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RABIES AS ANIMAL AND PUBLIC HEALTH PROBLEM: ITS CONTROL AND PREVENTION

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ABSTRACT

Rabies is caused by negative strand RNA-viruses belonging to the genus *Lyssavirus*. According to the International Committee on Taxonomy of Viruses (ICTV), *Lyssavirus* species segregate into two phylogroups. There is a significant serological neutralization within phylogroups, but very limited crossneutralization has been detected between phylogroups. *Classical rabies virus (RABV)*, the prototype *lyssavirus*, is the causative agent of the classical rabies and is responsible for the vast majority of all human rabies cases. Interestingly, bats are primary or sole reservoir hosts for all *lyssaviruses* except *Mokola virus (MOKV)*. Rabies is one of the most terrifying diseases, is of a great concern from both public and animal point of view. Wild animals and carnivorous bats are the primary reservoirs for rabies in many parts of the world, but domestic carnivores are the principal source of transmission of rabies infection to human being. Human being acquired the disease mostly when bitten by rabid carnivorous. Control and prevention strategy is primarily driven by the necessity to prevent spread to people. In Ethiopia, the production size and distribution of human and animal anti rabies vaccine for domestic supply per annum has increased from six thousand to twenty thousand doses for the last nine years (2001-2009), however it does not meet the projected domestic demand of eighty thousand doses at national level. The retrospective data for rabies diagnosis, post exposure prophylaxis and fatal human cases were underestimated due to the absence of rabies diagnosis laboratory across the country. Therefore, it is of a paramount

importance to assess and map the national picture of rabies within a given time interval to launch a national rabies control strategy. The control should be based on control in domestic and wild carnivorous, bats, mass immunization of the principal vector and stray dog control. Pre-exposure immunization is strongly recommended for all people in high risk groups particularly for veterinary practitioners and post-exposure treatment for humans should be made available to all medical practitioners found in the rabies affected areas.

KEYWORDS: *Animal, Bite, Control, Human, Prevention, Rabies.*

1. INTRODUCTION

Rabies is one of the oldest known, most feared human and all warm blooded animal diseases recognized since the early period of civilization. Democritus (500 B.C) and Aristotle (322 B.C) have been described this disease. It is caused by a virus that belongs to the order *Mononega virales*, family *Rhabdoviridae* and genus *Lyssavirus* (Murphy *et al.*, 1999). Rabies is one of the main zoonotic diseases prevalent throughout much of the world and is widely known in Ethiopia. It is a fatal Central nervous system disease which is highly contagious, responsible for approximately 60,000 annual deaths of peoples in the world. Recently, the number of human deaths caused by rabies is estimated to be 40,000 to 50,000 worldwide and 10 million people receive post exposure treatments each year after being exposed to rabies suspected animals. Rabies in Africa constitutes a serious public and animal health problem. In Ethiopia it is an important disease that has been here for many centuries. Currently the mortality rate for rabies in Ethiopia is around 18.6 per 100,000 people. According to EHNRI, 2010, the fatal human cases during the period of study (2001-2009) in Addis Ababa and its surounding were 386 humans with annual range of 35-58 (Asefa *et al.*, 2010).

Worldwide the dog is the principal vector in transmitting rabies to man, irrespective of whether the reservoir hosts are wild animals or dogs themselves. In exceptional circumstances, rabies may be acquired by inhaling aerosol containing rabies virus in infected bat caves or by virus passing through intact mucous membranes and corneal transplants from infected donors (Hirsh and Zee, 1999). The disease poses an important extinction risk for a number of carnivore populations as indicated by empirical evidence and population viability analysis. Rabies principally affects carnivores and insectivorous bats (Aiello and Mays, 1998). Furthermore, as the global humans and domestic animals grow, the threatened carnivore populations are also increases (Haydon *et al*., 2002). Wild Canids are particularly at risk from generalist pathogens transmitted from domestic dogs as a result of their close

genetic relationship, and making them susceptible to the same diseases, and high rates of contact in areas where wild canids coexist with humans and their domestic dogs (Woodroffe *et al*., 2004).

At present, the Ethiopian Health and Nutrition Research Institute (EHNRI), is the only institute which provides diagnostic services and produces about 10,000 doses of vaccine for dogs and a similar amount for human use per year. In Ethiopia, the production size and distribution of human and animal anti rabies vaccine for domestic supply per annum has increased from six thousand to twenty thousand doses for the last nine years (2001-2009), however, it does not meet the projected domestic demand of eighty thousand doses at national level. Although limited amount of vaccines are also said to be imported in to the country, there seems to be no mechanism to certify their quality and safety before being used, the type of vaccines used, their handling and the storage mechanisms are not regulated (OIE, 2011).

It is estimated that among the 150,000-200,000 dogs found in Addis Ababa, 50% of them roam freely without any control. Even though some efforts have been put to control and prevent rabies in Ethiopia, the low amount of vaccine produced per year and the presence of only one rabies diagnostic laboratory shows that no organized action is being taken yet to safeguard the public and animal from this dreadful disease. Moreover, unreasonably excessive service charges of vaccination requested by Private practitioners may also have contributed to the low number of dogs that get vaccination in those private clinics (MOA, 2011).

Therefore the objectives of this paper was:

- To indicate and review the current animal and public health significance of rabies.
- To highlight the current control and prevention strategies practiced.
- To give brief account on post exposure management of animals and humans.
- To forward appropriate recommendation on the alternative control and prevention strategies.

2. REVIEW ON RABIES VIRUS INFECTION AND DISTRIBUTION

2.1. Etiology, Pathogenesis and Clinical signs

Rabies is caused by *Lyssavirus, which* is enveloped, rod shaped, non segmented negatively stranded RNA genomes, 180nm height (long) x 75nm diameter in size, have a helical nucleocapsid surrounding by a lipid envelop with surface glycoprotein antigen (Murphy *et al*., 1999).

Rabies virus is almost always transmitted by bite of rabid animal. The saliva of most infected animals contains the infectious virus (David *et al.,* 2001). After inoculation of infectious saliva by bite, 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. After peripheral nerve entry, virus moves centripetally with in axons to the CNS at the estimated rate of 3 mm/hour. Once virus reaches the brain, it spread centrifugally to a variety of organs, the spread in to the salivary gland, which represents the final phase of infection, is important from animal to animal and from animal to humans (Knipe *et al.,* 2001).

The clinical features of rabies are similar in most species, but there is great variation between individuals. Following the bite of rabid animal the incubation period is usually between 14 and 90 days, but may be considerably longer. Even though the disease has three stages, there are two recognized clinical forms of the disease: Furious form and Dumb or Paralytic form. Animals often exhibit one of the two forms of rabies. Rare human cases have been observed in which the last opportunity for exposure occurred from 2 to 7 years before the onset of clinical disease. This is due to the different factors that lead the longest incubation period. Since there is no pathognomonic sign for this disease, the diagnosis shoud be based on laboratory confirmation of the suspected cases (Hirsh and Zee, 1999).

2.2. Epidemiology of the disease

Rabies occurs in most countries of the world except in few island countries, which are able to exclude it by strict quarantine measures or prohibition of the entry of dogs. Australia and Newzealand have never had the disease, and Great Britain (GB), Hawaii-islands, Japan, Pacific islands, Antarctica and Scandinavia are currently free. In some islands of east Africa, the disease does not recorded because of the segregation of the island (Radostits *et al.,* 1994).

2.2.1. Lyssa virus species, host range and susceptibility

Any warm-blooded animal, including humans, may become infected with the rabies virus, although birds have and only been known to be infected in experiments. The virus has even been adapted to grow in cells of poikilothermic ("cold-blooded") vertebrates (Wong *et al*., 2007). However the degree of susceptibility is different. Foxes and wolves have extreme high susceptibility. Domestic Cats, Cattle, and rodents have high susceptibility while dogs, sheep, goats, horses and non-human primates have moderate susceptibility. Dog rabies is still most important in many parts of the world and is the cause of most human rabies case. Cattle rabies is important in central and south America. In many countries wild life rabies has become of increasing important as a threat to domestic animals and humans (Murphy *et al*., 1999).

The most important animal families in maintaining rabies cycles are *Canidae* (dogs, foxes, jackals, wolves etc.), *Mustelidae* (skunks, martens, weasels, ferrets stoats etc.), *Viverridae* (mongooses, meerkat etc.), *Procyonidae* (raccoon etc.), *Chiroptera* (> 1,200 Species 0f bats). 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 (MOA, 2011). Recently, eleven distinct species can be distinguished within the genus *Lyssavirus*. In addition, a newly identified *lyssavirus*, *Shimoni bat virus* (*SHIBV*) and *Bokeloh bat lyssa virus (BBLV)* had been isolated from a bat in Kenya and Europe respectively and are awaiting official classification as depicted in table-1(Kuzmin *et al*., 2010; Freuling *et al*., 2011).

Table-1: Different *Lyssavirus* species with their potential vector(s)/reservoirs, and distributions.

No	Species name/abbreviations	Distribution	Host range/ reservoirs
1	*Classical rabies virus (RABV)*	Worldwide except few islands	All warm blooded animal
2	*Lagos bat virus (LBV)*	Nigeria, Togo, Egypt, France	Frugivorous bats, Dogs*, Cats*, Mongoose*
3	*Mokola virus (MOKV)*	Africa (Central)	Rodents?
4	*Duvenhage virus (DUVV)*	Africa (South)	Insectivorous bats, human*
5	*European bat Lyssa virus 1 (EBLV-1)*	Europe	Insectivorous bats, domestic cat*, human*
6	*European bat Lyssa virus 2 (EBLV-2)*	Europe	Insectivorous bats, human*

7	*Australian bat Lyssa virus (ABLV)*	Australia?	Frugivorous/insectivorous bats, flying fox*, human*
8	*Aravan virus (ARAV)*	Central Asia	Insectivorous bats
9	*Khujand virus (KHUV)*	Central Asia	Insectivorous bats
10	*Irkut virus (IRKV)*	Eastern Siberia, Russian Far-east	Insectivorous bats, human*
11	*West Caucasian bat virus (WCBV)*	South-eastern Europe, Caucasian region, Kenya	Insectivorous bats
12	*Shimoni bat virus (SHIBV)*	East Africa (Kenya)	*Hipposideros commersoni*
13	*Bokeloh bat lyssa virus (BBLV)*	Europe	*Myotis nattereri*

Source: (Kuzmin *et al.*, 2010; OIE, 2011), *=Spillover of infection from bats to human and animals.

Proposed species (*SHIBV*: Kuzmin *et al.*, 2010, *BBLV*: Freuling *et al.*, 2011).

RABV is found worldwide, and is responsible for the overwhelming majority of reported animal and human rabies cases. Other *lyssaviruses* appear to have more restricted geographical and host range, with the majority having been isolated from bats and use it as a reservoir hosts with the exception of Mokola virus for which the reservoir species has not been clearly identified as of yet but assumed to be rodents. However, all *lyssaviruses* tested to date cause clinical disease (fatal encephalitis) indistinguishable from classical rabies both in humans and other mammals (Kuzmin *et al.*, 2010).

Conserved antigenic sites on the nucleocapsid proteins permit recognition of all *lyssaviruses* with modern commercial preparations of anti-rabies antibody conjugates used for diagnostic tests on brain tissue. The *Lyssaviruses* have been divided into two phylogroups with distinct pathogenicity and immunogenicity. For *RABV, DUVV, EBLV* and *ABLV,* conserved antigenic sites on the surface glycoproteins allow cross-neutralisation and cross-protective immunity to be elicited by rabies vaccination. A reduced protection with pre-exposure vaccination and with conventional rabies post-exposure prophylaxis was observed against *IRKV, ARAV,* and *KHUV* and all of the above mentioned *lyssavirus* species were assigned to phylogroup one. Little or no cross-protection against infection with the members of phylogroup two (*MOKV, LBV* and *SHIBV*) is elicited by rabies vaccination and most anti-rabies virus antisera do not neutralise these lyssaviruses. *WCBV* does not cross-react serologically with any of the two phylogroups (Hanlon *et al.*, 2005).

2.2.2. Transmission and maintenance of different cycles

The source of infection is always an infected animal and the mode of transmission is usually by bite of an infected animal, although contamination of skin wounds by fresh saliva may result in infection. Because of the natural occurrences of rabies in animals in caves inhabited by infected insectivores and hematophagus bats, inhalational route of infection can possible. Inter bat spread and spread from bats to other species occurred principally by bites but ingestion of the virus has now been assumed to transmit the infection if the dose is large enough. Corneal transplantation has also been incriminated as means of rabies virus transmission. The only known cases of human-to-human transmission of rabies occurred in patients who received corneal transplants from persons who had died of unrecognized rabies. Recently, a few human rabies cases (six in number) have been reported from recipients of cornea transplants from infected donors (Hirsh and Zee, 1999). Bats play special role in the epidemiology of rabies, as they have been known to be symptomless carriers which can retain the virus for long periods of time in their fatty tissue and this may be the basis of 'reservoiring' mechanism in these species. Depending on the species of animals that plays role as a major vector, three rabies cycles have been distinguished (Radostits *et al.,* 2000).

The urban rabies cycle: This type of cycle is the one in which most human cases of rabies have by far been recorded in cities or urban centers due to bites of rabid dogs and cats. This type of canine rabies accounts for more than 90% of all human and domestic animal cases. The major vector is dog and the most common victims are cattle and humans (Radostits *et al.,* 2000).

Wild (sylvatic) rabies: This is a type of rabies cycle in which wild carnivores such as jackals, foxes, skunks, mongooses, wolves etc. do play an important role as vector. This rabies cycle usually reverts to urban cycle due to frequent contact between rabid wild carnivores and stray dogs. The most common victims are dogs, cattle and man (Quinn *et al*., 2002).

The vampire rabies (paralysa): This type of rabies is particularly important in Latin America and is transmitted by bite of bats. These bats usually transmit the bovine paralytic rabies and maintain the cycle in endemic areas while cattle and man are victims (Kuzmin *et al.,* 2011).

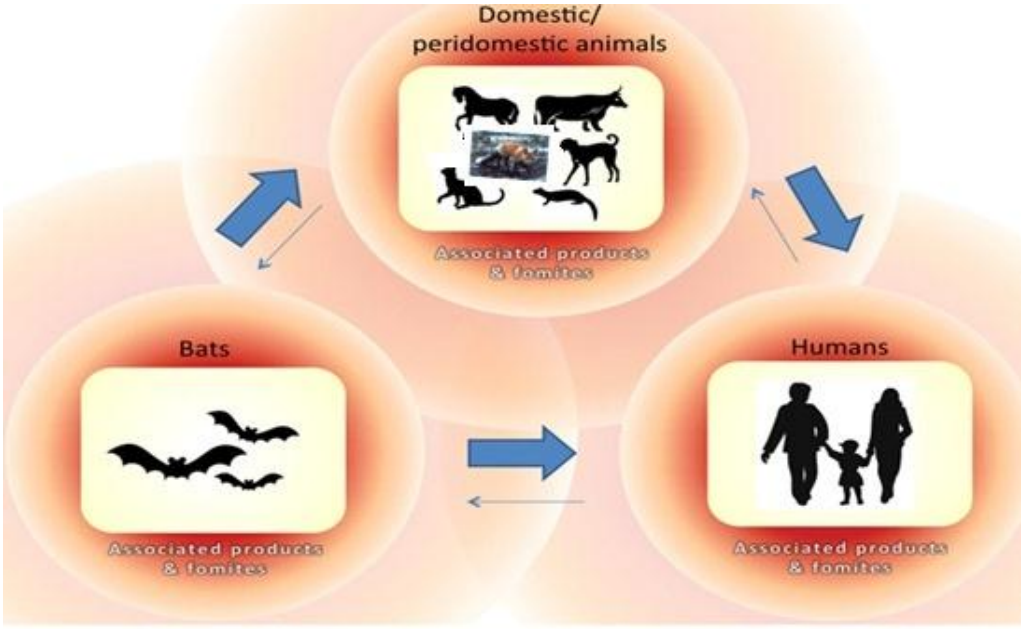

Figure: Transmission of rabies virus infection among different hosts/reservoirs species. Source: (Kuzmin *et al.*, 2011)

2.3. Current status and health significance of rabies in Ethiopia

Human rabies, transmitted by dogs is an important public health issue in Ethiopia. A well organized diagnostic laboratory for rabies is lacking at present rendering diagnostic difficulty. The only laboratory that provides accurate diagnostic service for rabies is the zoonoses laboratory at Ethiopian health and nutrition research institute. The coverage of this laboratory is limited to Addis Ababa and its surrounding. Thus, the vast majority of rabies cases remain undiagnosed, none registered and this results the number of rabies diagnosis, post exposure prophylaxis, and fatal rabies cases presented in the country are under estimated (MOA, 2011).

The incidence of human post exposure treatments and human rabies cases per million population of Ethiopia were 73.6 and 12.6, respectively. In a study conducted from 1999-2002 in and around Addis Ababa, it was reported that a range of domestic and wild animals and humans were affected. During this time, among the 902 brain samples examined for rabies, dogs were found to be the most affected (89.7%) followed by cats (4.2%) and cattle (3.4%) (Yimer *et al*., 2002).

A retrospective data were used from the EHNRI rabies case record book registered between 2001 and 2009 with the objective of reviewing recorded data to generate information on the status of rabies in Ethiopia for the year 2001-2009. According to this data, the fatal human

cases during the period of study were 386 humans with annual range of 35-58. Reports of EHNRI (2010) have also shown that many people, especially children and women are under high risk of being attacked by dogs, cats and others both in urban and rural areas of the country. The age and sex specific distribution in the year 2001-2009, showed that the most fatal cases were 42% from the age group 0-14 category. In the same period (2001-2009), out of 3,261 brain samples of different animals, mainly dogs, submitted for examination, 2,458 (75%) were found to be positive for rabies by FAT. The proportion of rabies among dogs was 88.7% in 2004, where as it was 68.65 % in 2008. The production and distribution of anti-rabies vaccine reached 130,673 treatment doses for human vaccine and 85,055 doses for animal vaccine respectively in the period of 2001-2009 (Asefa *et al.*, 2010).

Even though the epidemiology of rabies in Ethiopia wild life is not well studied, there are some reports that indicate the disease as a problem in Ethiopian wild life as indicated in table-2.

Table-2: Result of examination of animals/brain from 1990-2000 at EHNRI.

Species	Total examined	Number and positive (%)	Individual spp examined from total spp examined(%)
Dog	13,364	1951(14.6)	96.22
Cat	321	116(36.5)	2.31
Cattle	86	63(73.3)	0.62
Sheep	19	10(52.6)	0.136
Goat	6	3(50.0)	0.043
Donkey	10	8(80.0)	0.072
Horse	2	1(50.0)	0.014
Hyena	13	9(69.2)	0.093
Monkey	47	2(4.3)	0.34
Jackal	7	4(57.1)	0.05
Mongoose	2	1(50.0)	0.014
Rabbit	1	-	0.007
Cerval cat	1	1(100.0)	0.007
Cheetah	1	1(100.0)	0.007
Civet cat	1	-	0.007
Rat	3	-	0.021
Human	5	2(40.0)	0.036
Total spp	13,889	2172(15.64)	100 %

Source: (Yimer *et al.*, 2002)

The recent history of rabies outbreak affecting the red fox (wolf) in Bale Mountain National Park in 2003 and some occasional media reports about invasion of human settlement areas by fearless wild animals during day times are suggestive of the extent to which the disease may

have been distributed across the country and established itself even in our wild life population (MOA, 2011).

Table-3: The brain of animals examined for rabies from Addis Ababa and its surrounding areas between 2001 and 2009.

		Dog		Cat		Others
Year	Brain examined	Number(%) positive	Brain examined	Number(%) positive	Brain examined	Number(%) positive
2001	379	274(72)	15	11(73)	1	0
2002	1259	919(73)	20	17(85)	19	14(73.68)
2003	400	302(75)	12	10(83)	10	5(50)
2004	115	102(88.7)	9	5(55)	5	3(30)
2005	297	237(79.8)	17	12(70)	3	2(66)
2006	280	193(68.9)	11	5(45)	7	5(71.43)
2007	240	202(84)	15	10(66)	7	3(42.8)
2008	67	46(68.65)	12	10(83)	10	7(42.8)
2009	224	183(81.7)	15	11(73)	11	5(45)
Total	3261	2458(75.37)	126	91(72)	73	44(60)

Source: (Asefa *et al.*, 2010), Others=cattle, fox, horse, sheep, hyena, donkey etc.

The disease has been of major health hazard for centuries and the magnitude of the disease has been increasing due to some socio economic factors. Some of the factor that contributed to high incidence of the disease includes the duration of time rural residents spend outdoors, frequent contact with animals, the existing traditional belief, and lack of medical care and shortage of rabies vaccines supply in the country (Mekonnen *et al.*, 1996). These factors have not only maintained higher incidence and endemicity but also hampered the effective control of rabies and prevention of human exposure to rabies. Although majority of the victims are aware of danger of rabies, most of people reported to have died of rabies because they are misled by the existing traditional belief that exposed persons can be effectively treated with local medicine (herbs) and advice given against the use of modern post exposure treatment. One of the plants used for rabies treatment traditionally is known by its vernacular name as Haya (Amharic), Alaltu (Oromiffaa), and by its botanical name as *Salix subserrata and* the parts of the plant used are its leaf and root (Girma *et al*., 2002).

3. RABIES CONTROL AND PREVENTION STRATEGIES

3.1. Principles and major intervention areas

Control and prevention programs of rabies are based on the principles that rabies may not have significant importance to disrupt export trade of animals and animal products. However, it stands out as uniquely terrifying because of its fatality once the clinical signs appear. Its

prevention and control strategy is primarily driven by the necessity to prevent spread to people. The first line of defense against rabies is the continued implementation of preventive and control measures. The bite and aggression of a dog is sufficient indication for a man to react. Empirical observation and models of the transmission of canine rabies indicate that rabies can be eradicated if 70% of the dog population is vaccinated repeatedly to achieve herd immunity (Coleman and Dye, 1996).

For the prevention and control of rabies, the following terms are used: Infected animal (an animal that has confirmed rabies or is believed to have rabies), Dangerous contact animal (an animal that has been in direct contact with an infected animal), Suspected animal (other animals that may have been in the same area as the infected animal). All animals in direct contact with a rabies case or that have had access to the same cage, pen or yard or which have been separated only by a single wire fence, within 14 days before the disease was detected, will be treated as dangerous contact animals (Murphy *et al.*, 1999).

Preventive and control measures should include any or all of the following major intervention areas and methods. Of which early recognition of rabies cases in animals and reporting of animal bite cases in humans, quarantine and movement control, delineation of the geographic area of the outbreak, destruction of all infected and dangerous contact animals, compulsory vaccination of all dogs and cats, vaccination and identification of other animals, detention or destruction of all stray and uncontrolled dogs and cats which are not properly controlled or vaccinated, detection and management in wildlife, provision of safe and effective vaccines, conducting public education campaigns, and prophylactic treatment in humans (MOA, 2011).

3.1.1. Reporting of animal bite cases to concerned bodies

The reporting of animal bite cases in humans in an area where rabies has spread to a number of domestic pets and other animals including wildlife is essential for early evaluation and institution of post-exposure treatment of the human patient by the physician. Qualified on-site advice on post-exposure treatment and on the epidemiology of the disease would be essential. An epidemic surveillance system is an important instrument in rabies control, particularly for the effective and economic application of control measures in animals and post exposure treatment in man (WHO, 2009).

3.1.2. Quarantine and movement control

When there are reasonable groups of infected animal, it should be detained and isolated. Isolation of susceptible animals is possible by classical procedures of veterinary control which include quarantine measures, restriction of movement such as prohibition of free movement outside houses and farms, leashing, muzzling, and surveillance of animals into and out of infected areas. The availability of secure accommodation for a period of up to six months is a factor in deciding whether to detain or destroy suspects. If rabies is confirmed in an animal in quarantine, any animals kept in close proximity to the rabid animal and animals released within the previous 15 days would need to be recalled. Such animals, if previously vaccinated for rabies, should be serologically tested for rabies antibodies. Dogs and cats entering from abroad will be quarantined and finally vaccinated before released unless they are accompanied with valid vaccination certificates (OIE, 2011).

Where a rabid animal has been at large in an area and there are a number of possible contacts, declaration of a restricted area and introduction of general confinement and movement controls for appropriate species in that area should be practiced. Household pets need to be confined at home until the emergency is considered to have passed. The emergency must be regarded as continuing for at least 6 months following the completion of the vaccination program or of the occurrence of the last case (Quinn *et al.*, 2002).

When outbreaks occur, movement restriction will be imposed on dogs and cat and if wildlife involvement is suspected, domestic animals will be restricted not to have contact with affected species and consideration would have to be given to vaccination and movement restrictions of farm animals in the area. In the restricted area the owner of a dog or cat is responsible to ensure that the animal is at all times securely confined within their home. All dogs and cats should be vaccinated and must not come into contact with any animal within 30 days of the rabies vaccination. Vaccinated animals will be permanently identified in an approved manner and recorded. Dog registration is often considered as a basis for immunization and dog population control through spaying of females and castration of males. In some countries, particularly where fees or taxes are associated with registration, these measures counter act with the desired community participation in rabies control. An unvaccinated dog or cat may be moved to another place within the same area with the approval of a veterinarian provided it is either carried in a secure container or muzzled and

does not come into contact with any other animal at the premises to which it has been moved (MOA, 2011).

3.1.3. Destruction and Detention of uncontrolled and unvaccinated animals

Most control programs call for destruction of stray dogs (unless the owner is prepared to pay fine). When a case of rabies in an animal has been confirmed, the index case should be destroyed, the appropriate area disinfected and other susceptible animals on the premises should be quarantined and vaccinated and remain there until the official veterinarian decides. All infected and dangerously contact domestic or wild animals and those animals which are exposed to a rabid animal will be destroyed and their head will be submitted to a designated laboratory. To destroy all stray and uncontrolled dogs and cats, a team of experts drown from the veterinary and public health authorities, police, municipality and wild life will be established at various levels and conduct regular monitoring of the presence of stray dogs and cats. All Stray, unvaccinated and unidentifiable dogs and cats should be destroyed if not claimed soon after capture. Stray dogs registered and vaccinated against rabies should be captured and held for about 24 hours for the owner to claim the animal, failing which, the animal would be destroyed. Any animals released back to their owners subject to confinement and vaccination (WHO, 2009).

For controlling urban rabies, elimination or dramatic reduction in the number of stray or uncontrolled dogs and cats should be done. If there has been a single rabid dog that has had little or no opportunity to bite other dogs, owners of straying dogs may be given a short period of grace to control their dogs. However, in a situation where a rabid animal was free to roam, then stray dogs should be controlled promptly, a restricted area declared, contacts between animals reduced to the minimum and vaccination programs implemented (Murphy *et al.*, 1999).

3.1.4. Disposal of killed animals, animal products and decontamination

Stray or uncontrolled pets will be destroyed by suitable means and be immediately removed and buried. Dead and destroyed animals should be burnt or buried after the necessary diagnostic specimens have been taken. Where a suspected or known rabid animal is found on a farm, attention should be given to the disposal of farm products from both suspect and contact animals. Milk from affected or suspect cows should be disposed off as unsuitable for human or animal consumption. The areas that the animals occupied will need to be cleaned and disinfected. The infectivity of rabies virus is destroyed by most organic solvents, by

oxidizing agents, and by surface-active agents (quaternary ammonium compounds, soaps, and detergents) (OIE, 2011).

Oxidizing agents such as hypochlorite used for environmental decontamination. Quaternary ammonium compounds are also useful for personal disinfection. If rabies is detected or suspected in an animal held or handled in a quarantine center, laboratory, or household, the areas contaminated by the rabid or suspect animal should be cleaned and disinfected with warm soapy water, an oxidizing agent such as sodium hypochlorite or an acid or alkali after the animal has died or been destroyed. Vehicles used to transport dogs, cats and other animals to a detention center or to a laboratory should be periodically cleaned and sprayed with one of the disinfectants stated above (Hanlon *et al.,* 2005). Laboratories working with lyssaviruses or suspect material must comply with national biocontainment and biosafety regulations and they should also comply with the guidelines for risk group three pathogens in biosafety and biosecurity in the veterinary microbiological laboratory and animal facilities (WHO, 2004).

3.2. Rabies control in domestic animals

Rabies is considered a serious candidate for disease eradication at this time, because of numerous and diverse wild reservoirs. However, the correlation between canine rabies and human fatalities lead to the successful application of herd health initiatives using vaccination, particularly in developed countries. For farm animals there are two useful control techniques: The prevention of exposure and vaccination. The prevention of exposure can be achieved to a higher degree by control of wild animal, muzzling, restraint and Compulsory vaccination of all cats and dogs at regular intervals and keeping farm animals in doors. Depending on actual needs and the availability of vaccines, other domestic animals and wild life may also be vaccinated (Radostits *et al.,* 1994).

3.2.1. Management of dogs and cats that have bitten man.

Healthy dogs or cats biting a person should be confined for 14 days for observation of signs of rabies following biting. The purpose of the 14 days observation is to determine if the bitten person was exposed to rabies. This determination is based on the knowledge that 6 days before the onset of clinical signs of rabies, the earliest rabies virus have been detected in the saliva of dogs or cats (Quinn *et al.,* 2002). Therefore, if the dog or cat remains healthy for 14 days after the bite, the person was not exposed to rabies virus. There are no provision for confinement and observation of other species due to lack of information on the length of time that they may shed virus before the onset of clinical signs of rabies. As a result all “biters”

except owned healthy dogs and cats should be euthanatized immediately after the bite and examined for rabies virus. Dogs showing signs of neurologic disease at the time of biting a human or a stray dog or cat that have bitten a person should be euthanatized immediately and the brain is examined for rabies virus. If rabies virus is not detected in the brain of the animal, the person was not exposed to rabies virus, if found positive rabies post exposure immunization should be initiated as soon as possible (Quinn *et al.*, 2002).

3.2.2. Management of dogs and cats exposed to rabies.

Depending on vaccination status, antibody titer result, and factors relating to the extent of exposure to the rabid animal, either further quarantine or destruction of the animal be considered (WHO, 1984; MOA, 2011). Dogs or cats that are currently immunized to rabies according to recommendations for rabies vaccination and that are bitten by a proven rabid animal or that are bitten by a wild animal in rabies endemic area should be revaccinated immediately and observed for 90 days. Unvaccinated dogs or cats that have known exposure to rabies virus should be euthanatized or confined in strict isolation for 6 months if the owner is unwilling to consent to euthanasia. The dog or cat should be vaccinated at the fifth months and then they may be released to the owner at 6^{th} months. The maximum incubation period given in the OIE Code, for regulatory purposes, is six months. The purpose of this requirement is to prevent secondary exposure of other animals or humans if the bitten dog or cat should develop rabies (Aillo and Mays, 1998).

3.3. Rabies detection, control and management in wildlife

In general rabies should be suspected, if terrestrial wildlife acting abnormally. For example, rabid foxes and Coyotes frequently invade yards or even houses, attacking dog and people. The same is true of bats that are seen flying in day time, resting on the ground, attacking people and animals. Rabies in wild mammalian populations fluctuates, probably as a function of density of the principal vector. It requires moderate to high densities of medium-sized carnivores, over large areas (>5000 square km) in order to persist. Therefore mass killing of vector to reduce their density has always been attractive possibility for controlling the disease. This also resulting in reduction of the contact rate between susceptible animals, however this proved ineffective. Experience indicates that local rabies infections are adapted to be spread by only a small number of species. Although any mammal may be infected by any of the variants, only 1–5 species are involved in persistence and spread of a particular form (Aiello and Mays, 1998). Prevention of introduced rabies to susceptible wildlife may be

best achieved by the control and confinement of domestic animals in the area. In Europe and Canada use of oral vaccines distributed in baits to control fox rabies is widespread and effective. Prompt and effective measures to detect and eliminate any outbreak in wildlife are essential to stop the disease at an initial focus before it becomes widespread. The following methods are used how to control rabies in wildlife (Quinn *et al*., 2002).

Population reduction: When sampling demonstrates rabies presence in wildlife in a discrete and controllable area, actions should be undertaken to reduce the population density of involved species to below the threshold for rabies persistence in the area. Threshold densities for reservoir species are widely variable, and the rate of rabies movement through populations is not a species constant. The decision for stamping out will be much more difficult, if the species affected are endangered native species such as red fox or red wolf in our context. Wildlife population reduction may not achieve disease control if the level of reduction is inadequate (Macinnes, 1988).

Oral vaccination: When rabies in wildlife is accepted to be widespread and to have established a sylvatic cycle, serious consideration should be given to large-scale wildlife vaccination based on baiting with accepted oral vaccines for the target species (Quinn *et al*., 2002).

Trap–vaccinate–release (TVR): If wildlife reduction is unacceptable for some reasons or the outbreak is in an urban area where shooting and poisoning of target animals cannot be undertaken, TVR programs may be initiated. TVR may become also the only option where vaccine baits have not been developed for a species (Hirsh and Zee, 1999).

3.3.1. Control methods in bats

Bats should be eliminated from house and surrounding structures to prevent direct association with people. Such structures should then be made bat-proof by sealing routes of entrance with screen or other means. When a bat or other wild animal have bitten a person, they should be killed and sent to a laboratory examination (Crawford *et al*., 1982).

3.4. Management of wounds (Local treatment of wounds)

When accidental exposure occurs as a person is bitten, saliva is splashed on the hands or face, or suspensions containing virus are spilled or splashed, first aid should be applied immediately. Immediate and thorough washing/irrigation of all bite wounds and scratches

with 20 % soft soap solution or normal saline solution and water is perhaps the most effective measures for preventing rabies in humans and animals bitten by rabid animals (Radostits *et al.*, 1994). Immediate washing and flushing with soap and water, detergent, or water alone is imperative and is probably the most effective procedure in the prevention of rabies. Suturing the wound should be avoided if possible. The mortality may be markedly reduced when deeply exposed limbs are cauterized or amputated arguing for an initial productive infection in muscle cells (Knipe *et al.*, 2001). However, depending up on types of wounds, its management is different and all wounds should be the open wound healing except in very extensive wounds (Kaplan, 1996).

Table-4: Types of wounds and its management against rabies virus infection.

Types of wound	Character of wound	Management
Type I (1st degree wound)	Scratch of skin and no blood	Washing with soap, water and normal saline solution
Type II (2nd degree wound)	There is blood and nerve cells are not exposed	Washing with soap, water and normal saline solution
Type III (3rd degree wound)	Deeply injure nerves are exposed	Washing with soap, water, normal saline solution, and local immunoglobulin
Type IV (4th degree wound)	Most severe wounds	Washing with soap, water, normal saline solution, and local immunoglobulin

Source: (Kaplan, 1996).

3.5. Vaccination of animals and humans

The major goal of rabies control in domestic and wild animals is for reduction or elimination of human rabies. The most international approach for reducing human rabies is to reduce the prevalence and incidence of disease in animals. This has been accomplished by vaccination of dogs and cats and leaving much rabies in wildlife population. In countries without wildlife reservoirs, such as the Philippines, it would be economically advantageous to eliminate dog rabies only. Worldwide, more than 95% of all human rabies cases are caused by dog bites, even in those areas where wildlife rabies is predominant (Quinn *et al.*, 2002).

According to statistics, on an average of only 15-20 % of people who have been bitten by proven rabid animal and received no post exposure treatments die of the disease. Animals and humans vaccinated with rabies vaccine develop circulating neutralizing antibodies to the

virus in three weeks after primary vaccination. Both T and B lymphocytes are necessary for optimum clearance of rabies virus from the CNS (Quinn *et al.*, 2002).

July 6, 1885 is a millstone in the history of rabies. On that date, 9-years old Joseph Meister was bitten at multiple sites by a rabid dog and received the first post exposure prophylaxis with pasture's vaccine, Remarkably Joseph survived. Pastures vaccine with all its modification, become an accepted rabies prophylaxis throughout the world in the early 20th Century. However, problems remained because improperly inactivated virus has caused rabies, and animal brain tissue induced allergic reactions leading to neuroparalytic accidents. Moreover, most importantly the vaccine was not very effective in the cases of severe bites, such as those infected on the face and neck by a rabid wolf. Today the combination of serum and vaccine is the recommended standard for prophylaxis in human rabies exposure. In the 1960's, a rabies virus grown in human diploid cells was used for production of safe and efficacious vaccines, eliminating many of the problems connected with vaccines produced in brain tissue. This vaccine is being used widely through the world, although for economic reasons several developing countries still use nervous tissue vaccines (David *et al.*, 2001).

3.5.1. Pre-exposure prophylaxis

The spread between susceptible animals is greatly reduced by mass vaccination and possibly by stray dog control. Compulsory mass vaccination of dogs, cats may be carried out at designated vaccination centers or at the premises of owners in rabies outbreak areas. Cats are particularly at risk, if wildlife is infected because of their nocturnal hunting behavior. Pleasure horses, valuable stud animals and any other animal that comes into frequent human contact during the incursion should be considered for vaccination. Vaccination of at-risk, valuable farm animals may also be a sensible precaution. The identification of vaccinated animals by some suitable means (for example, by serially numbered dog tag or collar of colored rope inside plastic tubing) and an effective recording system would be necessary (OIE, 2011).

Pre-exposure prophylactic immunization would be required for people with a high-risk of exposure to rabies. Veterinarians and their assistants in clinics and at the diagnostic laboratory, stray dog and cat catchers, slaughter house personnel, animal handlers at quarantine centers and laboratories, wildlife control workers, game keepers and forest warder in endemic areas, people working in the rabies vaccine production factories should all be considered at high-risk and be immunized. With the exception of those in the diagnostic

laboratory and quarantine centers, where immunization should be carried out before an outbreak, all the others should only receive the required course of vaccinations at the onset of an outbreak (Davis, 1990).

All dogs should be vaccinated against rabies commencing three months of age, revaccinated with one of the 3 year vaccine one year later, and revaccinated every three years thereafter. All cats should be vaccinated at 3 months of age with rabies and revaccinated annually thereafter (David *et al.,* 2001). Different types of vaccines for humans and animals are available depending on the need of the person, owner and species of animals (Davis, 1990). Modern rabies vaccines are available for dogs, cats and domestic livestock species. These are broadly classified into three types: attenuated ('live') virus vaccines, inactivated nervous tissue vaccines, and inactivated tissue culture vaccines. Live attenuated rabies vaccine is a weakened rabies virus to stimulate antibody production or cellular immunity against the virus up on administration. An inactivated

virus vaccine used for pre- and post-exposure immunization against rabies includes human diploid cell vaccine and purified chick embryo cell vaccine (MOA, 2011).

Chick embryo adopted vaccine: Such vaccines include those that contain the flury low egg passage (LEP), or the more desirable high egg passage (HEP) variant strain which is safe for some animal species such as cat. The facts that dogs inoculated IM with 3 ml of the LEP virus resist challenge with street virus for as long as 3 years. The vaccine is very suitable for mass prophylactic vaccine in dogs. LEP strain is used in adult dogs but not to puppies under 3 months of age, cats and any other species. The HEP strain of flurry virus strain is more highly attenuated and is recommended for use in puppies, adult dogs, cats, wild animals and cattle (OIE, 1996).

Brain tissue vaccines (sheep brain vaccine): Such vaccines have been shown to be effective in mass canine immunization programs. Semple or Fermi type phenol inactivated fixed virus vaccines have the disadvantage of being derived from nervous tissue and may sensitive about 1 in 4000 to 1 in 10,000 patients who will develop side effects during a course of infections varying from transient nervous signs and paralysis to serious allergic reactions, encephalitis and death which is more frequent in previously rabies vaccinated people (Diaz, 1996; Singh, 1996).

Recombinant vaccines (V-RG): The advantage of V-RG includes improved stability and inability to cause rabies. Recombinant vaccines appear to be the preferred vehicles for future wild life vaccination program. The vaccine is stable under relatively high temperatures and can be delivered orally, making mass vaccination of wildlife possible by putting it baits. The plan for immunization of normal populations involves dropping bait containing food wrapped around a small dose of the live virus. The bait would be dropped by helicopter concentrating on areas that have not been infected yet. Such a strategy of oral immunization of foxes in Europe has already achieved substantial reductions in the incidence of human rabies (Reece, 2006).

Human diploid cell vaccine (HDCV): Three doses of HDCV are given one on day 0, 7 and 21 for Pre-exposure immunization of humans which stimulates the rapid development of specific antibodies (Coleman and Dye, 1996).

3.5.2. Post exposure treatment

Includes local treatment of wound, passive immunization with rabies immunoglobulin and vaccination is recommended for all severe exposure to rabies. Hyper immune rabies immunoglobulin (H-RIG) is proved effective in preventing rabies and its use in combination with vaccine is considered to be the best post exposure prophylaxis. The full dose of RIG should be infiltrated around wound(s) and any remaining volume should be administered IM at anatomical site distant from vaccine administration. The RIG should not be administrated in the same syringe as vaccine, since RIG might partially suppress active production of antibody, and no more than the recommended dose should be given (David *et al.*, 2001). Human diploid cell vaccine (HDCV) is recommended for persons with both pre- and post exposure to rabies virus, for people who have had previous exposure immunization. The treatment consists of only two doses of HDCV take three days apart regardless of how long it has been since they were vaccinated. For a person who has not had pre exposure treatment consists of five doses HDCV each on day 0, 3, 7, 21, and 28 and rabies immunoglobulin at dosage of 20 IU/Kg on first day (day 0) only (Ettinger, 1999).

3.6. Public education/creating awareness

Mobilization of community participation by Public education and cooperation are essential for a wide range of activities in canine rabies control programs (Girma *et al.*, 2002). The roles and responsibilities of veterinary and medical practitioners and local government, wildlife and public health authorities in an outbreak area should be clearly defined and made known

to all concerned. The public should be kept informed on the public health aspects of rabies, the requirements related to the control and eradication campaign including the reporting of animal bite cases. Considering this issue, world rabies day has been cerebrated since September 2007 aims rabies control by raising awareness about the impact of rabies on humans and animals provide information and advice on how to prevent the disease, and how individuals and organizations can help eliminate the main global sources (http://www.worldrabiesday.org/EN/).

4. CONCLUSION AND RECOMMENDATIONS

The prime importance of rabies is its transmissibility to humans, with veterinarians being at special risk. World human mortality from endemic canine rabies was estimated to be 55, 000 deaths per year (90 % CI: 24,500–90,800) with 56% of the deaths estimated to occur in Asia and 44% in Africa. Wild animals and carnivorous bats are the primary reservoirs for rabies in many parts of the world, but domestic carnivores are the principal source of transmission of rabies infection to human being. Over 99% of all human deaths that are caused by infected dogs usually occur in Africa and Asia, especially in regions with large numbers of unvaccinated community and domestic dogs. Human rabies is extremely rare in countries where canine rabies is controlled by regular vaccination. In Africa, the highest recorded human death due to rabies for the year 1998 was 43 and reported from Ethiopia. Rabies occur in more than 150 countries and territories, 40% of people who are bitten by suspected rabid animals are children under 15 years of age. *Lyssavirus* epidemiology is influenced by host species, distribution, abundance, demographics, behavioral ecology, dispersal and interactions with humans. The diagnosis of rabies is one of the most difficult and important duties that a veterinarian is exposed to perform. The disease is a great concern (risk) specially, for veterinarian, animal control officers, rabies diagnostic laboratory workers, and people traveling to countries in which canine rabies is endemic. Recently, a few human rabies cases have been reported from recipients of cornea transplants from infected donors.

Therefore, taking the above facts into consideration, the following points were recommended.

- Detailed and coordinated epidemiological studies should be under taken both in Veterinary and public health sectors to generate enough data on the status of rabies both in animals and humans for effective control and preventive measures.
- It is very important to design a comprehensive prevention and control strategy that can initially be implement in all cities and towns that are administered by municipalities and

gradually expanded to cover the rest of the country with the objective of minimizing its incidence to an acceptable level for public health reasons and prevent its spread to both domestic and wild animals.

- Public health education and creating awareness of the health effects associated with poor handling of dogs and cats both at house hold and community level need to be improved.
- Sheep brain tissue vaccine is very expensive, primitive and brings unwanted side effects and the human diploid cell vaccine is much cost therefore other better alternative methods should be implemented and the vaccine preparation should consider the two phylogroup species and *west Caucasian bat virus.*
- Pre-exposure immunization is strongly recommend for dogs, cats, high risk valuable animals and people in high risk groups particularly for veterinary practitioners and post-exposure treatment regimens for humans Should be available to all suspected people.
- Control of stray dogs through spaying of females or castration of males or by destruction is highly recommended.
- Avoid possible contact of bats in the Caves, old houses, other man-made structures and buildings from which bats may live, should be encouraged.
- Tissues from persons who die of encephalitis of unknown etiology should not be used as donor transplants to avoid possible corneal transmission.

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