Int. J. Curr. Res. Med. Sci. (2023). 9(7): 19-35

International Journal of Current Research in Medical Sciences

ISSN: 2454-5716

(A Peer Reviewed, Indexed and Open Access Journal)

www.ijcrims.com

Review Article

Volume 9, Issue 8 -2023

DOI: http://dx.doi.org/10.22192/ijcrms.2023.09.08.004

Rabies disease and its current status in Ethiopia: A review

Tewodros Sadado Samago

Wolaita Zone Agricultural Department, Animal Heath Directorate, Wolaita Sodo, Ethiopia.

Corresponding author: *sadadotewodros@gmail.com*

Abstract

Rabies is a neglected zoonotic disease with a global burden of approximately 59,000 human deaths per year. There is also an estimation of 21,476 human deaths occurs each year in Africa due to dog-mediated rabies. Its caused by *Lyssavirus* genus belonging to the *Rhabdoviridae* family The disease is characterized by course of clinical signs in 3 phases; namely prodromal, excitatory (excitement) and paralytic or end stage in which development of severe nervous symptoms that lead to paralysis and death. The primary route of infection in rabies is through the bite of a rabid animal that contains infectious virus in its saliva. More than 99% of all human deaths from rabies occur in the developing world among which 99% is also caused by dog bite and this is mostly true in Ethiopia. Current report of WHO and OIE revealed that globally there is total loss of 8.6 US$ billion per year. In Ethiopia, the national annual estimates from official reports indicate 12 exposure cases per 100,000 population and 1.6 rabies deaths per 100,000 populations and on average 2 million USD treatment costs per year countrywide even if there is no detail surveillance data available. The direct fluorescent antibody test (FAT) is suggested as a confirmatory diagnostic test for rabies disease confirmation. Although canine vaccination is most important to control rabies disease, canine vaccination has neither been enforced as compulsory nor promoted as a public good in Ethiopia, and as such very few dog owners vaccinate their dogs in the country. So increasing awareness and effective dog vaccination, with creating and adopting policies to control human and animal rabies is effective way to rabies control in general. This review

Keywords: Dog; Epidemiology; Ethiopia; Lyssavirus; Rabies; Virus.

Introduction

Rabies is a fatal zoonotic viral disease that affects the central nervous system of all warm-blooded animals, including humans leading to the development of fatal encephalitis [1, 2]. Rabies is caused by *Lyssavirus* family Rhabdoviridae that principally affects carnivores and insectivorous bats which are also carriers of the virus, although it can affect any mammal [3]. There are many strains of the rabies virus; each strain is maintained in a particular reservoir hosts even though these viruses can readily cause rabies in other species [4]. Dogs remain the primary reservoir in developing countries, whereas wildlife species serve as hosts in developed nations [5]. The disease is characterized by the development of severe nervous symptoms that lead to paralysis and death [6]. Once symptoms of the disease develop, it is invariably fatal and can only be prevented but not cured [7].

The animal usually contracts rabies from the bite of an infected animal. The virus may also enter the body if the mucous membranes (the wet part of the eyes, nose, or mouth) or a scratch or break in the skin have contact with saliva containing the rabies virus [8]. Once the rabies virus enters the body, it begins to multiply in the area near the entry site. If the infection is not stopped at this point, the virus will eventually invade the nerve cells in the area [9]. Following access to the muscle cells at the wound site, peripheral nerves and subsequently the central nervous system, the virus travels retrogradely from the CNS via peripheral nerves to various tissues, most importantly the salivary glands, from which it is shed, completing the transmission cycle [10].

Rabies is maintained in two epidemiological cycles, one urban and another sylvatic. In the urban rabies cycle, dogs are the main reservoir host. This cycle predominates in areas of Africa, Asia, and Central and South America where the proportion of unvaccinated and semi owned or stray dogs is high and the sylvatic (or wildlife) cycle is the predominant cycle in Europe and North America [11]. Although rabies is generally well controlled among domesticated animals in developed nations, canine rabies continues to be a serious problem in some areas of Africa, the Middle East, Asia and Latin America. Wildlife reservoirs have become increasingly important where canine rabies is under control [11].

The disease occurs throughout the world and it is also endemic in Ethiopia [3]. On estimation, 59,000 people die from rabies each year 40% of whom is children living in Asia and Africa [12]. In Ethiopia, the national annual estimates from official reports indicate 12 exposure cases per 100,000 population and 1.6 rabies deaths per 100,000 populations [13]. From the total, 99% of rabies cases are dog-mediated and the burden of disease is disproportionally occur in rural poor populations, with approximately half of cases attributable to children under 15 [10]. Rabies has great public health concern and economic importance; however, the disease remains as a neglected tropical disease in most part of developing countries including Ethiopia [14]. But there is also low level of political commitment to rabies control in dog vaccination and other practices due to lack of accurate data on the true public health impact of the disease [15, 16].

The production of the Fermi type rabies vaccine started in Ethiopia since 1944 E.C. and it is in use until now even though it is not recommended by World Health Organization currently; and now annual consumption of the vaccine is more than 36,000 doses for human and 12,000 doses for animals in Ethiopia [17]. But there is low level practice of dog vaccination trend in Ethiopia which is from 10%-30% [18, 19], as surveyed in different regions which is very different from WHO recommendation of 70% [12]. So to maintain the rabies-free status, much more practices should be done including strict continuous monitoring and control, and applicable regulations in dog vaccinations and stray dog control to reduce disease status in the country. Therefore; the aim of this review is to highlight rabies disease and its current status in Ethiopia.

Rabies disease

Etiology

Rabies is caused by the genus *Lyssavirus* belonging to the *Rhabdoviridae* family. It is a bullet shaped virus, containing a negative sense single-stranded RNA genome [20, 21]. The causative agent of rabies is a highly neurotropic virus and member of the 16 currently recognized viral species of the *Lyssavirus* genus [22]. The virus is not viable outside the host and is fragile and easily inactivated by desiccation, ultra-violet radiation, and detergents like sodium hypochlorite, 45-75% ethanol, iodine preparations, quaternary ammonium compounds, formaldehyde, phenol, ether, trypsin, β-propiolactone, and some other detergents. It is rapidly destroyed by temperatures above 50 ^{0}C (122° F) and destroyed within a few hours at room temperature, however, the virus may persist for years when frozen. Rabies virus can also be inactivated by a very low pH (below 3) or very high pH (greater than 11). It is rapidly inactivated by sunlight and drying, and (in dried blood and secretions) it does not survive for long periods in the environment [23].

There are many strains of the rabies virus; each strain is maintained in a particular reservoir hosts. Although these viruses can readily cause rabies in other species, they usually die out during serial passage in species to which they are not adapted [4]. Closely related lyssaviruses, which are known as rabies-related lyssaviruses or non-rabies lyssaviruses, can cause a neurological disease that is identical to rabies. To date now, seven strains have been associated with rapidly-progressive fatal encephalomyelitisin humans [4, 24]. Lagos bat virus (genotype 2, serotype 2) is found in bats in parts of Africa, and has caused fatal cases of neurological disease in cats, dogs and a water mongoose. Mokola virus (genotype 3, serotype 3) is the only rabies-related lyssavirus that has not been found in bats. This virus has been isolated from rodents and shrews in Africa, but its reservoir host is unknown [25, 26]. It has caused fatal neurological disease in cats, dogs and humans, including rabies-vaccinated cats and dogs. Duvenhage virus (genotype 4, serotype 4) occurs among bats in Africa. It has caused fatal rabies-like disease in several people. The European bat lyssaviruses (EBLVs 1 and 2, genotype 5 and 6, respectively) are very similar to the Duvenhage virus, but are found in limited to western and Eastern Europe. The Australian bat lyssavirus (ABLV; genotype 7) has been isolated in Australia [4].

Epidemiology

Rabies is prevalent throughout the world except in Islands. Many of the countries are endemic for rabies, except Australia and Antarctica [27]. Across the globe, particularly in Africa, Asia and India, domestic dog-adapted RABV wages a neglected epidemic that claims an estimated 59,000 human lives annually [28]. As per the WHO global vaccines research forum, over 3 billion people are affected with dog rabies and more than 30,000 deaths occur annually in Asian continent, among which 15% of mortality occurred in children under 15 years of age [27]. This usually also happens in the most of developing countries, especially in Africa [29]. While in WHO South East Asian Region member countries, it is more serious public health problem accounting for approximate 99%human mortality worldwide [30], and among which rabies virus circulating in dogs are responsible for more than 99% of the cases in humans worldwide [31].

Among the African countries Cape Verde, Congo, Libya, Mauritius, Reunion and Seychelles are free from rabies [27]. Report of WHO indicated that canine rabies has been eliminated from western Europe, Canada, the United States of America (USA), Japan, Malaysia and a few Latin American countries; while Australia is free from carnivore rabies, and many Pacific island nations have always been free from rabies and related viruses [32]. In Ethiopia, the national annual estimates from official reports indicate 12 exposure cases per 100,000 population and 1.6 rabies deaths per 100,000 populations [13]. However, the actual numbers are expected to be higher as many cases are not reported [33]. The reliability of the reported incidence data is expected to differ among the regions in Ethiopia due to geographical as well as cultural differences. For instance, in rural Ethiopia, individuals who are exposed to rabies often prefer to see traditional healers for the diagnosis and treatment of the disease because of cultural background, lack of knowledge [17], or limited accessibility to medical treatment [34, 35]. These widespread traditional practices of handling rabies cases might interfere with medical treatment seeking practice, resulting in an under reporting of the actual number of rabies cases and its related health burden [35]. To fill the disparities between officially recorded and likely occurring rabies cases, researchers have applied approaches like extensive animal bite case searching, and predictive modeling [35].

Rabies has also emerged as a threat to conservation after outbreaks in highly endangered populations of Ethiopian wolves (*C. simensis*) in the Bale Mountains National Park (BMNP) [36], in African wild dogs (*Lycaon pictus*) in eastern and southern Africa [37]. This threat became a reality when rabies caused significant mortality in the web valley wolf population in 1991–1992 and was probably responsible for the death of wolves on the Sanetti Plateau in 1990 [38]. This mortality due to rabies accounts for the steep decline in BMNP wolf population from year to year [38]. Ethiopian wolves and African wild dogs are among the world's most highly endangered carnivore species, and transmission of rabies virus from more abundant primary hosts (such as domestic dogs) is considered a threat for extinction of several populations [32].

Epidemiologically, there are two cycles of rabies which are the urban and sylvatic (wildlife). The major reservoir host of urban rabies is dogs although in Africa, Middle East, Latin America and Asia few sylvatic cases of rabies have been reported [11]. In the urban rabies cycle, dogs are the main reservoir host. This cycle predominates in areas of Africa, Asia, and Central and South America where the proportion of unvaccinated and semi-owned or stray dogs is high. It has been virtually eliminated in North America and Europe; although sporadic cases occur in dogs infected by wild animals, the urban cycle is not perpetuated in the canine population [4,11].

The sylvatic (or wildlife) cycle is the predominant cycle in Europe and North America. It is also present simultaneously with the urban cycle in some parts of the world. The epidemiology of this cycle is complex; factors affecting it include the virus strain, the behavior of the host species, ecology and environmental factors [4]. In any ecosystem, often one and occasionally up to 3 wildlife species are responsible for perpetuating a particular strain of rabies. The disease pattern in wildlife can either be relatively stable, or occur as a slow moving epidemic. Recent examples of epidemics include a fox rabies epidemic that moved slowly west in Europe, and a raccoon rabies epidemic that moved north along the east coast of the USA and into Canada [4, 11].

Risk Factors

Rabies remains endemic in Ethiopia suggesting wildlife may play a role in rabies persistence or that there is re-introduction of dog maintained rabies virus variants from neighboring regions. The interaction of wild and domestic animals in grazing areas, water points and backyard or slaughterhouse waste disposal areas can also facilitate the circulation of the virus in the country [39]. Dog slaughterhouses are also considered as vital risk factor in the epidemiology of rabies in some of the Asian and African countries. RABV recovered from Burkinafaso [40] and Vietnam [41] having homology with isolates recovered from Mauritania and China, respectively, indicated that transboundary spread of RABV, which indicates importance of trading and slaughtering of dogs in the rabies epidemiology [42]. Although effective and economical control measures are available [43], rabies remains a neglected disease throughout most of these countries [44].

A major factor in the low level of political commitment to rabies control is a lack of accurate data on the true public health impact of the disease. It is widely recognized that the number of deaths officially reported greatly underestimates the true incidence of disease [45]. Patients may not present to medical facilities for treatment of clinical disease; few cases receive laboratory confirmation; and clinical cases are often not reported by local authorities to central authorities [45]. There is also limitation of knowledge, attitude and practice on rabies disease in different aspects between communities [16, 46, 47]. Another factor is only centrally limited rabies diagnosis capacity to the center and not available in various regions of the Ethiopia [48] and there is also no enforcement and or promotion of canine vaccination as a public good, and as such very few dog owners vaccinate their dogs in Ethiopia which paves way to increment of rabies in the country [15, 16].

Reservoirs of Lyssaviruses

Lyssaviruses have been detected in bats throughout the world, although different species are present in different regions. Bats have been identified as vectors for all *Lyssavirus* species except Mokola virus and Ikoma lyssavirus, for which the true primary host is yet to be found. This observation strongly suggests that bats are true primary hosts for lyssaviruses. At least four lyssavirus species are known to circulate in populations of insectivorous and frugivorous African bats, namely Lagos bat virus, Duvenhage virus, Shimoni bat virus and Mokola virus [32].

Of the many animals that are susceptible to rabies, several species, including foxes, skunks, wolves, raccoons, mongooses, coyotes, and vampire, insectivorous and fruit-eating bats are important reservoirs for the disease. A particular species usually serves as the important reservoir for a certain geographic region, for example, foxes for Western Europe, skunks and raccoons for North America, mongooses for Africa and Asia. Now a day the role of cats in human rabies exposures has also increased [49]. Among warm blooded animals, Squirrels, chipmunks, rats, mice, hamsters, guinea pigs, gerbils, rabbits and hares are not usually infected with rabies [50]. The domestic dog, however, remains the most important source of rabies in humans in most developing regions of the world and account for the majority of deaths that occur due to human rabies all over the world [49]. Although animals like horses, deer and cattle can be infected with rabies and transmit to other animals and human this seldom occur [32]. Spread of the disease is often seasonal, with the highest incidence in the late summer and autumn because of large scale movement of wild animals at mating time and in pursuit of food [49].

Figure 1: Schematic representation of the pathophysiological cycle of the rabies
Source: The Ethiopian Health and Nutrition Research Institute, 2012 [17].

Pathogenesis

The primary route of infection in rabies is through the bite of a rabid animal that contains infectious virus in its saliva [51]. The *lyssavirus* enters the body via abrasions or by direct in touch with mucosal membranes. It is not able to intersect undamaged skin. The rabies virus replicates inside the bitten muscle tissue and then it achieves entry towards the central nervous system [52]. The virions are passed in carrying vesicles [53] and move to the central nervous system (CNS) completely via rapid retrograde transport beside motor axons, by means of no uptake through sensory or sympathetic endings [54]. Once infection is established within neuronal cells the virus usurps host cell machinery to reach cell bodies in the spinal cord or brainstem or in sensory ganglia (dorsal root ganglia) where replication occurs. The motility of rabies virus along neuronal processes has been exploited to map neuronal circuitry [55]. The virus is transported by fast axonal transport through the spinal cord to the brain. Until this stage the patient shows no clinical signs.

Host detection of virus intracellularly occurs through the retinoic acid-inducible gene 1 pathway ([56] through the detection of cap structures on the virus mRNAs and through Toll-like receptors [57]. This detection stimulates an early interferon response that is antagonised by the virus phosphoprotein [58].

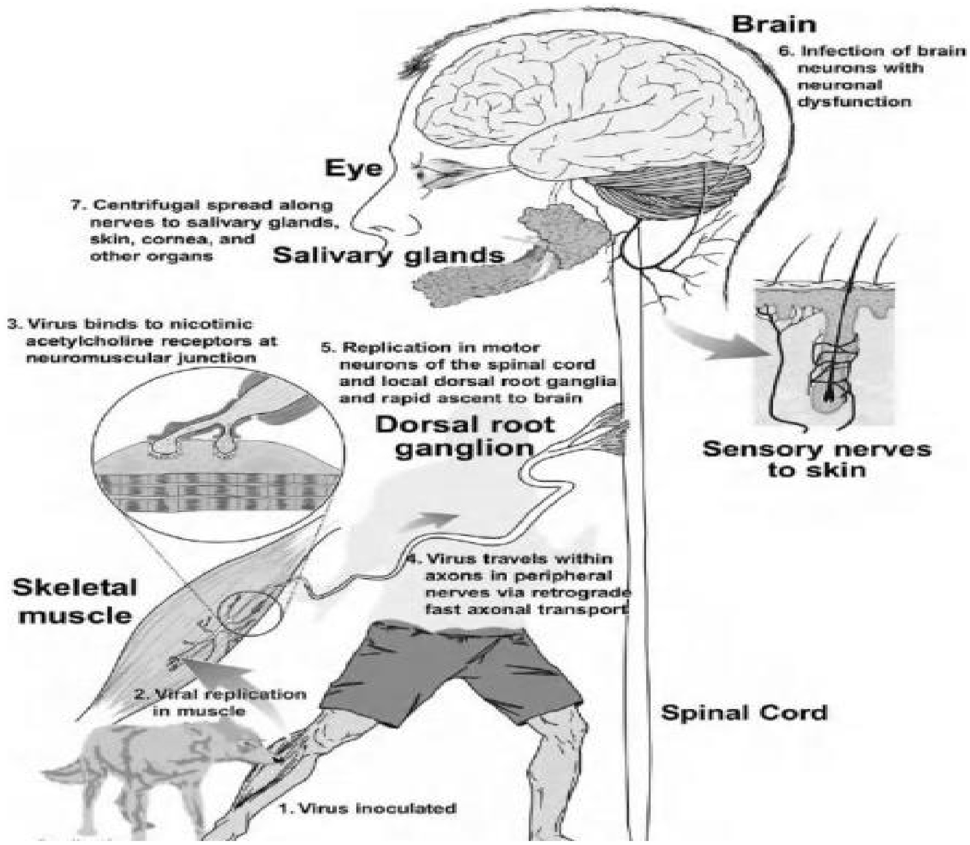

Figure 2: Schematic representation of the pathophysiological cycle of the rabies (Jackson and Fu, 2013) [59].

The entrance of virus inside tissues of the brain leads to death, usually through respiratory dysfunction and secondary metabolic and circulatory defects [60]. Several factors, including the virulence of strain, the quantity of infectious virus in the saliva, and the susceptibility of the species, play a role in establishing rabies in the recipient animals [51]. The disease is always fatal, but infrequently an experimentally infected animal shows clinical signs of the disease but recovers. There are two recent records of spontaneous recovery in man, and the occurrence of non-fatal rabies in all species has been reviewed as reported by Radostits and his coworkers [49]. There appears to be no field occurrence in domestic animals of the finding in experimentally infected mice that some strains of virus invade only peripheral nerves and spinal ganglia leaving a number of survivors with permanent nervous disability [49].

Transmission

Transmission of animal rabies is similar to that of human rabies, with virus-laden saliva from infected animals entering the body through wounds or by direct contact with mucosal surfaces [10]. Infection occurs primarily via bite wounds, or infected saliva entering an open cut or wound or intact mucous membrane, such as those in the mouth, nasal cavity or eyes. In exceptional circumstances, rabies may be acquired by inhalation of aerosol containing rabies virus in infected bat caves. Recently, a few human rabies cases have been reported from recipients of cornea transplants from infected donors [51, 61]. Transmission of rabies virus can also occur from bat bites that may be small and insignificant [62].

Diagnosis

Clinical observations may only lead to a suspicion of rabies because signs of the disease are not pathognomonic and may vary greatly from one animal to another. The only way to undertake a reliable diagnosis is to identify the virus or viral antigen/viral RNA using laboratory tests [61]. The diagnosis of rabies is carried out by either *in vivo* or through autopsy [63]. Although hydrophobia is highly suggestive, no clinical signs of disease are pathognomonic for rabies and differential diagnosis can involve many agents and syndromes (eg, other viral encephalitides, tetanus, listeriosis, and poisoning) and coinfections, such as malaria, can lead to misdiagnosis. Historical reliance on the detection of accumulations of negri bodies is not this much applicable due to low sensitivity and alternative laboratory-based tests have been developed to conclusively confirm infection [6].

Laboratory techniques are preferably applied on samples from the central nervous system of the suspected animal by opening of the skull. If the skull cannot be opened there are two alternative routes for collection of brain samples: the occipital foramen route and retro-orbital route. But mostly for confirmatory diagnosis samples from the brain stem and cerebellum are taken [27, 61]. The best impression smears from the brain includes sampling of the hippocampus, medulla oblongata, cerebellum or gasserian ganglion [64].

The brain smears are utilized for the human discovery of virus antigen by means of the fluorescent antibody test (FAT), designed mutually for human as well as for animal samples. In most animals, the direct FAT is suggested as a confirmatory diagnostic test. Molecular methods, such as the reverse transcription polymerase chain reaction (RT-PCR) and other amplification techniques like Enzyme-linked immunosorbent assay (ELISA), Rapid immunodiagnostic test (RIDT), rabies tissue culture infection test (RTCIT) and Immunochemical tests are playing an increasingly important role in many countries but are not recommended currently for routine post-mortem diagnosis of rabies if brain tissue is available, when the FAT should be used [61].

In Ethiopia the laboratory confirmation is done using Fluorescent Antibody test (FAT), and Mouse Inoculation Test (MIT). Furthermore, the Institute has introduced Direct Immunohistochemistry Test (dRIT) that detects antigen. There is no established diagnosis on human rabies at the EHNRI except clinical observation and Pre Exposure Prophylaxis (PEP) [17].

Table 1: The diagnostic techniques for rabies disease

Techniques	Sample	Benefits/ disadvantages
Polymerase Chain Reaction (PCR)	Body fluids, saliva, urine, cerebrospinal fluid	Applicable in all tissue conditions but, requires experienced technicians
Mouse Inoculation Technique (MIT)	liver, brain, salivary glands, spleen and pancreas are the most appropriate sample	In this technique only fresh tissue is used for an accurate result
Direct Fluorescent Antibody Technique (DFA)	Similar to MIT	Applicable with most tissue sources. Not applicable in decomposed tissues.

Clinical signs

The initial clinical signs are often nonspecific and may include anxiety, fearfulness, restlessness, anorexia or an increased appetite, vomiting, diarrhea, a slight fever, dilation of the pupils, hyperactivity to stimuli and excessive salivation. The first sign of post-vaccinal rabies is usually lameness in the vaccinated leg [65]. The animals regularly comprise behaviorally and personality changes, and might turn into either curiously aggressive or uncharacteristically dedicated [65]. The typical histological signs, found in the central nervous system, are multifocal, mild, polioencephalomyelitis and craniospinal ganglionitis with mononuclear perivascular infiltrates; diffuse glial proliferation, regressive changes in neuronal cells and glial nodules. Negri bodies can be seen in some but not all cases. The incubation period in naturally occurring cases is about 3 weeks, but varies from 2 weeks to several months in most species, although incubation periods of 5 and 6 months have been observed in cattle and dogs [49, 61]. The course may be divided into 3 phases; namely prodromal, excitative (excitement) and paralytic or end stage [20].

1.1. Prodromal Stage

During the prodromal period which lasts approximately 1-3 days, animals show only vague central nervous system signs, which intensify rapidly [20]. Following a definite incubation phase, the beginning of clinical symptoms starts. During this first stage, slight behavioral modification may occur, *i.e.* anger in domestic animals, day time tricks in nocturnal animals, no fright of humans in the wild animals or else irregularities in the appetite [32].

1.2. Excitement (Furious) Phase

The term "furious rabies" refers to animals in which aggression (excitatory phase) pronounced [20]. The furious type is described via agitation, wandering, weeping, polypnea, drooling and attacks upon other animals, community or unresponsive objects. Infected animals frequently ingest foreign items for instance firewood and gravels. The wild animals often drop their fright of humans, and may harass humans or another surrounding animal that they would usually avoid (*e.g.*, porcupines). On the other hand, the nocturnal animals may be observable throughout the day. In cattle, strange attentiveness can be an indication of this phase [65].

1.3. Paralytic (Dumb) Phase

Furthermore, this stage is also characterized by dropping of foamy salivary secretion and paralysis of hind limbs eventually leading complete paralysis followed by death [32]. It is first manifested by paralysis of the throat and masseters muscle often with profuse salivation and in ability to swallow [66]. Laryngeal paralysis can cause a change in vocalization, including an abnormal bellow in cattle or a hoarse howling in dogs, facial paralysis or the lower jaw may drop. Ruminants may separate from the herd and can become somnolent or depressed. Rumination may stop, ataxia, incoordination and ascending spinal paresis or paralysis are also seen [20].

Public health and economic burden of rabies

Rabies, a fatal but neglected disease, constitutes a major public health problem worldwide [67]. Estimates of the global burden, based on models of incidence of dog bites included from country-specific data from published studies and online surveys, giving a more comprehensive global estimate Knobel *et al*. (2005) [31] suggest that almost 60,000 human deaths occur from rabies globally per year, which is more than that attributed to any other single zoonotic disease [28]. An estimation of 21,476 human deaths occurs each year in Africa due to dog-mediated rabies. Africa is estimated to spend the least on PEP and have the highest cost of human mortality [10]. According to the study done in 2018 by universities of united kingdom, from 2020 to 2035, they estimated that under the status quo1074000 dog-mediated rabies deaths in humans will occur in the 67 endemic countries considered (580000 deaths in Gavi-46 countries) which is around 67000 deaths per year. Approximately 10% of 1074000 deaths are children younger than 5 years and most deaths are in sub-Saharan Africa (347000 in the east Africa cluster and 231000 in the West Africa cluster) and Asia (464000), with much fewer in the Americas (33000). Current levels of post-exposure prophylaxis prevent approximately 56000 deaths or 2764000 DALYs per year [68].

As health and economic burden of rabies based on the cost classification of Jo with the post exposure treatment (PET) and indirect costs in terms of disability-adjusted life years (DALYs) [69], the large number of children among these fatalities indicates rabies is estimated to cause more than 2 million disability-adjusted life-years (DALYs) lost per year [31]. Current report of WHO and OIE revealed that globally there is total loss of 8.6 US$ billion per year among this; 54% accounts productivity losses due to premature death, 37% treatment costs, livestock losses 2% dog vaccination & population control and 0.01% cost on rabies surveillance data [12].

Rabies is one of the most feared infectious diseases in Ethiopia [70]. In a zoonotic disease prioritization workshop held as Ethiopia's first step in engagement in the U.S. CDC Global Health Security Agenda, rabies was identified as the number one priority disease followed by anthrax, brucellosis, leptospirosis, and echinococcosis [71]. Estimates of the global burden of rabies showed that some 2,700 humans die of rabies in Ethiopia every year making it the country with the second highest annual number of human rabies deaths in Africa [28]. Preliminary findings of community based national rabies base line survey showed 12 incidence of rabies exposure / 100,000 population and human death of 1.6/100,000 population.

Current status of rabies in Ethiopia

The current situation analysis and statement of rabies problem in Ethiopia shows primarily a serious threat of canine rabies virus transmission in the rapidly growing human population with equally growing stray dog population of the nation [72]. There is no clear cut demarcation between owned and scavenging dogs, as free movement of dogs from place to place is not restricted, and 80% herd immunity level is not yet maintained. Similarly, the population dynamics of dogs in urban and rural setting is not yet documented for feasible national intervention plan [73].

In Ethiopia, the dogs, cats, and wild life species are known to transmit rabies virus to both humans and livestock [13]. At present, although rabies control associated working groups have been established across the regions of Ethiopia, there is no national strategic plan to clearly define targets for rabies control [74]. The relative burden of rabies compared to other neglected tropical diseases is also not known [75]. In countries like Ethiopia, where financial resources are limited, there is a need **for** quantitative data on the costs of certain diseases to support intervention prioritization [76].

National level surveillance data compiled by EHNRI since 2007 to September 2012 indicated that 15,178 exposure cases (3.4 /100,000 populations), 272 fatal cases with more than 88% of the exposure cases were due to dog bites. Among the exposed people 59.2% of the cases are males while 40.8% females. Out of the total exposure 98.9% (15,008) of exposure cases and 97.1% (264) of fatal cases were from Addis Ababa, Oromia, Amhara, SNNPR and Tigray regions. As the surveillance report, the national data indicates an exposure of 2.6/100,000 people. The highest incidence is registered from Tigray (11.4/100,000), followed by Oromia (3.5/100,000), Benshangul (3.3/100,000), Amhara (1.5/100,000), SNNPR (1.2/100,000) and Addis Ababa (0.8/100,000) [17].

Study done at three districts of Ethiopia (namely Bishoftu, Lemuna-bilbilo and Yabelo) in September 2013 to August 2014 revealed that a total of 655 animal bite cases were traced of which 96.5% was caused by dog bites. 73.6% of the biting dogs were suspected to be potentially rabid dog. Annual suspected rabid dog exposures were estimated per evaluated urban, rural highland and rural lowland district at, respectively, 135, 101 and 86 bites, which led, respectively, to about 1, 4 and 3 deaths per 100,000 populations was registered. Extrapolation of the district results to the national level indicated an annual estimate of approximately 3,000 human deaths resulting in about 194,000 DALYs per year and 97,000 exposed persons requiring on average 2 million USD treatment costs per year countrywide [35].

As a retrospective cross-sectional study done in northwestern Gonder, Addis Alem district level hospital data in 2017, a total of 924 human rabies exposure cases were recorded. The overall human rabies incidence per 100, 000 population was 6.5 in 2015 and 7.5 in 2016. Males (55.2%, 510/924) and children of age less than fifteen (46.3%, 428/924) were most affected groups. The majority of human rabies exposure cases (71.9%, 664/924) were from rural settings. Dogs were the principal sources of exposure (96.3%) followed by cat (1.5%) and donkey (1.3%). High incidence rate of rabies exposure was reported during spring (360, 39%) and summer (244, 26.4%) seasons [77]. According to Gebreyohans *et al.* (2019) [14] in Tigray region in 2016, a total of 368 human rabies exposure cases were collected during the study period.

On another hand researcher reported that, in and around Addis Ababa between the years 2008 and 2011, a total of 1,088 dogs were examined for rabies, of which 801 (73.62%) were confirmed to be rabid. The proportion of rabid female dogs (87.5%) was higher than that of males (73.44%), and dogs 3 to 12 months old were diagnosed with rabies more frequently (76.6%) than dogs belonging to other age category. The highest proportion of rabid dogs was recorded in dogs whose ownership was not known followed by ownerless dogs. Rabies cases were confirmed both in vaccinated and non-vaccinated dogs [70].

Table 2: Current situation of human rabies related cases in Ethiopia

Study area	No. of Affected	Author
Bishoftu	189 by rabid dog	[35]
Lemuna-bilbilo	189 by rabid dog	[35]
Yabelo	87 by rabid dog	[35]
In and around Addis Ababa	386 death in 2001-2009	[39]
Northwestern Tigray	14.4% in urban	[14]
	85.6% in rural	
Northwestern Amhara	55.2% male	[77]
	44.8% female	
	28.1% urban	
	71.9% rural	
Hawassa Zuria	55.3 per 100,000	[78]
Mareka woreda	13.6 per 100,000	[78]
Soro woreda	12.1 per 100,000	[78]
Tembaro woreda	116.3 per 100,000	[78]
Gena Bossa	5.4 per 100,000	[78]
Northwestern Tigray	35.8 per 100,000 in 2012	[79]
	63 per 100,000 in 2013	
	89.8 per 100,000 in 2014	
	73.1 per 100,000 in 2015	
Southern, Eastern, South East and Mekelle zones in Tigray region	392 per 100,000 in 2012	[80]
	422 per 100,000 in 2013	
	278 per 100,000 in 2014	
	308 per 100,000 in 2015	
	317 per 100,000 in 2016	

Table 3: Current situation of knowledge, attitude and practice of rabies related cases in Ethiopia

Study area	No. of respondents	Level of KAP in %	Author
South Gondar	384	Poor 51% Good 49%	[34]
Aksum town and Laelay Machew district	558	Urban poor 56% Rural poor 62%	[81]
Southern, Eastern, South East and Mekelle zones in Tigray region	1440	72.2%	[80]
		66.0%	
		62.4%	
Around Debre Tabor	422	Good 49.5%	[82]
Around Gonder	384	Good 51%	[83]

Table 4: Current situation of animal rabies related cases in Ethiopia

Study area	No. of studied	No. of Affected in %	Author
Northwestern Tigray	Male(dog bite)	63%	Gebreyohans *et al.*, 2019
	Female(dog bite)	37%	
In and around Addis Ababa	20,414	10%	[39]
In and around Addis Ababa	1,088 dogs	73.62%	[70]

2. Rabies vaccination in Ethiopia

The development of rabies vaccines passed through 4 historical stages (1) the production of neural tissue vaccines, (2) followed by non-neural vaccines, (3) cell culture vaccines and recently (4) rabies recombinant DNA vaccines. During these stages, various living attenuated or inactivated vaccines were tested among which the killed vaccines were less efficient due to poor immunogenic and inflammatory response required for effective T- and B- cell responses [84]. One of the most widely used cell lines for human vaccine production currently is the non-tumorigenic Vero cell line which is expensive and not readily available in developing countries where rabies is endemic [85].

The production of the Fermi type rabies vaccine started in Ethiopia since 1944 E.C. and even though it is not recommended by World Health Organization the vaccine is still in use in Ethiopia. Annual consumption of the vaccine is more than 36,000 doses for human and 12,000 doses for animals. Currently, EHNRI is working on tissue culture vaccine and, the institute has already produced over 100,000 doses of cell culture based vaccine for animal use. Cell culture based vaccine production for humans is under way and shortly the institute will replace the Fermi vaccine with the aim of increasing safety and potency [17].

Dog vaccination is a key to stopping rabies transmission between dogs, and from dogs to humans and it is a cost–effective and sustainable way to save lives [86]. But different studies occurred at different regions of Ethiopia revealed that many dog guardians do not vaccinate their dogs or vaccinate them irregularly.

For example, in a study conducted by Jemberu and his associates (2013) [18], only 20% of surveyed dog guardians residing in North Gondar vaccinated their dogs regularly; 11% vaccinated their dogs occasionally and the remaining dog guardians indicated they never vaccinated their dogs; Similarly, there is also similar findings from the earlier study in Addis Ababa indicated that only one third of the surveyed dog guardians vaccinated their dogs regularly [19].

Prevention and control

The large dog population size in combination with poor dog management contributes to a high endemicity of canine rabies in Ethiopia [72]. So, the use of wider measures to control the spread of rabies should be followed. Measures will be focused on controlling and eradicating the disease as quickly to protect public health and to prevent establishment of disease in any animal population [87]. So, engaging communities to improve rabies education and awareness is essential to prevent human deaths by effective post exposure prophylaxis rather using traditional treatment and reporting of possible exposures to medical professionals [28, 31].

As dog is the main source of rabies in humans, at least 70% mass vaccination of dog should be used to eliminate human dog-mediated rabies in countries as recommended by World Organization for Animal Health (OIE) and World Health Organization [12]. Stray dogs, cats, and ferrets should also be removed from the community [88]. Then, expanding access to high-quality, affordable PEP for populations at risk of rabies is also one way to control rabies disease [12] and there should be also clear guidance, strategies and frameworks applied to adapt, own and implement and establishment of reporting structures with defined linkages between departments to ensure continuity and progress of elimination activities in the context of changing political environments and personnel [12].

Conclusion and Recommendations

Rabies is a fatal viral zoonotic disease and a serious public health problem by which an estimate of 59000 people die each year worldwide. Though its occurrence is worldwide, it is important in developing countries like in Ethiopia. This is because of wide spread occurrence of large number of stray dogs. In Africa, the Ethiopian wolf (*Canis simensis*) and African wild dogs (*Lycaonpictus*) are also threatened by this virus which may cause economic loss on the aspect of tourism and natural resource damage. Poor enforcement and/or promotion on canine vaccination as a public good with low level of political commitment to rabies control and lack of accurate data on the true public health impact of the disease to take serious attention is one of the main challenge of rabies disease control in Ethiopia. Due to this the number of deaths officially reported greatly underestimates the true incidence of disease. However, preliminary findings of community based national rabies base line survey indicated 12 incidence of rabies exposure / 100,000 population and human death of 1.6/100,000 population which might be greater if there is detailed surveillance. So, there should be adequate laboratory surveillance system in different regions for case reports to update national picture of human and animal rabies incidence in Ethiopia which also uses the distinction of serotype/s and genotypes of rabies virus type on phonological study and molecular characterization work for further documentation of rabies strains in Ethiopia. In general, rabies control can be effective through engaging communities to build awareness of rabies, and vaccination of dogs to prevent human disease, requires collaboration between, at a minimum, the human and veterinary health sectors and other concerned bodies. Coherent, standardized, evidence-based tools and strategies for effective dog vaccination, Strengthened, vitalized and supportive regional networks, improved availability and access to dog rabies vaccines and Local, regional and global reporting structures should also be established to facilitate data collection and sharing.

References

1. World Health Organization WHO (2005): World Health Organization Expert Consultation on Rabies. World Health Organization Technical Report Series; no. 931: 111-121.
2. Black T.P. and Rupprecht C.E. (2004): Rhabdo viruses. In: Mandell GL, Bennett JE, Dolin R, editors.Principles and Practice of Infectious Diseases. Philadelphia: ELSEVIER Churchill Livingstone; 6th edition. Pp. 2047-56.
3. Drug Administration and Control Authority (DACA) (2006): Year book, Standard Treatment guide lines for veterinary practice, Drug Administration and Control Authority, Addis Ababa, Ethiopia, Pp. 335-336.
4. Center for Food Security and Public Health (CFSPH) (2009): Rabies. Iowa State University; Institute for International Cooperation in Animal Biologics.
5. Rupprecht C.E., Barrett J., Briggs D., Cliquet F., Fooks A.R., Lumlertdacha B. and Tordo N. (2007): Can rabies be eradicated? *Developments in biologicals*, 131: 95-121.
6. Abera E., Assefa A., Belete S. and Mekonen N. (2015): Review on Rabies, with Emphasis on Disease Control and Eradication Measures. *International Journal of Basic and Applied Virology*, 4(2): 60-70.
7. Blackmore C. (2014): Rabies Prevention and Control in Florida, Division of Disease Control and Health Protection. 122P.
8. Langley R.L. (2009): Human fatalities resulting from dog attacks in the United States, 1979–2005. Wildern. *Environ. Med*. 20(1): 19-25. *https://doi.org/10.1580/08-WEMEOR-213.1*
9. Morbidity and Mortality Weekly Report (MMWR) (2011): Compendium of Animal Rabies Prevention and Control: Recommendations and Reports/Vol.60/No.6:1-17.
10. World Health Organization WHO (2020): Animal rabies. *https://www.who.int/rabies/about/home_animal_rabies/en/*
11. Office of International des-epizootic (OIE) (2009): Rabies/lyssa/hydrophobia. http://www.oie.gov/rabies//
12. World Health Organization, Food and Agriculture Organization of the United Nations and World
Organisation for Animal Health (WHO-FAO-OIE) (2018): Zero by 30: the global strategic plan to end human deaths from dog-mediated rabies by 2030.
13. Deressa A., Sefir D., Mamo H., Ali A, and Akililu M. (2013): Rabies diagnosis and surveillance for the period 2010–2012 in Ethiopia. 11th SEARG meeting, Dar es Salaam 11–15 February 2013, South Africa.
14. Gebreyohans G., Gebremedhin R., Abrha A., Haftom H. and Muluberhan B. (2019): Risk Factors and Spatio-Temporal Patterns of Human Rabies Exposure in Northwestern Tigray, Ethiopia. *Annals of Global Health*; 85(1): 1–12. DOI: https://doi.org/10.5334/aogh.2518.
15. Ali A., F., Mengistu K., Hussen G., Getahun A., Deressa E. and Yimer E. (2010): Overview of Rabies in and around Addis Ababa, in Animals Examined in EHNRI Zoonoses Laboratory Between, 2003 and 2009, *Ethiopian Vet. J*. 14 (2): 91–101.
16. Kabeta T., Deresa B., Tigre W., Ward M.P. and Mor S.M., (2015): Knowledge, attitudes and practices of animal bite victims attending an anti-rabies health center in Jimma Town, Ethiopia, *PLoS Negl. Trop. Dis*. 9 (6): e0003867.
17. Ethiopian Health and Nutrition Research Institute (EHNRI) (2012): The National Workshop on Rabies Prevention and Control in Ethiopia.
18. Jemberu W. T., Molla W., Almaw G. and Alemu S. (2013): Incidence of Rabies in Humans and Domestic Animals and People's Awareness in North Gondar Zone, Ethiopia, PLoS Neglected Tropical Diseases, vol. 7, no. 5.
19. Yimer E., Mesfin A., Beyene M., Bekele A., Taye G., Zewdie B. and Alemayehu, T. (2012): Study on knowledge, attitude and dog ownership patterns related to rabies prevention and control in Addis Ababa,

Ethiopia. *Ethiopian Veterinary Journal*, vol. 16, no. 2.

20. Moges N. (2015a): Epidemiology, prevention and control methods of rabies in domestic animals. *Eur. J. Biol. Sci.* 7(2): 85-90.
21. Wunner, W.H. and Conzelmann, K.K. (2013): Rabies Virus. In Jackson, A. C. (Ed.), Rabies: Scientific basis of the disease and its management, 17-60, San Diego, CA: Elsevier.
22. International Committee on Taxonomy of Viruses (ICTV) (2018): 10th Report of the International Committee on Taxonomy of Viruses Online 2018b Release EC50, Washington DC, USA. *http://www. ictvonline.org/virusTaxonomy.asp*.
23. Leung A.K., Davies H.D., Hon K.L. (2007): Rabies: Epidemiology, pathogenesis, and prophylaxis. *Adv Ther*. 24: 1340–1347.
24. Arnaud T. (2018): Epidemiology as a tool to improve prevention of human rabies: local and global health implications of postexposure prophylaxis data, Institut Pasteur du Cambodge, 2003-2014. Santé publique et épidémiologie. Université Sorbonne, Paris.
25. Gould A.R., Hyatt A.D., Lunt R., Kattenbelt J.A., Hengstberger S. and Blackwell S.D. (1998): Characterization of novel lyssa virus from Pteropid bats in Australia. *Virus Res*. 54: 165–187.
26. Fauquet C.M., Mayo M.A., Maniloff J., Desselberger U. and Ball L.A. (2004): Virus taxonomy: the classification and nomenclature of viruses. Eighth report of the International Committee on Taxonomy of Viruses. San Diego (CA): *Academic Press*; Pp. 623–631.
27. Yousaf M.Z., Qasim M., Zia S., Ashfaq U.A. and Khan S. (2012): Rabies molecular virology, diagnosis, prevention and treatment. *Virol. J.* 9(1): 1p. *https://doi.org/10.1186/1743- 422X-9-50.*
28. Hampson K., Coudeville L. and Lembo T. (2015): Global alliance for rabies control partners for rabies prevention. Estimating the global burden of endemic canine rabies. *PLoS Negl. Trop. Dis.* 9: e003709p.
29. Tenzin M. and Ward P. (2012): Review of rabies epidemiology and control in South, South East and East Asia: past, present and prospects for elimination. *Zoonoses Public Health*, 59 (7): 451–467.
30. World Health Organization (WHO) (2002): Rabies vaccines. Wkly Epidemiol Rec. 77: 109–119.
31. Knobel D.L., Cleaveland S., Coleman P.G., Fevre E.M., Meltzer M.I., Miranda M.E., Shaw A., Zinsstag J. and Meslin F.X. (2005): Reevaluating the burden of rabies in Africa and Asia. Bull World Health Organ. 83: 360–368.
32. World Health Organization WHO (2013): World Health Organization Expert consultation on rabies, 2nd Report (No. 982).
33. Moges N. (2015b): Rabies in Ethiopia: Review Article. *Academic Journal of Animal Diseases* 4(2): 74–81.
34. Bihon A., Meresa D. and Tesfaw A. (2020): Rabies: Knowledge, Attitude and Practices in and Around South Gondar, North West Ethiopia. Diseases, 8; 5; http://doi:10.3390/diseases8010005
35. Beyene T.J., Mourits M.C.M., Kidane A.H. and Hogeveen H. (2018): Estimating the burden of rabies in Ethiopia by tracing dog bite victims. PLoS ONE 13(2): e0192313. https://doi.org/10.1371/ journal.pone.0192313.
36. Mebatsion T., Sillero-Zubiri C., Gottelli D & Cox J.H. (1992): Detection of rabies antibody by ELISA and RFFIT in unvaccinated dogs and in the endangered Simien jackal (Canis simensis) of Ethiopia. *J. Vet. Med. Ser. B,* 39: 233–235.
37. Dye C. (1996): Serengeti wild dogs: what really happened? *Trends in Ecology and Evolution*, 11: 188-189.
38. Sillero-Zubiri C. and King A.A., Macdonald D.W. (1996): Rabies and mortality in Ethiopian wolves (canis simensis). *Journal of wild life diseases*, 32: 54-56.
39. Deresa A., Ali A., Beyene M., Newayesilasie B., Yimer E. and Hussen K. (2010): The status of rabies in Ethiopia: A

retrospective record review. *Ethiop.J. Health Dev*; 24 (2):105-112.

40. De Benedictis P., Sow A., Fusaro A., Veggiato C., Talbi C., Kabor e A., Dundon W.G., Bourhy H. and Capua I. (2010): Phylogenetic analysis of rabies viruses from Burkina Faso, 2007. *Zoonoses Public Health*. 57(7–8):e42–e46.
41. Nguyen A.K., Nguyen D.V., Ngo G.C., Nguyen T.T., Inoue S., Yamada A., Dinh X.K., Nguyen D.V., Phan T.X. and Pham B.Q. (2011): Molecular epidemiology of rabies virus in Vietnam (2006–2009). *Jpn J Infect Dis*. 64(5): 391–396.
42. Atuman Y.J., Ogunkoya A.B., Adawa D.A.Y., Nok A.J. and Biallah M.B. (2014): Dog ecology, dog bites and rabies vaccination rates in Bauchi State, Nigeria. *Int J Vet Sci Med*. 2: 41–45.
43. Cleaveland S., Kaare M., Tiringa P., Mlengeya T. and Barrat J. (2003): A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine*; 21: 1965-73.
44. Warrell D.A. and Warrell M.J. (1995): Human rabies: a continuing challenge in the tropical world. *Schweizerische Medizinische Wochenschrift*; 125: 879-85.
45. Fekadu M. (1997): Human rabies surveillance and control in Ethiopia. In: Kitala P., Perry B., Barrat J. and King A.A., editors. Proceedings of the Fourth International Conference of the Southern and East African Rabies Group, Nairobi, Kenya, 4-6 March, 7-8. Lyon : Editions Fondation Mérieux ; Pp. 78-79.
46. Digafe, R., Kifelew, L., & Mechesso, A. (2015): Knowledge, attitudes and practices towards rabies: questionnaire survey in rural household heads of Gondar Zuria District, Ethiopia. *Bmc Research Notes*, 8 (1): 1-7.
47. Kansas department of health and environment (KDHE) (2019): Rabies Investigation Guideline.
48. Deressa A., Pal M., Mamo H., Haile A. and Dasgupta R. (2015): Rabies: A major fatal viral disease of humans and animals in Ethiopia; *journal of natural history*; v o l. 11(2): 19-26
49. Radostits, O. M., Gay, C.C., Hinchcliff, K. W. and Constable, P.D. (2007): Special Medicine. In: Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs and Goats. 10th ed. Spain: sounders Elsevier, pp: 1384-1393.
50. Wu X.R., Hu Y., Zhang G., Dong and Rupprecht C.E., (2009): Reemerging rabies and lack of systemic surveillance in People's Republic of China. *Emerging Infectious Disease*, 15: 1159-1164. *https://doi.org/10.3201/eid1508.081426*
51. Dwight C.H. and Yuan C.Z. (1999): Veterinary Microbiology. California: Blackwell science. Pp. 412-416.
52. Ugolini G. (2007): Use of rabies virus as a transneuronal tracer of neuronal connections: implications for the understanding of rabies pathogenesis. *Develop. Biologic*. 131: 493-506.
53. Klingen Y., Conzelmann K.K. and Finke S. (2008): Double-labelled rabies virus: live tracking of enveloped virus transport. *J. Virol*. 82(1): 237-245. https://doi.org/10.1128/JVI.01342- 07.
54. Hemachudha T., Ugolini G., Wacharapluesadee S., Sungkarat W., Shuangshoti S. and Laothamatas J. (2013): Human rabies: Neuropathogenesis, diagnosis and management. Lancet Neurol. 12(5): 498-513. *https://doi.org/10.1016/S1474-4422(13)70038-3*.
55. Ginger M., Haberl M., Conzelmann K.K., Schwarz M.K. and Frick A. (2013): Revealing the secrets of neuronal circuits with recombinant rabies virus technology. Front Neural Circuits; 7: 2.
56. Hornung V., Ellegast J. and Kim S. (2006): 5´-Triphosphate RNA is the ligand for RIG-I. *Science*; 314: 994–97.
57. Rieder M. and Conzelmann K.K. (2011): Interferon in rabies virus infection. *Adv Virus Res*, 79: 91–114.
58. Chelbi-Alix MK., Vidy A., El Bougrini J. and Blondel D. (2006): Rabies viral mechanisms to escape the IFN system: the viral protein P interferes with IRF-3, Stat1,

and PML nuclear bodies. *J Interferon Cytokine Res*; 26: 271–80.
59. Jackson A.C. and Fu Z.F. (2013): Chapter 8 - Pathogenesis. In: Jackson A.C., ed. Rabies 3rd Edition. Boston: Academic Press: pp. 299–349.
60. Bishop G.C., Durrheim D.N., Kloeck P.E., Godlonton J.D., Bingham J. and Speare R. (2003): Rabies guide for the medical, veterinary and allied professions. Rabies Advisory Group, South African Department of Agriculture and Health, Pretoria.
61. Office of International des-epizootic (OIE) (2014): Rabies: Aetiology, Epidemiology, Diagnosis, Prevention and Control
62. Center for Disease Control (CDC) (2008): Human Rabies Prevention – United States, Recommendations of the Advisory Committee on Immunization Practices. Morbidity Mortality Weekly Report, 57: 205-210.
63. Consales C.A. and Bolzan V.L. (2007): Rabies review: immunopathology, clinical aspects and treatment. *J. Venomous Anim. Toxins Trop. Dis.* 13(1): 5-38. *https://doi.org/10.1590/s1678-91992007000100002.*
64. Shite A., Guadu T. and Admassu B. (2015): Challenges of Rabies. *International Journal of Basic and Applied Virology*, 4(2): 41-52.
65. Banyard A.C., Horton D.L., Freuling C., Müller T. and Fooks A.R. (2013): Control and prevention of canine rabies: the need for building laboratory-based surveillance capacity. *Antivir. Res*. 98(3): 357-364.
66. Chernet B., Nejash A. (2016): Review of rabies preventions and control. Int. J. Life Sci. 4(2): 293-301.
67. Office of International des-epizootic (OIE) (2018): Rabies (Infection with rabies virus and other Lyssa viruses). OIE terrestrial manual. http://www.oie.int/en/our-scientific-expertise/reference-laboratories/list-of-laboratories/
68. Katie H. and Caroline T. (2019): The potential effect of improved provision of rabies post-exposure prophylaxis in Gavi-eligible countries: a modelling study; WHO Rabies Modelling Consortium. *Lancet Infect Dis*; 19: 102–11. http://dx.doi.org/10.1016/S1473-3099(18)30512-7.
69. Jo C. (2014): Cost-of-illness studies: concepts, scopes, and methods. *Clinical and molecular hepatology*, 20(4): 327–337. https://doi.org/10.3350/cmh.2014.20.4.327 PMID: 25548737
70. Reta T., Teshale S., Deresa A., Ali A., Mengistu F., Sifer D. and Freuling C. M. (2014): Rabies in animals and humans in and around Addis Ababa, the capital city of Ethiopia: A retrospective and questionnaire based study. *Journal of Veterinary Medicine and Animal Health*, vol. 6(6): 178-186.
71. Pieracci, E. G., Hall, A. J., Gharpure, R., Haile, A., Walelign, E., Deressa, A., Bahiru, G. and Ermias, B. W. H. (2016): Prioritizing zoonotic diseases in Ethiopia using a one health approach. One Health, 2: 131-135.
72. Yimer E., Newayeselassie B., Teferra G., Mekonnen Y. and Bogale Y. (2002): Situation of rabies in Ethiopia: a retrospective study 1990–2000. *Ethiopian Journal of Health Development*, 16(1): 105–112.
73. Pal M. and Deressa A. (2016): 5th Animal Health and Veterinary Medicine Congress; *J Vet Sci Med Diagn*, 5:5p. Valencia, Spain. *http://dx.doi.org/10.4172/2325-9590.C1.009*
74. Coetzer A., Kidane A.H., Bekele M., Hundera A.D. and Pieracci E. G. (2016): The SARE tool for rabies control: Current experience in Ethiopia. *Antiviral Research*, 135: 74–80. *https://doi.org/10.1016/j.antiviral. 2016.09.011 PMID: 27746249.*
75. Deribe K., Meribo K., Gebre T., Hailu A. and Ali A. (2012): The burden of neglected tropical diseases in Ethiopia, and opportunities for integrated control and elimination. *Parasit Vectors*, 5(1): 240p.
76. Murray C. (1994): Quantifying the burden of disease: the technical basis for disability-adjusted life years. Bulletin of the World Health Organization, 72(3): 429p.
77. Yizengaw E., Getahun T., Mulu W., Ashagrie M., Abdela I. and Geta M. (2018): Incidence of human rabies virus exposure in northwestern Amhara, Ethiopia. *BMC Infectious Diseases*, 18: 597p. *https://doi.org/10.1186/s12879-018-3500-3*

78. Mulugeta Y., Lombamo F., Alemu A., Yohanise M., Assefa Z., Shibru E., Beyene M., kitila G., Getahun G., Sifer D., Aklilu M., Regasa F. and Deresa A. (2020): Assessment of the current rabies situation and its management in epidemic areas of southern Ethiopia. Highlights in BioScience, Volume 3. *http://dio:10.36462/ H.BioSci.20212*
79. Teklu G.G., Hailu T.G. and Eshetu G.R. (2017): High Incidence of Human Rabies Exposure in Northwestern Tigray, Ethiopia: A Four-Year Retrospective Study. *PLoS Negl Trop Dis* 11(1): e0005271. doi:10.1371/journal.pntd.0005271
80. Ebuy Y., Alemayehu, T., Reda, M., Berhe M. and Bsrat, A. (2019): Community Knowledge, Attitude and Practice on Rabies, Incidence in Humans and Animals and Risk Factors to Rabies in Selected Districts of Tigray Region, Ethiopia. *Nigerian Veterinary Journal*, 40(2): 147-163. *https://dx.doi.org/10.4314/nvj.v40i2.7*
81. Letebrhan G., Gebretsadik B., Aregawi G.B. and Alefech A. (2018): Rabies prevention and control practice and associated factors among dog owners in Aksum town and LaelayMachew district, north Ethiopia: community based comparative cross-sectional study. *https://doi.org/10.1101/436493*
82. Awoke A., Ashenafi A., Samuel D. and Birhanu A. (2015): Assessment of Knowledge, Attitude and Practice on Rabies in and Around Debretabor, South Gondar, Northwest Ethiopia *International Journal of Basic and Applied Virology* 4(1): 28-34.
83. Amare B., Desalegn M. and Abraham T. Rabies: (2020): Knowledge, Attitude and Practices in and Around South Gondar, North West Ethiopia. *Diseases*, *8*; 5.
84. McGettigan J. (2010): Experimental rabies vaccines for humans. *Expert Rev Vaccine*; 9: 1177–86.
85. Montagnon B., Fanget B. and Nicolas A.J. (1981): The large scale cultivation of Vero cells in micro-carrier culture for virus vaccine production: preliminary results for killed poliovirus vaccine. *Dev. Biol. Stand*, 47: 55- 64.
86. World Health Organization (WHO) (2018): Expert Consultation on Rabies: 3rd report: Geneva.
87. Gemechu R. (2017): Review on Economic Importance's of Rabies in Developing Countries and Its Controls.
88. Catherine M. and Brown (2011): Compendium of Animal Rabies Prevention and Control: Committee Compendium of Animal Rabies Prevention and Control.

Access this Article in Online

Quick Response Code	Website: www.ijcrims.com
	Subject: Medical Sciences

How to cite this article:
Tewodros Sadado Samago. (2023). Rabies disease and its current status in Ethiopia: A review. Int. J. Curr. Res. Med. Sci. 9(8): 19-35.
DOI: http://dx.doi.org/10.22192/ijcrms.2023.09.08.004