 2000, the dog population was estimated at around 1.6 million, with 10 percent of the population being stray dogs (Harrak, 2008). According to the OIE World Animal Health Information System, in 2011, Morocco reported 64 cases of rabies in dogs, with 62,851 dogs routinely vaccinated. In the following year, 2012, 91 dogs died from rabies, while 114,790 animals were routinely vaccinated. 44 dog rabies cases were confirmed in the first half of 2013 (OIE, 2011) [45].

Nonetheless, a significant number of livestock, especially cattle, die from rabies every year. In 2011, 187 cases were reported, 255 cases in 2012, and 133 in 2013. PEP treatment is entirely funded by the government and is available at 120 PEP centers all over the country (EL Harrak, 2011) [45].

Tunisia

Rabies is endemic in Tunisia, with the Northern provinces being most affected. The most common lyssavirus present is Genotype 1 (Rabies virus, RABV), with human infections being mostly due to the canine biotype (ELHarrak, 2011) [45]. Human rabies is a notifiable disease in Tunisia (OIE, 2011) [45]. And the surveillance system for both humans and animals (except bat specific surveillance) is relatively well established. Human rabies cases are sometimes laboratory confirmed, but mostly diagnosed on clinical grounds only. According to the OIE World Animal Health Information System in 2011 Tunisia reported one case of rabies in humans, 3 cases in 2012, and 6 cases in 2013(OIE, 2011) [45]. A significant number of livestock, especially cattle, die from rabies in Tunisia every year. In 2011, 34 cases were reported, 114 cases in 2012, and 160 in 2013(OIE, 2011) [45]. Rabies in wildlife is present in Tunisia, with one case reported in 2013 (species unknown) (OIE, 2011) [45]. The main vector for rabies in Tunisia is the domestic dog.

In 2011, it was estimated that vaccination coverage amongst the dog population is 48 percent (ELHarrak, 2011) [45]. In 2011, Tunisia reported 64 cases of rabies in dogs, with 4,379 dogs ring vaccinated and 395,835 routinely vaccinated (OIE, 2011) [45]. In the following year, 2012, 167 dogs rabies cases were reported, 4,722 animals were ring vaccinated and 399,732 dogs received routine vaccination. In 2013, there were 199 dog rabies cases, 2,681 ring and 467,507 routine vaccinations. PEP treatment is entirely funded by the government and is available free of charge in the 360 antirabies medical centres, with around 40,000 PEP are administered annually (Bourhy, 2013).

2.11. Status of rabies in Ethiopia

2.11.1. General Consideration

Rabies in Ethiopia is primarily a disease of dogs. Many people are at increased risk of being exposed to rabies since man-dog contact is very common (Eshetu *et al.*, 2014). Ethiopia has been considered among the most rabies affected country in the world with an estimated annual occurrence of 10, 000 cases of human rabies which makes it to be one of the worst affected countries in the world (Fekadu *et al.*, 1997) [25]. Deressa *et al.*, in their study have indicated the available data during the years 2001 to 2009 at the Ethiopian Health and Nutrition Research Institute (EHNRI) showed that 35 to 58 annual human deaths were recorded mostly in Addis Ababa, the capital city of Ethiopia (Deressa *et al.*, 2010). Meseret and Debasu, in their three year retrospective study at Gonder Health Center indicated that a total of 261 human rabies exposure cases were reported to the Gondar Health Center from 2011 to 2013(Meseret *et al.*, 2015) [46].

Vaccination is below the WHO recommended coverage for herd immunity where 33% of dogs from dog owning households had been vaccinated (Mekona *et al.*, 2012). Thus, an increasing number of stray dogs in Ethiopia and the absence of legislation to determine and certify the status of vaccinated and non vaccinated dogs create difficulty to control the disease. Moreover, lack of utilization of modern anti-rabies vaccines, low level of public awareness, lack of nationwide animal rabies surveillance and poor attention and resource allocation by government are major important problems that hinder the control of rabies 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(Meseret *et al.*, 2015) [46]. 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 (Berhanu *et al.*, 2013).

2.11.2. Community awareness on rabies in animals and humans

A number of community knowledge, attitude and practice (KAP) studies have been conducted across the country. The results showed a very variable magnitude in KAP levels in different localities across the country. In a study conducted in Addis Ababa, for instance, most of the respondents are well aware of the risks associated with the disease, the importance of modern human post exposure treatment (vaccination) and proper wound treatments. A significant proportion of the interviewed households 2323 (97.2%), indicated that rabies is transmitted to humans when they are bitten, scratched or licked by rabid dogs, cats and other animals. In addition, most of the households 2053 (85.9%) indicated that treatment of wound and vaccination is important to prevent the occurrence of rabies in humans when bitten by suspected or known rabid dogs and cats (Eshetu *et al.*, 2012). Almost all (83.0%) study respondents had previously heard about rabies. Half of the respondents reported that informal/non mass media (family, teacher, traditional healer, professionals and friends) were the main sources of information for them about rabies. (30.97%) claimed to possess the basic knowledge of what rabies is and that it is a deadly disease. The vast majority of study participants (71.9%), knew that it can affect all warm blooded animals including human beings and dogs are the major vector for rabies in Addis Ababa as reported by (73.5%). Moreover, 81.5% of respondents recognize that it affects all human races regardless of the age. Thirty four percent of the study respondents were able to identify most recognized clinical signs of the disease both in animals and human. However, It was widely perceived among respondents that bite was a main mode of rabies transmission from animal to animal (67.8%), animal to human (75.6%) and human to human (42.4%)(Abraham *et al.*, 2013).

Majority of the respondents know that rabies can be prevented in animals (46.6%) through regular vaccination against the disease. Only 28.7% of the respondents recognize the availability of rabies preventive measures in human and of these, 85.7% of them correctly answered that both diate medical seek and taking post exposure treatment as effective preventive measures. More than 98% of the respondents were willing to vaccinate their pets, and almost all respondents (98.2%) agreed to consult health professionals if they were bitten by dogs. However, 58.3% the respondents had strong believe on traditional medicine for rabies prevention and treatment (Desalegn *et al.*, 2013) [2] In Eastern Ethiopia, one

study confirmed that majority of the respondents have heard about the disease from their family in both urban and pastoralist households which implied government based awareness creation might not be adequate or practiced. In the same study, overall poor knowledge about the disease has been reported in pastoralists (Tschopp *et al.*, 2016) ^[74].

2.11.3. Incidence and prevalence studies

The available information on rabies in Ethiopia is largely based on passive reports to EPHI zoonoses laboratory (Eshetu *et al.*, 2000; Paulos *et al.*, 2000). Passive reports usually underestimate incidence and are poor indicator of the status of the disease in countries where human and animal health information systems are inadequate (Kitalaa *et al.*, 2000; Kayali *et al.*, 2003).

- In the 1980's Bogel and Motschwillor had also reported 12 cases per million people which made Ethiopia the second worst affected by rabies next to India (Bogel and Motschwiller, 1986).
- An estimate of incidence of magnitude with 2.33 per 100, 000 was reported in North Gondar zone
- In a hospital-based study in Asella, an average 101 people was infected annually in the years 2008-2013 (Fetene *et al.*, 2014).
- Same type of hospital-based study in North Gondar Zone from 2011 to 2013, a total of 261 human rabies was reported, with 140, 81, and 40 exposure cases in 2011, 2012, and 2013, respectively. Both data from Gonder and Asella showed a decreasing trend.
- In another publication by Jemberu *et al.* (2013) a slight decline to estimate of 2.33 per 100,000 was recorded, but most suspected rabies victims do not die in hospital.
- In Ethiopian Somali Regional State (ESRS), various rabies outbreaks had been repeatedly reported. For instance, in one of the major outbreak, about 288 human cases of affected domestic animals were reported in Afder and Gode zones from 3rd February, 2009 that covered East and South Afdher, Central Gode, border area with Koraha zone. In Afder Zone, 477 animal cases were reported with an unknown numbers in other woredas. Yusuf (2016). On the other hand, Ayalew *et al.* (2015) ^[4] had documented incidences of outbreak in two woredas of Fafan zone- Jigjiga and Kebribayah. in which 70 cattle (in one heard) were bitten by a suspected rabid stray dog, of which five of them showed clinical sign of rabies and dead at different times. Also cases were reported in two camels that had shown typical signs in less than a month (Ayalew *et al.*, 2015) ^[4].

In general, rabies is virtually underreported which leads to lack of accurate quantitative information on rabies both in humans and animals (WHO, 2010b; Wilde and Lumlerdacha, 2011) ^[73]

2.11.4. Control and Prevention in Ethiopia

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 4.5 Opportunity for rabies elimination in Ethiopia inadequacy has resulted in uncoordinated and largely ineffective actions. (Birhanu *et al.*, 2013) ^[46].

3. Conclusion and Recommendation

Elimination of human rabies is dependent on the elimination of dog rabies simply because dogs remain the major epicenter in the epidemiology in most African nations. No single country in Africa had ever eradicated the disease to date. Moreover, most passive reports often practiced in African countries had underreported the disease. A neglected tropical disease by its nature, the disease is hurting millions of rural communities comprising major proportion of populations as PEP services are not well accessible and thus killing hundreds of thousands per year. More often than not, information, education and communication activities for rabies control are insufficient in many African nations including Ethiopia. Not to mention feeble intersect oral and regional coordination among various agencies like Ministry of Health, Ministry of Agriculture, OIE, WHO, it adds major headache on the control. It is generally agreed that a full-fledged control and eradication of this deadly disease is doom and gloom in near future. Also vaccination of dogs is below the recommended coverage almost in all nations.

Based on the above conclusions the following recommendations could be forwarded:

- Most passive reports need to be streamlined with active laboratory confirmations to combat underreporting of the disease.
- PEP services should be accessible in rural health facilities
- Vaccination of dogs should be improved and brought in range of WHO-OIE-recommended coverage.
- Information, education and communication activities should be routinely practiced.
- Improvement Intersectoral and regional coordination among various agencies is very mandatory.
- Regulations for stray dog management should be enforced and supported by law.

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