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A REVIEW OF RABIES IN LIVESTOCK AND HUMANS IN ETHIOPIA

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Abstract

Rabies, a viral disease caused by lyssa virus of family Rhabdoviridae, is a fatal zoonotic disease with worldwide occurrence and endemic in developing countries of Africa and Asia. Rabies generally affects all warm-blooded animals, but it is primarily a disease of dogs in Ethiopia because access to suspected domestic canids and pets are not controlled indoor or by immunization. The major means of transmission of the disease is through any types of bite, scratch, or other situation in which saliva, cerebral, spinal fluid, tear, or nervous tissues from suspected or known rabid animal or person enters an open wound, is transplanted into, or comes in contact with mucus membrane of another animals or person. One of retrospective study of rabies in Addis Ababa from 1990 – 2000 indicated that an average of 2,200 people per year received post – exposure antirabies treatment while 95% of the reported fatal human rabies case was due to dog bites. The widespread use of traditional medicine among urban and rural population of Ethiopia could be attributed to cultural acceptability, physical accessibility and economic affordability. Individuals who are exposed to the rabies virus often see traditional healers for the diagnosis and treatments of the disease. Once the virus entered into body of exposed individuals through wound (abrasion) or direct contact with mucosal surface, then there, it replicates in the site of deposit (bitten site), where local viral proliferation occurs, and get access (viral attachment) to motor endplates. The clinical sign of the disease is nonspecific and difficult to differentiate without laboratory test, but some of signs such as pupil dilation in some case, paralysis (last stage) and hydrophobia are some characteristic signs. The control of access to domestic canid to other suspected animals is not only prevention method but also is treatment measures. Mass vaccination of dogs and removal of stray canids are the best measure of control. In general, this study provides an overview of the current status of Rabies in livestock and human in Ethiopia.

Keywords: Rabies; Epidemiology; Warm-Blood; Canids; Vaccine; Lyssa Virus.

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1. Introduction

The dictionary tells us that rabies is derived from the Latin *rabere*, "to rage or to rave", as is the corresponding adjective rabid; *rabere* possibly may have earlier origin in the *Sanskrit rabhas*, for "violence" (Drew, 2004). The Greeks adopted their own word, *Lyssa* meaning "madness", for rabies; this in turn is still reflected in English in *Lyssophobia*, described in the oxford English Dictionary as "a morbid dread of hydrophobia, the symptoms of which sometimes simulate those of the actual disease" (Shite *et al*., 2015) and also according to Chernet and Nejash, (2016), the name *Rhabdo* comes from the Greek and identifies the characteristic bullet or rod-shape of the viruses.

Rabies is a deadly zoonotic disease with world-wide occurrence and is transmitted mostly by carnivores to humans and livestock. It is known to cause large number of deaths in humans and animals each year. It is the most serious zoonotic disease of virus which is released in the saliva of infected animals that someone might encounter (Deressa *et al.,* 2010; Reta *et al.,* 2014).

Rabies, a viral disease that affects all warm-blooded animals, is widespread in many regions of the world. Rabies is viral disease that affects warm blooded mammals. The virus shades in the saliva of clinically ill animals and is transmitted through a bite (Windsor, 2004; Deressa *et al.,* 2010). The virus affects virtually all mammals and infected species invariably die from the disease once clinical signs are manifested. Once clinical symptoms appear, it is almost 100% fatal. More than 95% of human rabies cases are due to dog bites and the rest associated with cat, fox and other carnivores (Windsor, 2004; Jemberu *et al.,* 2013; Admasu *et al.,* 2014; Aga *et al.,* 2015).

Rabies is a disease of brain causing encephalitis, almost inevitably fatal zoonotic disease. It has worldwide distribution. Humans and nearly all mammals are susceptible. Beside poliomyelitis and pox, rabies is one of the longest known infectious diseases in human history. Rabies virus infection most commonly occurs when a rabid animal bites an animal or a person (Guadu *et al.,* 2014; Shite *et al.*, 2015) and causes an acute viral disease of the central nervous system (CNS) that affects humans and other mammals.

The main reservoir for humans is known to be carnivores. Rabies is almost invariably fatal once the clinical signs develop (Reta *et al.,* 2013; Shite *et al.,* 2015) and it is endemic in developing countries of Africa and Asia where it is responsible for causing deaths in human and livestock. The annual cost of rabies in Africa and Asia was estimated at 583.5 million USD most of which is due to cost of post exposure prophylaxis (PEP). Ethiopia being one of the developing countries is highly endemic for rabies. Globally, human mortality from endemic canine rabies was estimated to be 55,000 deaths per year and 56% of the estimated deaths occur in Asia and 44% in Africa and was responsible for 1.74 million disability adjusted life years (DALYs). About 98% of the human rabies cases occur in developing countries that possess large number of dogs, many of which are stray dogs (WHO, 2004, Jemberu *et al.,* 2013; Guadu *et al.,* 2014; Moges, 2015).

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Rabies is a major public-health problem in most of the parts of the developing world, where the dog plays a principal role as a reservoir and transmitter of the disease to humans. Human rabies, transmitted by dogs, is an important public health issue in Ethiopia (Esayas *et al.,* 2012). It is a particular problem in the larger cities of developing countries, with sprawling, impoverished suburbs and high densities of dogs. In Ethiopia it is an important disease that has been recognized for many centuries. The first major outbreaks in dog were reported in many parts of Ethiopia in 1884 and reported in and around in Addis Ababa in August, 1903s (Windsor, 2004, Ali *et al.,* 2010; Deressa *et al.,* 2010; Esayas *et al.,* 2012).

Urban rabies is essentially maintained by dogs wherever it is endemic world-wide. It is a problem of veterinary and public health importance because of the relationship which exists between man and animals. Regardless of whether or not rabies is present in wildlife reservoirs, over 90% of human deaths from rabies are caused by dog bites (Zewudie, 2009). There is lack of accurate quantitative information on rabies both in humans and animals and little is known about the awareness of the people about the disease to apply effective control measures in Ethiopia (Moges, 2015).

Animal attacks on people are still a huge medical and social problem worldwide resulting in millions of injuries and thousands of deaths (Reta *et al.,* 2014). Animal bites are the main source of rabies virus infection, a dreadful infectious disease that has not yet been brought under control in many parts of the world (Ramos *et al.,* 2015). Deaths due to rabies occur despite the availability of effective vaccines which can prevent the development of fatal rabies cases (Reta *et al.,* 2014).

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. Total of 488 labs confirmed human rabies cases in and around Addis Ababa had occurred between the period 1964 and 1975. The total fatal human cases between 2001 and 2009 were 386 humans with annual range of 35 to 58 people (Hurisa *et al.,* 2013). Surveillance of animal-related injuries could provide useful information for planning and evaluating public health interventions. It is important to know the epidemiology of animal bites and factors influencing post-exposure treatment for preventing human deaths due to rabies, and formulate rabies control strategies (Ramos *et al.,* 2015).

Therefore; the objective of this paper is to give an overview of the current status of Livestock and Human Rabies in Ethiopia.

2. Rabies Distribution in Ethiopia

Rabies, a fatal viral disease of humans and all other mammals, which has been associated with animal bites for centuries and it is the oldest infectious disease known to medical science. Dogs have long been recognized as the main transmitters of the disease to people and animals. When compared with other formidable human diseases such as bubonic plague and smallpox, and animal diseases such as Rinderpest and Anthrax, rabies has probably never caused comparably high numbers of deaths in humans and animals.

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Etiology

Lyssavirus is a causative agent that the members of order are ribonucleic acid (RNA) virus that contains non – segmented, negative and singled – stranded genomes (Radostits *et al*., 2007). Rabies is an acute encephalitis illness caused by rabies virus and virus is the prototype species of the genus *Lyssavirus* in the family of *Rhabdoviridae*. The virus affects virtually all mammals and infected species invariably die from the disease once clinical signs are manifested (WHO, 1989; Drew, 2004) and is a fatal viral zoonosis disease which causes encephalitis in all warm-blooded animals and humans (Krauss *et al.,* 2003).

The name *Rhabdo* comes from the Greek and identifies the characteristic bullet or rod-shape of the viruses (Drew, 2004). The virus is spread through infected saliva in bites, scratches and through licks from infected animals in open wounds or on mucosal (Krauss *et al.,* 2003; Windsor, 2004).

All the *lyssaviruses* share many biological and physicochemical features as well as amino acid sequence characteristics that classify them with other *rhabdoviruses*. These include the bullet shaped morphology helical *nucleocapsid* or ribonucleoprotein core. The five structural proteins of the virion include nucleocapsid protein, phosphoprotein (P), matrix protein (M), glycoprotein (G) and RNA – dependent RNA polymerase or large protein (L) (Jackson and Wunner, 2002).

Although a number of carnivore and bat species serve as natural reservoirs, worldwide rabies in dogs is the source of 99% of human infections and poses a threat to >3.3 billion people (WHO, 2004, Hurisa *et al.,* 2013) and human infection usually occurs following a transdermal bite or scratch by an infected animal. Globally, human mortality from endemic canine rabies was estimated to be 55,000 deaths per year and 56% of the estimated deaths occur in Asia and 44% in Africa (Ali *et al.,* 2013).

Beside *poliomyelitis* and pox, rabies is one of the longest known infectious diseases in human history (Shite *et al.,* 2015). The disease particularly affects developing countries in Asia and Africa. The disease is vaccine preventable and can be controlled through vaccination of exposed humans and source animals, mostly dogs (Aga *et al.,* 2015). The disease is widely distributed throughout the world but more than 95% of human deaths were reported in Asia and Africa. In Ethiopia, rabies is one of the most feared infectious diseases and it has been diagnosed from various parts of the country (Windsor, 2004; Reta *et al.,* 2013).
There are an estimated 60,000 human rabies related deaths worldwide each year. Of these, most cases occur in Asia and Africa (Hurisa *et al*., 2013). About 98% of the human cases occur in developing countries that possess large number of dogs, many of which are stray (Ali *et al*., 2013). Domestic dogs are considered to be the main source (>90%) for human rabies in Africa. Once the symptoms have appeared, the disease ends almost always fatally (Tschopp *et al.*, 2015).

Epidemiology

Sylvatic and urban rabies cycles occur concurrently in some regions, while the sylvatic cycle predominates in others. Rabies can be a serious concern in some rare or endangered species. In

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Africa, the Ethiopian wolf (*Canis simensis*) and African wild dogs (*Lycaon pictus*) are threatened by this virus (Chernet and Nejash, 2016).

Geographic Distributions and Occurrence of Rabies in Ethiopia

An increase in incidence of rabies in foxes result in an increase in incidence of rabies in domestic animals such as cattle, sheep, horse, cat, dog and others (Chernet and Nejash, 2016). The first major outbreaks in dog were reported in many parts of Ethiopia in 1884, especially in the former province of Tigre, Begemder, Gojjam and Wollo. Like other big cities in developing country, the rabies problem has been greatest in Addis Ababa where the disease had been well established and become endemic. The reviewed rabies situation in Ethiopia revealed that 2172 cases of animal rabies had been confirmed in and around Addis Ababa during 1990-2000, where dogs constituted 89.83 % with the incidence rate of 73.2 % (Ali *et al.,* 2010, Deressa *et al.,* 2010).

Rabies occurrences in Human in Ethiopia

The annual reports of the EHNRI (Ethiopian Health and Nutrition Research Institute) indicated that a total of 488 human deaths had occurred from 1964 to 1975 (Deressa *et al.*, 2010). During the period between 1996 and 2000, a total of 9593 post exposure, and a total of 153 fatal human rabies cases were recorded. The cases were originated from Addis Ababa and its surroundings (122), and other regions in the country (31) (Yimer, 2001). Similarly, a study by Moges, (2015) also showed that fatal human rabies cases in Ethiopia reached up to 322 from period 1990 to 2000. Reports show that there is considerable higher dog to human ratio, approximately 1:6 and 1:8 in urban and rural areas, respectively. Such a large number of dogs in both urban and rural settings along with low vaccination imply the risk of rabies circulation and spread to human and other domestic animal populations (Admassu and Mekonnen, 2014).

According to a study finding by Deressa *et al.* (2010), a total of 11,017 (64%) humans from Addis Ababa and 6,187 (35.96%) humans from areas outside of Addis Ababa were advised to take post exposure *antirabies* prophylaxis between 2001 and 2009. Annual post exposure prophylaxis for human rabies ranged from 1026 to 1580 and 300 to 1922 every year for the last nine years in Addis Ababa and for areas outside Addis Ababa respectively.

As stated in the study conducted by Yimer, (2001), dogs contributed to 91.6% of the fatal human rabies cases and 91.6% of the human rabies post exposure cases that necessitated post exposure anti rabies treatments. This result agreed with the study result in Ramos *et al.*, (2015). According to Fekadu, (1982), the study showed that of the 488 humans who died of rabies, 136 (28 per cent) of the patients were bitten on the head, 201 (41 per cent) on the upper extremities and 151 (31 per cent) on the lower extremities. This agrees with the result in Ali *et al.*, (2013) and Admassu and Mekonnen, (2014).

According to the study result in Yibrah and Damtie, (2015), a large proportion human rabies exposure cases were reported among children under 15 years of age (38.5%) and the agreed with the result in Yimer, (2001) and Fekadu, (1982).

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Rabies is an urban human problem in developing countries characterized by the presence of disease in domestic animals such as pet dogs and cats (Shite *et al.,* 2015). In Ethiopia, it is primarily a disease of dogs and many people are at increased risk of being exposed to rabies since man – dog contact is very common (Hurisa *et al.,* 2013). Approximately 10,000 people were estimated to die of rabies annually in Ethiopia which makes it to be one of worst affected (Moges, 2015). Another retrospective study of rabies in Addis Ababa from 1990- 2000 indicated that an average of 2,200 people per year received post-exposure *antirabies* treatment while 95% of the reported fatal human rabies cases was due to dog bites (Admassu and Mekonnen, 2014).

Rabies occurrences in Livestock and wildlife in Ethiopia

During the years (1996 – 2000) in Ethiopia, a total of 7749 animals were observed and examined for rabies and 1228 of them found to be positive. Dogs accounted for 95% of the total animals examined. Most of the time, hyena, jackals, mongooses and cerval cats were animals that were encountered in the occurrence of rabies (Yimer, 2001).

Reta *et al.* (2013), also reported that 87.19% of the dogs examined 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 proportion of dogs diagnosed with rabies was 96.67%% in dogs categorized into this group. This result is agreed with the result in Reta *et al.,* (2014).

Ali *et al.* (2010), conducted research and reported that, out of 2517 animal brain tissue samples examined, 76.9% were positive for Rabies virus. The total of 1936 rabies laboratory confirmed cases in and around Addis Ababa during 2003-2009, 1724 were dogs, 116 cats, 37 cattle, 13 Horses, 19 Donkeys, 13 sheep & goats, 7 Hyenas and 7 Monkeys. Assefa, (2012) and Yimer, (2001) have an agreement with this result.

Myths and Beliefs in Rabies treatment in Ethiopia

It is widely believed in Ethiopia that the skill of traditional health practitioners is 'given by God' and knowledge on traditional medicines is passed orally from father to a favorite child, usually a son or is acquired by some spiritual procedures. Traditional Healing knowledge is guarded by certain families or social groups (Deribe *et al.,* 2006, Shite *et al.,* 2015). The widespread use of traditional medicine among urban and rural population of Ethiopia could be attributed to cultural acceptability, physical accessibility and economic affordability as compared to modern medicine. Healing in Ethiopian traditional medicine is not only concerned with curing of diseases but also with the protection and promotion of human physical, spiritual, social, mental and material wellbeing (Deribe *et al.,* 2006, Adimasu and Mekonnen, 2014).

Perceptions of local people in Ethiopian show that rabies outbreak occurs annually between July and September. Further interviews of elder from different regions of the country indicated that these seasonal outbreaks were expected phenomena and could be associated with breeding season of dogs (Fekadu, 1982, Moges, 2015).

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In 2010, a total of 750 human rabies exposures and 18 Human rabies fatal cases were reported from different regions in Ethiopia with incidence of 2.4%. Total exposure cases (750) were varying with months (figure 2). As a result, the Ethiopian Health and Nutrition Research Institute (EHNRI) have distributed 20,000 rabies post exposure prophylaxis to safeguard the public. The highest number of exposure to rabies and human fatal rabies cases report from Oromia Regional State. Amhara Regional state is second in fatal rabies cases, but Tigray has no fatal rabies cases even though second in exposure to rabies (Abraham *et al.,* 2010).

The domestic dog is the most important vector of human exposure. Annual reports of the Ethiopian Health and Nutrition Research Institute indicated a total of 488 human deaths that occurred in 1964 and 1975 (Deressa *et al.,* 2010, Hurisa *et al.,* 2013). Most human deaths from the disease occur in endemic countries. Human mortality from endemic canine rabies was estimated to be 55, 000 deaths per year and was responsible for 1.74 million disability adjusted life years (DALYs) losses each year (Jemberu *et al.,* 2013). The magnitude of the problem is higher in big cities like Addis Ababa linked with the presence of large population of stray dogs and associated factors (Ali *et al.,* 2013).

There are 50,000–55,000 people dying from rabies worldwide each year and over 3 billion people continue to be at risk of rabies virus infection in over 100 countries in the 21st century. In Ethiopia, approximately 76 persons per million of the population receive anti-rabies post-exposure treatments annually due to the widespread nature of rabies in the country (Reta *et al.,* 2014, Ramos *et al.,* 2015).

The outbreak of rabies is believed to occur annually between July and September in traditional Ethiopian believes and interviews of elders from different regions of the country indicated that these seasonal outbreaks were expected phenomena (Fekadu, 1982). To test this belief, a survey on the incidence of rabies was carried out between 1964 and 1975, mainly in the capital city of Addis Ababa and the surrounding area. This report thus reviews the incidence of rabies in the capital and its vicinity and the control measures taken; it also identifies some factors related to the maintenance and spread of the disease (Fekadu, 1982, Deressa *et al.,* 2010). In Ethiopia, individuals who are exposed to rabies virus often see traditional healers for the diagnosis and treatment of the disease. These widespread traditional practices of handling rabies cases are believed to interfere with timely seeking of Post exposure prophylaxis (PEP) (Moges, 2015).

The Ethiopian wolf is endemic to Ethiopia and is the world's most endangered *canid*. Less than 400 individuals now survive in six fragmented populations in the afroalpine highlands of Ethiopia and only two of these populations may be viable in the long term. The species is ultimately threatened by habitat loss as expanding human populations push into afroalpine habitat (Laurenson *et al.,* 1999, Randall *et al.,* 2004).

Transmission

Rabies virus is usually transmitted from animal to animal through bites (Windsor, 2004, Shite *et al.,* 2015). A rabies exposure is any bite, scratch, or other situation in which saliva, cerebral spinal fluid, tears, or nervous tissue from a suspect or known rabid animal or person enters an open wound, is transplanted into, or comes in contact with mucous membranes of another animal

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or person. The common mode of transmission of rabies in man is by bite of a rabid animal or the contamination of scratch wounds by virus infected saliva (Chernet and Nejash, 2016) and of both wild and urban rabies occurs mainly when an animal that is shedding virus in its saliva bites another susceptible animal or humans. Spread of the disease is often seasonal, with high incidence in late summer and autumn because of large scale movement of wild animals at the mating time and in pursuit of food (Shite *et al.,* 2015). Rabies virus is transmitted by contamination of a fresh wound with infected saliva from the bite of a rabid animal or from licking abraded skin or mucous membranes. Respiratory and oral transmission can also occur. The main determinant of transmission is the population density of non-immunized susceptible key host species that are free roaming within an ecosystem (MoARD, 2010).

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 (Windsor, 2004, Deressa *et al.,* 2010). Once the rabies virus enters the body, it begins to multiply in the area near the entry site (Deressa *et al.,* 2010, Moges, 2015).

Usually transmission occurs by bite with rabid canine and also under unusual circumstances by inhalation of large amounts of aerosolized rabies virus and through organ transplantation from rabies infected patients (Jemberu *et al.,* 2013). Rabies-infected animals have rabies virus in their salivary glands at high titers which can be even greater than in the brain (Esayas *et al.,* 2012).

The presence of high population of dogs with improper management contributes for high endemic condition of canine rabies in Ethiopia. In canine rabies endemic countries like Ethiopia, rabies has also significant economic importance by its effect on livestock, and in Africa and Asia, the annual cost of livestock losses as a result of rabies is estimated to be US$ 12.3 million (Jemberu *et al*., 2013, Serebe *et al.,* 2014, Guadu *et al.,* 2014).

Rabies is mainly rural transmitter, the hematophagous bat (*Desmodus rotundos*), that transmits the disease to herbivores, as these are the most common food source. Cycle in wild disease is transmitted to animals like fox, wolf, monkey, coon, skunk, among others. These animals can be a source of food for the hematophagous bat (Shite *et al.,* 2015). Transmission to people occurs predominantly via infected animal bite or scratch as well as via their saliva through mucosa and broken skin (Tschopp *et al.,* 2015). Rabid dogs are the principal sources for the transmission to human. The transmission almost always occurs by an animal bite that inoculates the virus into the wounds. Virus inoculated into a wound does not enter the bloodstream directly bur is taken up at a nerve synapse to travel to the brain; it causes encephalitis (Serebe *et al.,* 2014).

Host Range

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) (Chernet and Nejash, 2016). Many animal species can be regarded as accidental hosts or ‘dead end’ hosts and these species have no epidemiological significance in sustaining rabies epidemics. These include humans and other primates, horses, cattle, sheep and pigs. The most common hosts are domestic dogs, cattle and man in Ethiopia (Moges, 2015). All warm-

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blooded animals are susceptible to rabies (MoARD, 2010), 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). An epizootic occurs when the incidence of disease increases markedly in the reservoir species (Admasu and Mekonnen, 2014, Chernet and Nejash, 2016).

Pathogenesis and Clinical Signs

Rabies virus enters the body through wounds or by direct contact with mucosal surfaces, but cannot cross intact skin. 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 (Shite *et al.*, 2015, Chernet and Nejash, 2016).

The initial clinical signs are often nonspecific and may include fearfulness, restlessness, anorexia or an increased appetite, vomiting, diarrhea, a slight fever, dilation of the pupils, hyperreactivity to stimuli and excessive salivation. The first sign of post-vaccinal rabies is usually lameness in the vaccinated leg (Chernet and Nejash, 2016). The course may be divided into 3 phases namely prodromal, excitative (excitement) and paralytic or end stage. During the prodromal period which lasts approximately 1-3 days, animals show only vague central nervous system signs, which intensify rapidly. The term "furious rabies" refers to animals in which aggression (excitatory phase) pronounced (Moges, 2015).

Prodromal Stage

After a certain incubation period, the onset of clinical symptoms follows. Behavioral changes might occur, i.e. aggressiveness and no fear of humans in wild animals or abnormalities in appetite (Chernet and Nejash, 2016). The period lasts approximately 1-3 days, animals show only vague central nervous system signs, which intensify rapidly (Moges, 2015, Shite *et al.*, 2015).

Excitement (Furious) Phase

The animal often bites any material. Rabid dogs, for example, may develop a typical high barking sound during furious rabies (Chernet and Nejash, 2016). The furious phase is characterized by an increase in aggressiveness and hyperexitability and there is a tendency to bite at inanimate objects and at other animals. Affected animal may roam over long distances. (Moges, 2015) and is characterized by restlessness, wandering (aimless movement with speed), howling, polypnea, drooling and attacks on other animals, people or inanimate objects. Affected animals often swallow foreign objects such as sticks and stones (MoARD, 2010). Nocturnal animals may be visible during the day (Chernet and Nejash, 2016).

Paralytic (Dumb) Phase

The "dumb" form of rabies is characterized by progressive paralysis (MoARD, 2010, Chernet and Nejash 2016). It is first manifested by paralysis of the throat and masseters muscle often

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with profuse salivation and in ability to swallow: Hydrophobia (Shite *et al.*, 2015, Chernet and Nejash, 2016) and it can salivate profusely. 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 (Moges, 2015).

The clinical signs of rabies are rarely definitive. Rabid animals of all species usually exhibit typical signs of CNS disturbance, with minor variations among species (Shite *et al.*, 2015). Several factors influence the duration of the incubation period. These include the virus strain, virus dose, the distance of the bite site from the central nervous system and the richness of the sensory enervation at the site of virus entry into the body (MoARD, 2010, Yibrah and Damtie, 2014). The animals become irritable and with the slightest provocation, may viciously and aggressively use its teeth, claw, horns or hooves (MoARD, 2010, Shite *et al.*, 2015).

The virus shades in the saliva of clinically ill animals and is transmitted through a bite. Once clinical symptoms appear, it is almost 100% fatal. More than 95% of human rabies cases are due to dog bites and the rest associated with cat, fox and other carnivores (Aga *et al.*, 2015).

After inoculation of infectious saliva by bite (Moges, 2015) and virus enters the body (Deressa *et al.*, 2010), the virus may either persist and replicate in the striated muscles of inoculation site for two weeks or follow a relatively rapid centripetal to the central nervous system, with replication and dissemination prior to the development of a significant immune response (Moges, 2015). It travels along the nerve to the center of multiplication (the brain). The virus may then spread to the salivary glands or other parts of the body. This incubation period lasts a varying amount of time; it can range from days to years, but the average length is 3-8 weeks (Deressa *et al.*, 2010). Centrifugal spread of virus may lead to the invasion of highly innervated sites of various tissues, including the salivary glands. During this period of cerebral infection, the classic behavioral changes associated with rabies develop (MoARD, 2010).

Once virus reaches the brain, it spread centrifugally to a variety of organs, the spread into the salivary gland, which represents the final phase of infection, is important from animal to animal and from animal to human transmission (Moges, 2015, Shite *et al.*, 2015). Destruction of spinal neurons results in paralysis, but when the virus invades the brain, irritation of higher centers produces manias, excitement and convulsions, and death is usually due to respiratory paralysis (drooling of saliva). The clinical signs of salivation, indigestion and pica, paralysis of bladder and anus and increased libido all suggest involvement of the autonomic nervous system, including endocrine glands (Moges, 2015).

Diagnosis

By history of animal exposure, diagnosis can be carried out (Shite *et al.*, 2015). Most diagnostic tests for rabies virus in animals need brain material for diagnosis and as such are often only possible post mortem. 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 (Chernet and Nejash, 2016).

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In Ethiopia, Rabies diagnosis is performed on live animals by inoculation, cell cultures, serological tests, histological examination, molecular methods and immunohistochemistry (Reta *et al.,* 2013) and Mouse Inoculation Test (MIT**)** is also used in our laboratory in case of FAT test result failure due to sampling and human error for further confirmation and after inoculation, suspected animals show sign of rabies (Deressa, 2012) and brain samples of animals that are submitted to the Ethiopian Health and Nutrition Research Institute's (EHNRI) (the only laboratory in Ethiopia responsible for diagnosis of rabies) laboratory live, suspected of being affected by rabies and are kept in quarantine and finally die or brain of animals submitted by health care seekers/customers after being killed or died (Deressa, 2012, Reta *et al.*, 2013).

Clinical diagnosis of encephalitis can be challenging and difficult, especially in area where rabies is uncommon, and all suspected and probable clinical cases of rabies should be confirmed by laboratory methods when possible (Moges, 2015). The clinical diagnosis of rabies is sometimes suggested by either epidemiological or clinical findings. Observation and quarantine for 10 days of dogs and cats, and euthanasia of suspect animals with examination by the direct fluorescent antibody test (DFA) is recommended (Ali *et al.*, 2014).

Laboratory Tests

The recommended laboratory procedure includes the following tests. The most commonly used and the gold-standard diagnostic test is the Fluorescent Antibody Test (FAT), which detects the virus antigens in brain samples using fluorescent labeled anti-rabies virus antibodies (Reta *et al.,* 2013) and on the impression smears from the brain current recommendations includes sampling of the hippocampus, medulla oblongata, cerebellum or gasserian ganglion. Enzyme linked immunosorbent assay (ELISA) is available for the detection of rabies antigen in animals. Because of false positive diagnosis the technique is in some disrepute (Shite *et al.,* 2015).

Laboratory diagnosis of rabies in humans and animals is essential for timely post-exposure prophylaxis. Although hydrophobia is highly suggestive, no clinical signs of disease are pathognomonic for rabies. Rabies diagnosis may be carried out either *in vivo* or postmortem so that laboratory-based tests based have been developed to conclusively confirm infection (Chernet and Nejash, 2016). Animal specimens should, therefore; be sent to the designated laboratory approved to be capable of undertaking the required laboratory examination (MoARD, 2010). Other methods for the detection of *lyssavirus* antigens, such as enzyme-linked immunosorbent assays (ELISAs) and direct rapid immunohistochemistry tests have provided consistently reproducible results in several laboratories (Moges, 2015). A Rapid Immunodiagnostic Test (RIDT) for detecting rabies virus in brain tissues has been developed. This test is based on the principles of immuno-chromatography (Reta *et al.,* 2013).

Differential Diagnosis

Rabies must be considered in the differential diagnosis of any suspected mammalian meningitis/ encephalitis, distemper, infectious canine hepatitis and cerebral cysticercosis (*Taenia solium*,) in dogs, sporadic bovine *encephalomyelitis* (*Chlamydia psittaci*), *heartwater* in cattle and sheep. Other conditions like mineral/ pesticide poisoning and plant poisoning from *Pennisetum clandestinum* (*kikuyu grass*) in cattle, *Cynanchum* spp (monkey rope) in sheep should be

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considered (Chernet and Nejash, 2016). Several diseases are characterized by signs of abnormal mental stages or paralysis or a combination of both. It should be differentiated from lead poisoning, deficiency (vitamin A), *polioencephalomalacia*, *listeriosis* and enterotoxaemia (Ali *et al.,* 2014).

Clinical signs of rabies can look similar to any illness that causes flaccid paralysis of the larynx, general depression or abnormal aggression and behavioral change may be the key clinical sign for wildlife and domesticated animals. The behavior changes described for rabies can also occur with *canine distemper* in dogs, foxes and ferrets (MoARD, 2010).

Treatment

Treatment is symptomatic for established disease. Non-drug treatment (thorough cleaning and careful management of the wound, nurse in quiet) and darkened room/place) and drug treatment (post exposure) human *antirabies* immunoglobulin (human), 20 IU/kg, human diploid cell strain vaccine (HDCV), 1 ml IM are the best measure (DACA, 2010, Chernet and Nejash, 2016).

The application of traditional medicine to veterinary medicine has been termed as *ethnoveterinary* medicine. It is mainly concerned with *folk* beliefs, knowledge, skills, methods and practices which are used in the healthcare of animals (Fullas, 2010). Traditional medicine is the sum total of the knowledge and practices, whether explicable or not, used in the diagnosis, prevention and elimination of physical, mental and/or social imbalance (Berhanu *et al.,* 2006). Most people use wide variety of traditional treatment in cases of bite by animals (mostly dogs) believed to be rabid (Aga *et al.,* 2015) and traditional medicine (TM) includes *folk* drugs composed of herbs, herbal materials, herbal preparations and finished herbal products (Contain as active ingredients of plant parts, or other plant materials). Herbal medicines include the medicinal products of plant roots, leaves, barks, seeds, berries or flowers (Admassu and Mekonnen, 2014, DACA, 2010). The effectiveness of and safety of these traditionally used *antirabies folk* drugs in the country was not well demonstrated and understood. Some of *folk* drugs include: *Datura Stramoniu, Cucumis ficifolius*, *Euphorbia abyssinica* and *Salix subserrata* (Adimasu and Mekonnen, 2014).

There is lack of information on rabies treatment and prevention both in humans and animals. People have clear understanding on the danger of the disease but believe to cure with different traditional and religious treatment rather than seeking effective post exposure prophylaxis (Aga *et al.,* 2015). Post exposure prophylaxis (PEP) consists of immediate wound cleansing and disinfection, followed by rabies vaccination and the administration of human rabies immunoglobulin (Shite *et al.,* 2015) and pre-exposure (i. e vaccination) and post-exposure treatment regimens for rabies in humans should be made available to all medical practitioners found in the rabies affected areas (MoARD, 2010). Rabies infection is always fatal unless prompt post exposure treatment is administered before symptoms begin (Aga *et al.,* 2015, Shite *et al.,* 2015).

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Control and Prevention

Domestic animal vaccination: The primary components of a rabies control program for companion animals are: immunization and licensing; stray animal control; reporting, investigation, and isolation of animals involved in bite incidents; and public education (Chernet and Nejash, 2016). Multiple vaccines are licensed for use in domestic animal species. Vaccines available include: inactivated or modified live virus vectored products; products for intramuscular and subcutaneous administration; products with durations of immunity from one to 4 years; and products with varying minimum age of vaccination (Moges 2015, Shite *et al.,* 2015).

Animal control: Principles of rabies prevention should focus on excluding wild animals from areas of human and domestic animal habitation and activity, and avoidance of contact with possibly rabid wild animals. 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 (Hurisa *et al.,* 2013, Chernet and Nejash, 2016).

Public health education: Understanding communities' perceptions of cause, mode of transmission, symptoms, treatment and possible intervention measures of rabies is an important step towards developing strategies aimed at controlling the disease and determining the level of implementation of planned activities in the future (Ali *et al.,* 2013) and creating responsible pet ownership, routine veterinary care and vaccination, and professional continuing education. Having about controlling animal and human exposures to rabies can be prevented by raising awareness concerning: rabies transmission routes, and avoiding contact with wildlife. Public education on the risks of rabies transmission from wild animals is paramount to effective disease prevention (Serebe *et al.,* 2014, Aga *et al.,* 2015, Shite *et al.,* 2015, Chernet and Nejash, 2016).

Vaccines, antiviral drugs such as ribavirin, interferon-alpha, passively administered anti-rabies virus antibodies (human immunoglobulin or monoclonal antibodies), ketamine and/or the induction of a coma have been tried in the past, but were usually ineffective (Shite *et al.,* 2015).
It is better to register, license and immunize all dogs in enzootic countries, collect and euthanize ownerless animals and stray dogs. To create awareness, pet owners and the public should be educated to educate about the importance of restriction for dogs and cats and advise them against keeping wild animals as a pet (Moges 2015).

According Chernet and Nejash, (2016), rabies control strategies include quarantine, confirmation of diagnosis, determining the origin and spread of an outbreak, and specific measures to terminate transmission. All local jurisdictions should incorporate stray animal control, leash laws, animal-bite prevention and training of personnel in their programs (Shite *et al.,* 2015).

3. Conclusion and Recommendations

Rabies is a zoonotic viral infection of all mammals with worldwide distribution. Its importance goes to those wild animals which are in great danger of extinction in the world as it causes high mortality. All the *lyssaviruses* are shared biological and physiochemical features as well as

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amino acid sequence characteristics that classify them with other *rabidoviruses*. In Ethiopia, the disease is endemic and a threat to both urban and rural community due to large numbers of stray dogs and varieties of wild carnivores. Rabies is a major public health problem in most parts of the country, where the dogs play a principal role as a reservoir and transmitters of the diseases to humans. For instance, a total of 2172 cases of animal rabies had been confirmed in and around Addis Ababa during 1990-2000, where dogs constituted 89.83 % of the cases. The transmission means of the disease in both wild and domestic rabies occurs mainly when an animal that is shedding virus in its saliva bites another susceptible animal or humans and the spread is often seasonal, with high incidence in late summer and autumn. The rabies disease virus encompasses wide ranges of host by affecting all warm- blooded both domestic and wild mammals including humans. Among clinical sign, the dumb or paralytic form is the final and last stage in infected individuals (human being) or livestock. After inoculation of infectious saliva bite and virus enters the body, the virus may either persist and replicate in the striated muscle of inoculation site for weeks or move rapidly centripetally to the central nervous system. The primary measures to prevent and control rabies is controlling in domestic animals, wild animals, health education, awareness creation in public (community) to not access to wild animals.

Generally, based on this review, the following recommendations are forwarded:

- Since rabies outbreaks are frequently occurring and the disease is life threatening, affects all warm blooded mammals, mass vaccination dog of population should be carried out in the country.
- The stray dogs and cats should be removed from the community because most are carrier and reservoirs.
- Post exposure treatment should be given immediately after exposure to bite or scratch by rabid animals.
- All local jurisdictions should incorporate in rabies control, animal and human bite prevention.

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