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REVIEW ON RABIES: EPIDEMIOLOGY, PREVENTION AND CONTROL METHODS

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ABSTRACT

The importance of zoonoses is increasing day by day in public health. Among zoonoses, rabies is a highly fatal viral anthropozoonosis that affects the central nervous system of all warm blooded mammals including humans. It is more prevalent in Asia, Africa and the Latin American countries. The first major outbreaks in dog were reported in many parts of Ethiopia in 1884. The transmission of virus occurs only when the saliva of the infected animal comes into contact with a broken skin or mucous membrane. Histophatological Reliance on the detection of accumulations of Negri-bodies is no longer regarded as suitable for diagnostic assessment because of low sensitivity and alternative laboratory-based tests findings have been developed to conclusively confirm infection. Detection of rabies virus antigen in rabies diagnosis may be carried out either in vivo or postmortem. The main reason for rabies to remain as a neglected zoonotic disease in many developing countries including Asia and Africa is lack of specific diagnostic and surveillance techniques. Generally, elimination of canine rabies is epidemiologically and practically feasible through mass vaccination of domestic dogs which is cost-effective approach to the prevention and elimination of human rabies deaths.

Key words: *Control, Diagnosis, Epidemiology, Rabies*

1. INTRODUCTION

The importance of zoonoses (diseases communicable from animals to humans) is increasing day by day in public health. These diseases have a great impact on health and economy. Among zoonoses, rabies is a highly fatal viral anthropozoonosis that affects the central nervous system of all warm blooded mammals including humans (Deressa *et al.*, 2011). It has been responsible for estimated annual human mortalities of 31,000 and 24,000 in Asia and Africa, respectively, with people mostly at risk of dying due to rabies being those who live in rural areas of these continents (Knobel *et al.*, 2005).

The main reason for rabies to remain as a neglected zoonotic disease in many developing countries including Asia and Africa is lack of specific diagnostic and surveillance techniques. Rabies is one of the major neglected tropical diseases. Its control is more difficult because it is a neglected zoonotic disease, and is endemic in most of the world. Therefore, the aim of this manuscript is to review the epidemiology and prevention strategies of rabies.

2. LITERATURE REVIEW

2.1. Etiology

Rabies virus is a, negative sense; single-stranded, enveloped, bullet shaped RNA virus of the genus *Lyssavirus* under the family *Rhabdoviridae*. Presently, 7 distinct genotypes of RABV have been found to circulate in nature. Classical rabies virus genotype 1 (street and laboratory strains) is the globally prevalent and causing disease in >99% cases in humans as well as animals. The other 6 genotypes named as rabies- related viruses (RRVs) such like Lagos bat virus (genotype-2), Mokola bat virus (genotype-3), Duvenhage virus (genotype-4), European bat Lyssaviruses (genotypes-5 and 6), and Australian bat Lyssavirus (genotype-7), are prevalent in certain areas of Africa, Western and Eastern Europe and Australia (Knobel *et al.*, 2005).

2.2. Epidemiology

Reservoirs of rabies vary throughout the world. The most important animal families in maintaining rabies cycles are *Canidae* (dogs, foxes, jackals, ferrets stoats etc.), *Viverridae* (mongooses, meerkat etc.), *Procyonidae* (raccoon etc.), *Chiroptera* (> 1,200 species of bats), and

Wild (sylvatic) rabies. Canine rabies is dominant in Africa, Asia, Latin America, and the Middle East. In North America and Europe, canine rabies has been practically eliminated; rabies is maintained in wild life (Finnegan *et al*., 2002). Some countries such as the United Kingdom, Ireland, Sweden, Norway, Iceland, Japan, Australia, New Zealand, and Singapore, most of Malaysia, Papua New Guinea, the Pacific Islands and some Indonesian islands have been free of this virus for many years. It has been reported that 98% of human rabies cases occurred in the developing countries of Asia, Africa and Latin America (Kahin, 2005).

It is more prevalent in Asia, Africa and the Latin American countries. Rabies affects all warm blooded animals and incidences have been reported from all continents except Australia and Antartica. Asia remains the hot spot in terms of both incidences and reservoirs. In Asia, over 3 billion human beings are at the risk of canine mediated rabies and it witnesses 30000 deaths annually (1 death every 15 minutes). The mortality rate in children below 15 years of age is more. The South Asian region records a maximum incidence of rabies outbreak, with India and Bangladesh in the lead (Singh *et al.*, 2017).

2.3. Rabies Distribution 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. 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 (Chernet and Nejash, 2016).

Ethiopia being one of the developing countries is highly endemic for rabies. Dogs are responsible for rabies in almost 90% of the cases. The human-animal interface is accelerating, expanding, and becoming increasingly more consequential. In Ethiopia, rabies is an important disease that has been recognized for many centuries. Historic and current emphasis on interdisciplinary approaches to rabies control provides a prime example of a zoonotic disease that is being managed more effectively via the One Health approach (Regea, 2017).

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. 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 (Oyda and Megersa, 2017a).

2.4. 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 (Table 1) (Oyda and Megersa, 2017b). (Reta *et al.*, 2014) 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.

Table 1: Prevalence of Rabies in Animals in Ethiopia

No of animals Examined	Number Positive	Prevalence	No of death	Study Area	Year	Citation
7749	1228	15.84%	-	All over the country	1996-2000	Eshetu, Y., 2001
20414	18243	89%	-	Within and around Addis Abeba	2001-2009	Asefa *et al*. 2010
3460 (brain sample)	2593	75%	-	Within and around Addis Abeba	2001-2009	Asefa *et al*. 2010
23	-	-	13	North Gonder Zone	2009-2010	(Jemberu *et al.*, 2013; Reta *et al.*, 2014)

2.5. 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.*, 2011). 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). 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 (Afework *et al.*, 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 *anti rabies* 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 (Table 2, Fig. 1).

Table 2: Prevalence of Rabies in Humans in Ethiopia

#of humans exposed	No people advised to take PEP	No of death	Study Area	Year	Citation
9593	-	153	All over the country	1996-2000	Eshetu, Y.,2001
-	17204	384	Within and around Addis Abeba	2001-2009	Asefa *et al.*, 2010
91683	683		Gambo Rural Hospital (West-Arsi zone)	2006-2010	Jose, 2015
32	-	3	North Gonder Zone	2009-2010	Jemberu, 2013
2180	-	-	Suhul Hospital, Shire Endeselase, Northr en Tigray	2012-2015	(Teklu *et al.*, 2017)

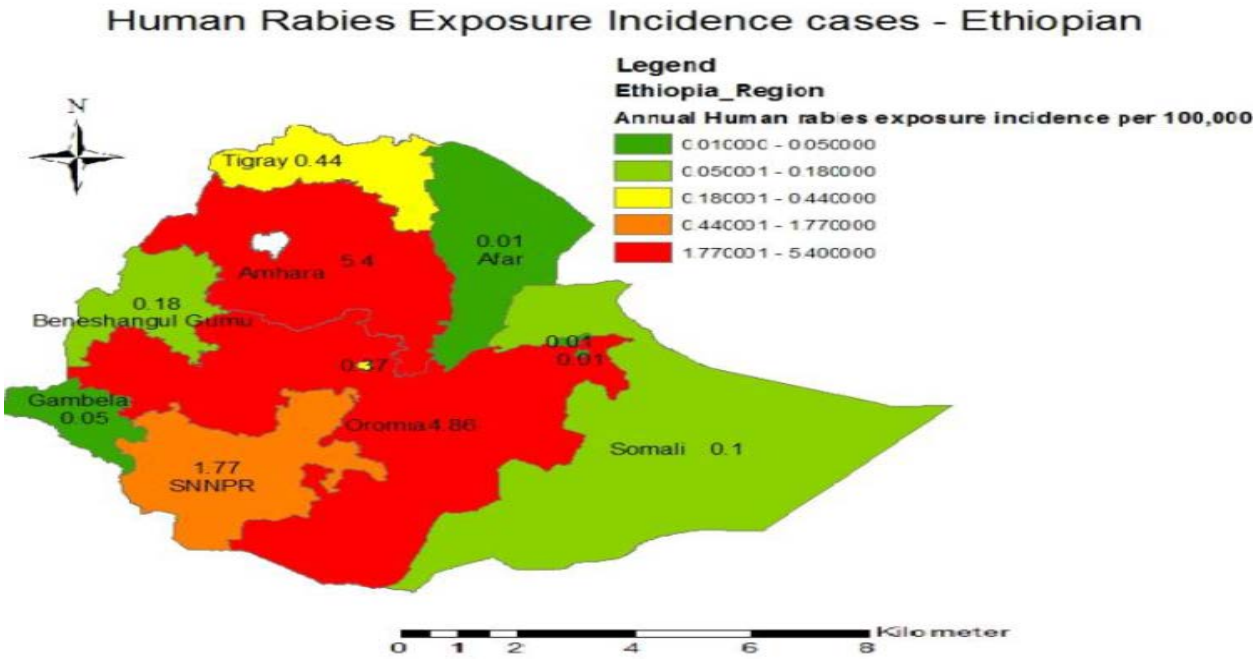

Fig1: Map of rabies outbreaks in 2010 by regions

Source: The National Workshop on Rabies Prevention and Control in Ethiopia (2012)\

2.6. Source of Infection and Transmission

The source of infection 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). In Africa, evidence indicates that the primary rabies virus maintenance cycle is among domestic dogs although other carnivores maybe involved as non-maintenance population Rabies in human beings develops from the bites of infected animals, predominantly dogs (91.5%) that have contracted the virus from feral or fellow infected creatures (Menezes, 2008).

The transmission of virus occurs only when the saliva of the infected animal comes into contact with a broken skin or mucous membrane. The risk associated with the infection is reported to be high through the bite (5%-80%) than scratches or licks (0.1% -1%) from the affected animal. Fatality depends on the site of bite and the quantum of virus in the saliva of bitten rabid animal (Hemachudha *et al.*, 2013). Exposure to live attenuated vaccines during the production stage may have potential risk. The persons who are involved in capturing the animals for birth control

programmes are also at potential risk because of the threat of bite and scratch (Sparkes *et al.*, 2015).

In Ethiopia, retrospective data registered between 2001 and 2009 at one center (EPHI) showed that fatal human cases were 386 with annual range of 35 to 58 (Asefa *et al*., 2013). Study done at North Gonder of Ethiopia indicated an annual estimated rabies incidence of 2.33 cases per 100,000 humans; 412.83 cases per 100,000 dogs; 19.89 cases per 100,000 cattle; 67.68 cases per 100,000 equines, and 14.45 cases per 100,000 goats. Dog bite was the source of infection for almost all fatal rabies cases throughout the country (Jemberu *et al.*, 2013).

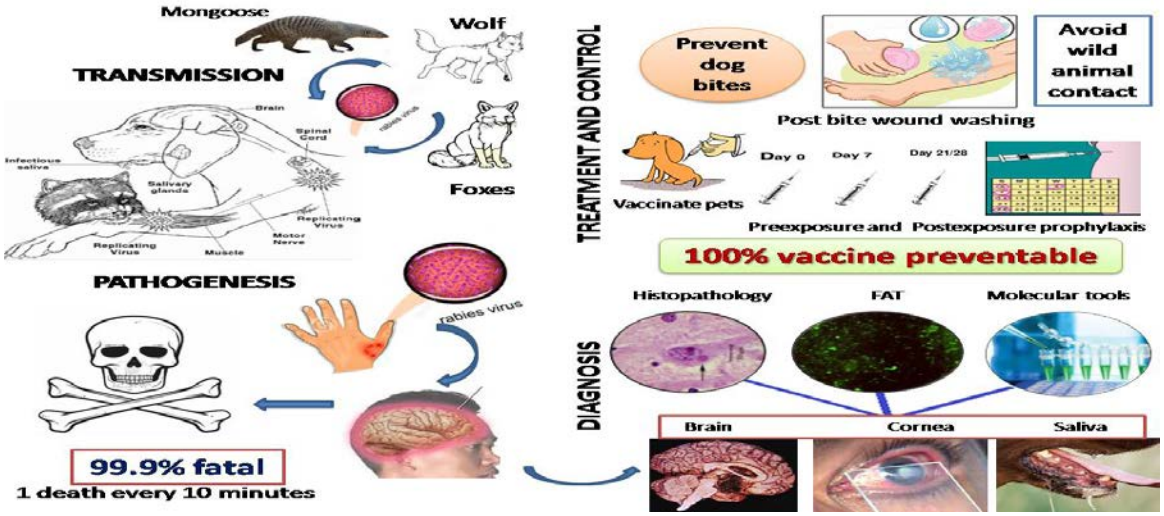

Figure 2: Transmission of rabies, diagnosis and elements of prevention and control

Source: (Singh *et al*., 2018)

2.7. Pathogenesis

Rabies virus enters the body through wounds or by direct contact with mucosal surfaces. It cannot cross intact skin (Ugolini, 2011). Subsequently, the virus infects local sensory and motor neurons and replicate locally in skeletal muscle cells or attach directly to nerve endings, in particular to nicotinic acetylcholine receptors at motor-end plates. After peripheral nerve entry, the virus migrates in centripetal retrograde axonal transport to the CNS at the estimated speed of 5–100 mm/day.

The incubation period varies from 5 days to several years (usually 2-3 months; rarely more than 1 year), depending on the amount of virus in the inoculum, the density of motor endplates at the wound site and the proximity of virus entry to the central nervous system. The overall outcome of an exposure to RABV depends in part upon the rabies genotype (different strains and mutants) or variant involved, its pathogenicity (apoptogenicity and neuroinvasiveness), the dose of virus inoculated (severity of exposure), the route as well as the host species and its susceptibility to the particular pathogen together with innate and adaptive immune responses of the host (Chalchisa *et al.*, 2018).

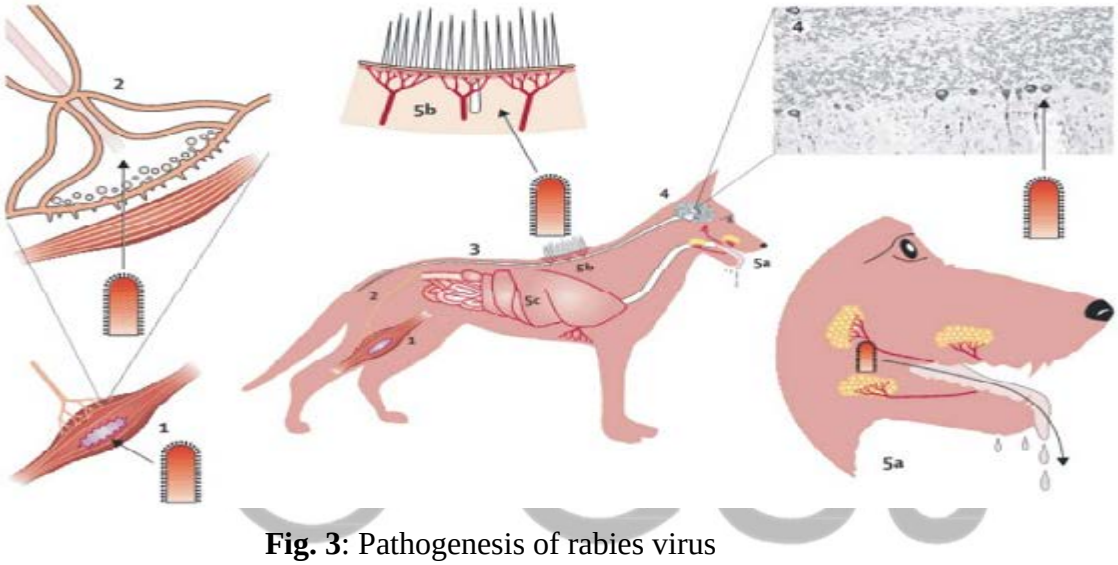

Fig. 3: Pathogenesis of rabies virus

Source: (Ugolini, G., 2011)

2.8. Clinical Findings

The clinical signs of rabies are rarely definitive. In humans, initial symptoms typically appear within 30 to 60 days following exposure and can include pain and itching at the site of the virus entrance into the body, restlessness, headache, fever, nausea, sore throat, and loss of appetite. Symptoms of rabies in animals include an evident change in behavior, loss of appetite, fever, change in phonation (e.g the sound of a dog's bark), greater excitement, aggression, paralysis (especially in the lower jaw), and increased salivation. All rabies infected species usually exhibit typical signs of CNS disturbance, with minor variations among species. The clinical course may be divided into three phases (Radostits *et al.*, 2006).

Prodromal phase after a certain incubation period, the onset of clinical symptoms follows. It usually lasts for about 1-3 days, minor behavioral changes might occur, i.e. aggressiveness in tame animals, daytime activities in nocturnal animals, no fear of humans in wild animals or abnormalities in appetite.

Excitement (Furious): This is "mad-dog syndrome" although it may be seen in all species. The animals become irritable and, with the slightest provocation, may viciously and aggressively use its teeth, claws, horns, or hooves. The posture and expression is one of alertness and anxiety, with pupils dilated. Noise may invite attack. Carnivores with this form of rabies frequently roam extensively, attacking other animals, including people, and any moving object. As the disease progresses, muscular in coordination and seizures are common. Death results from progressive paralysis.

Paralytic (Dump) phase: The paralytic (dumb) stage of rabies is characterized by progressive paralysis. In this form, the throat and masseter muscles become paralyzed; the animal may be unable to swallow and starts to salivate profusely. There may be facial paralysis or the lower jaw may drop. Death usually occurs within 2 to 6 days, as the result of respiratory failure

2.9. Diagnosis

Infection with rabies virus can be difficult to diagnose at ante-mortem. Although hydrophobia is highly suggestive, no clinical signs of disease are pathognomonic for rabies. Laboratory diagnosis: Histophatological Reliance on the detection of accumulations of Negri-bodies is no longer regarded as suitable for diagnostic assessment because of low sensitivity and alternative laboratory-based tests findings have been developed to conclusively confirm infection. Detection of rabies virus antigen in rabies diagnosis may be carried out either in vivo or postmortem. Most diagnostic tests for rabies virus in animals and humans need brain material for diagnosis and as such are often only possible post mortem. Brain samples are most readily taken by breaching the skull and sampling directly. Brain smears or touch impressions are used for the detection of virus antigen with the fluorescent antibody test (FAT) for both human and animal samples (Radosttis *et al*., 2006).

In Ethiopia Rabies diagnosis is performed on live animals and brain samples of animals that are submitted to the Ethiopian Health and Nutrition Research Institute's 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.

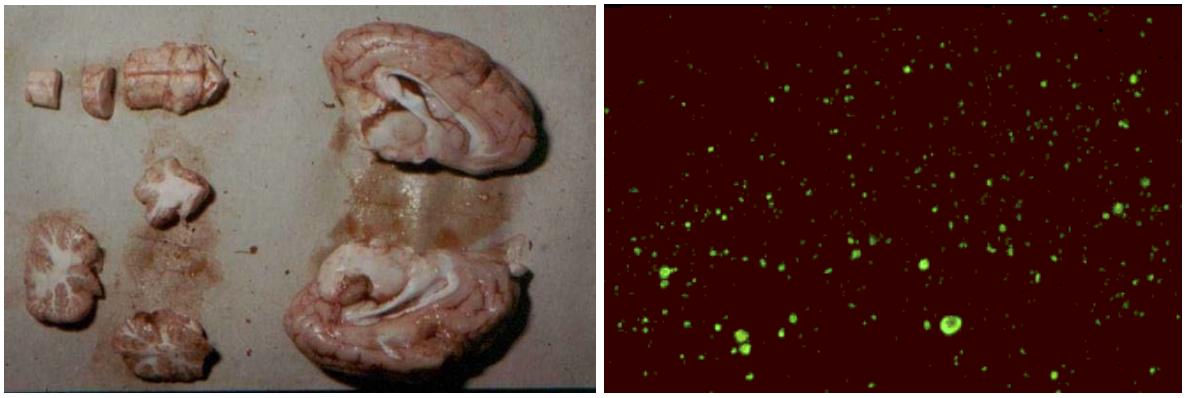

Figure 4: Brain tissue sample & detection of virus antigen with the fluorescent antibody test

Histopathological changes do not reflect the severity of the clinical disease. The presence of Negri bodies is considered as pathognomic for rabies, but these are only seen in about 50 - 75% of cases. These are found most commonly in ganglionic cells of the hippocampus and in Purkinje cells of the cerebellum. Spongiform lesions may be found in the grey matter, in the neuropil and in the neuronal cell bodies of thalamus and cerebral cortex. Spinal and cranial nerve ganglia particularly, gasserian ganglia may show an inflammatory response. There is no visible inflammatory response in the brain of some rabid individuals.

2.10. Differential diagnosis

Can involve many agents and syndromes (e.g. other viral encephalitis, tetanus, listeriosis and poisoning) and co-infections, such as malaria, lead poisoning, deficiency (vitamin A), *polioencephalomalacia*, enterotoxaemia can lead to misdiagnosis.

2.11. 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). Rabies infection is always fatal unless prompt post exposure treatment is administered before symptoms begin (Shite *et al.*, 2015).

The application of traditional medicine to veterinary medicine has been termed as *ethno-veterinary* medicine. It is mainly concerned with folk drugs, beliefs, knowledge, skills, methods and practices which are used in the health care of animals. 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. Most people use wide variety of traditional treatment in cases of bite by animals (mostly dogs) believed to be rabid 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). Herbal medicines include the medicinal products of plant roots, leaves, barks, seeds, berries or flowers (Admassu and Mekonnen, 2014).

2.12. Economic Impacts of Rabies

In canine rabies endemic countries like Ethiopia, it 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).

Table 4: The yearly impacts and economic burdens of canine rabies vary by continent (Hampson *et al.*, 2015)

Impact	**Africa**	**Asia**	**Latin America**
Death	21,502	37,266	182
PEP treatments	1,387,848	26,589,22	835,656
Cost of prevention (US$)	15,948,303	42,115,175	63,287,263
Dog vaccination	14,520,789	38,528,371	61,033,617

Dog popilation management	1,305,247	3,369,953	1,930,503
Surveillance	122,267	216,851	323,143
Productivity losses	773,352,665	3,852,276,021	30,242,012
Livestock losses	279,546,173	219,045,223	12,187,129
Preventable costs/person	1,282,4624121.23	1.67	0.54
Cost of prevention/person	0.02	0.01	0.12
Total costs (us$)	1,086,204,795	4,155,588,862	169,839,505.7

2.13. Major Challenges and Gaps in Rabies Prevention and Control

After all the deliberations, the major challenges clustered in four categories are: Low effort of animal rabies control (no defined legislation/guidelines, fragmented stakeholders efforts, lack of animal rabies surveillance, insufficient availability and misuse of vaccines, low vaccination coverage), Low effort in human rabies prevention (absence of modern tissue culture vaccine, low public awareness, limited PET service and in adequate skill on the use of PET, Weak human rabies surveillance), Limited rabies diagnostic capacity (rabies diagnoses technology, absence of trained manpower, only one laboratory facility, lack of inter-sectoral effort), and Coordination (lack of strong collaboration/networking among concerned stakeholders, no defined role and responsibilities of stakeholders in rabies prevention and control activities).

2.14. Prevention and Control

Long before the recognition of bat and other wildlife rabies and the availability of modern vaccines, rabies in Japan was successfully controlled through mass vaccination of dogs. Large-scale oral vaccination campaigns were first used to fight rabies epidemic successfully in foxes during 1980s. According to one health definition established by the paraprofessional One Health Task Force, the confluence of environmental, animal, and human interactions can be used as opportunity by working together to fight such diseases like rabies. The paraprofessional health team recognizes that there is no more important disease to begin educating and developing our

efforts than rabies. Progression of countries from endemic rabies to elimination of dog-mediated rabies by implementation of sustained mass dog vaccination programmers.

For developing countries like Ethiopia, strategy should be developed to prevent and control the disease. Sustainable resources for effective dog vaccination are likely to be available through the development of inter sectoral financing schemes involving both medical and veterinary sectors. Prevention of animal rabies through dog vaccination, better public awareness, improved access to cost-effective and high-quality human rabies vaccines, and improved local capacity in rabies surveillance and diagnostics are essential for the elimination of human rabies. Generally, elimination of canine rabies is epidemiologically and practically feasible through mass vaccination of domestic dogs which is cost-effective approach to the prevention and elimination of human rabies deaths (Aga *et al*, 2016).

Strategies for the prevention of human rabies are aimed at protecting those at highest risk of exposure, post exposure treatment and supportive management for the clinically ill. To mitigate those economic losses due to rabies, it is important to prevent through use of vaccine and environmental management. There should be magnificent importance of using awareness materials in particular Videos to mobilize the general public and relevant decisive actors vigorously act against the dreadful disease rabies (EHNRI, 2012). 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 (Semayat Oyda and Bekele Megersa, 2017).

Vaccination approaches in control of rabies: Pioneering anti-rabies immunization was performed on a boy (Joseph Meister) by Louis Pasteur in late phase of 19th century. After that plenty of effective and safe, second and third generation vaccines have been developed for use in animals and humans. Currently, a number of vaccines such as recombinant rabies virus strains or rabies antigen-glycoprotein (G protein), either as a component of non-pathogenic viruses, or in plants / form of DNA vaccines are being developed (Ohara *et al.*, 2013). To stimulate the host immunity against rabies infection, normally different forms (live intact, inactivated, attenuated) or purified components of pathogens (outer coat proteins of rabies virus) with high immunogenicity are used. This generates immune response within 2 weeks. These vaccines are administered by IM or ID routes.

If dog population is sufficiently (>70%) covered by rabies vaccination, it will reduce the disease burden in humans. Currently, the rabies vaccines are accessible to prevent and control rabies in animal population (dogs, cats, wild carnivores and bats). The vaccines administered within first few days of post-exposure are reported to decrease the disease by attenuating the virus considerably. Later on the 4 dose series (day 0, 3, 7 and 14) would take care.

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. Multiple vaccines are licensed for use in domestic animal species. It 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.

Wild animal (Wolf) Vaccination in Ethiopia: 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).

The endangered Ethiopian wolves *Canis simensis* are restricted to the Afroalpine areas of Ethiopia and live in small populations. Together with habitat loss, diseases transmitted by domestic dogs pose the major threat to their survival. Out of an estimated global population of some 500 individuals, around 300 live in the Bale Mountains National Park, where the Ethiopian Wolf Conservation Programme (EWCP) is based. This crucial population is threatened by recurrent epizootics of rabies, which can decimate local populations by two thirds, over a short period of time (Murray *et al.*, 1986).

2.15. 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 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).

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). 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

All rabies infected species usually exhibit typical signs of CNS disturbance. The source of infection includes members of the families Canidae (dogs, jackals, coyotes, wolves, foxes and raccoon dogs), Mustelidae, Viverridae, and Procyonidae (raccoons), and the order Chiroptera (bats). The transmission of virus occurs only when the saliva of the infected animal comes into contact with a broken skin or mucous membrane. Brain samples are most readily taken by breaching the skull and sampling directly. Brain smears or touch impressions are used for the detection of virus antigen with the fluorescent antibody test (FAT) for both human and animal samples. Histophatological Reliance on the detection of accumulations of Negri-bodies is no longer regarded as suitable for diagnostic assessment because of low sensitivity and alternative laboratory-based tests findings have been developed to conclusively confirm infection. Detection of rabies virus antigen in rabies diagnosis may be carried out either in vivo or postmortem. Generally, elimination of canine rabies is epidemiologically and practically feasible through

mass vaccination of domestic dogs which is cost-effective approach to the prevention and elimination of human rabies deaths.

Conflict of interests

The authors have no conflict of interest regarding the publication of this paper.

Authors' contributions

All authors equally drafted, edited, reviewed, read and approved the final manuscript.

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