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Mini-Review

Roles of wildlife in epidemiology of rabies: A mini-review

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ABSTRACT

The roles of wildlife in rabies transmission are still underestimated in many parts of the world. In the developed countries, epidemiology of rabies considering wildlife has been well documented. However, in the least developed and developing countries, emphasis has not given on this issue. Human population is increasing all over the world, and new localities are continuously developing. As a result, wildlife territory is decreasing, and the animals are coming in close contact with humans. Besides, many people are keeping wildlife as the sources of their pleasures. Due to the increased interaction among wildlife, domestic animals and human there is need to intensify efforts on mass education and building of awareness on the risks of rabies spreading by the wildlife, and to institute effective preventive measures to control over the disease. In this mini-review, roles of wildlife in epidemiology of rabies has been discussed considering the dynamics of wildlife in relation with associated intrinsic and extrinsic factors.

KEYWORDS

Awareness; Control; Epidemiology; Rabies; Wildlife

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INTRODUCTION

Wildlife, domestic animals and humans are constantly threatened by rabies which is a zoonotic disease characterized by encephalomyelitis. When wild animals are rabid, they approach towns and may attack both domestic animals and humans (Gortazar et al., 2006; Miller et al., 2013). The public health importance of rabies is great since its mortality rate can be up to 100 %. It is estimated that between 50,000-100,000 humans, uncountable domestic animals and wildlife die yearly due to rabies all over the world (CDC, 2008; Aiyedun, 2011). The aetiology of rabies are viruses of the Rhabdoviridae family. They have seven recognized genotypes in three phylogroups (CDC, 2008; Wu et al., 2009; Adedeji et al., 2010).

There are various biotypes of rabies virus and each biotype is host specific. They are usually highly pathogenic, highly excreted while exhibiting low immune response in the host specie (Wandeler, 2004). Bats, Jackals and Mongooseshabour rabies viruses of concern (Dzikwi et al., 2010). Although variants are adapted to their reservoir species, they can be transmitted to other species, (fox variant could be detected in a dog). However, molecular analyses are needed to identify the different virus variants (McElhinney et al., 2008; ASE, 2008).

Globally, information are increasing on the roles of wildlife in the epidemiology of rabies particularly in the developing world, for instance, rabies transmission risks and its link with wildlife have been enumerated by Daszak et al. (2000) and Caron et al. (2013). Hanlon (2005) in their epidemiological survey observed the limitations associated with rabies control given the compounded factors associated with wildlife and its ecology. They recommended a multiagency approach in the management and understanding the epidemiology of rabies and wildlife. The team also pointed out some constrains on available and feasible control methods compared with the broad range of public attitude and engagement in wildlife ventures and recreational activities (Hanlon et al., 2005), the team therefore suggested that the control of wildlife rabies should be multiagency and multidisciplinary. Economically, other scientists emphasised the fact that rabies have a multi-hosts and multi-infections scope with significant impacts on human efforts and income in the management and control of rabies in domesticated particularly in the wildlife (Gortazar et al., 2007; Martin et al., 2011).

Furthermore, several studies expanciated on the possible changes associated with the epidemiology of rabies in wildlife with particular references to its multi-species complexity and its dynamics regarding human demographic variability, animal instability, climate change, and viral mutations (Uhaa et al., 1992; Holmala and Kauhala, 2006). Hence, rabies in the wild is more complicated than envisaged hence the need for more research with a multidisciplinary approaches as recommended by these authors (Uhaa et al., 1992; Holmala and Kauhala, 2006). In this review specific sub-topics were enumerated under discussion to reveal more information on rabies' epidemiology in wildlife and control suggestions to the stakeholders are summarized under the conclusion.

Rabies-related viruses and complexity

One of the specific features of this viral agent is for the fact that a minimal of 7 different major genotypes of *Lyssavirus* species have been identified from mammals (Fauquet et al., 2004). This genus also covers those species isolated from Eurasia (Kuzmin et al., 2005). Six of these have similar clinical manifestations in humans

Table1: Classification of Lyssaviruses

Genotype	Phylogroup	Species	Abbrevation	Distribution	Potential vector (s)
1	I	Rabies virus	RABV	Worldwide	Carnivores (worldwide) Bats (Americas)
2	II	Lagos bat virus	LBV	Africa	Frugivorous bats
3	II	Mokola virus	MOKV	Africa	Unknown (isolated from shrews)
4	I	Duven-hage virus	DUVV	Africa	Insectivorous bats
5	I	European bats Iyssavirus 1	EBLV-1	Europe	Insectivorous bats (eg. *Eptessicusserotinus*)
6	I	European bat Iyssavirus 2	EBLV-2	Europe	Insectivorous bats (eg. Myotissp)
7	I	Australian bat Iyssavirus	ABLV	Australia	Frugivorus/insectivorous bats
Proposed	I	Aravan virus	ARAV	Central Asia	Insectivoruos bat (isolated from Myotisblthi)
Proposed	I	Khujand virus	KHUV	Central Asia	Insectivoruos bat (isolated from Mytismystacinus)
Proposed	I	Irkut virus	IRKV	East Siberia	Insectivoruos bat (isolated from Murinaleucogaster)
Proposed	II or III	West Caucasian bat virus	WCBV	Caucasus region	Insectivorous bat

(Aiyedun, 2011)

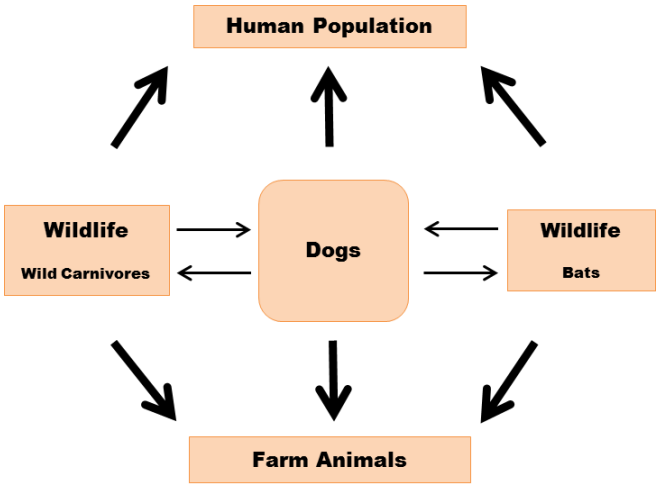

Figure1: Dynamics of rabies occurrence and transmission

(**Table 1**). However, genotype 2, is more important in wild animals as it has not yet been isolated in humans; more importantly are variants 1, 5 and 6 (Wilsmore et al., 2006). Genotype 1 viruses are globally distributed and can be found specifically in earthbound animals. Species from variants 5 and 6 are popularly referred to as European bat lyssaviruses (EBLVs). They are usually found in Europe and isolated from bats (Fauquet et al., 2004). Rabies is basically caused by species in genotype I, isolation of members of this group have not been reported in bats from Europe. There have however, been reports of their isolation in bats from North America. (Finnegan and Brookes, 2002).

Table 1 shows that there are emerging lyssavirus genotypes these include; Aravan (ARAV), Khujand (KHUV), Irkut (IRKV), and West Caucasian bat virus (WCBV) which were discovered in bats from Eurasia (Hanlon et al., 2005). Genotype I (RABV) is the classical rabies virus. The classification came to be after other viruses related to rabies were isolated in Europe and Africa in the 50s. They are designated as the typical members of the genus (Wilsmore et al., 2006).

Currently, four *Lyssavirus* species have been described in Africa out of which classical rabies virus occur worldwide however, Lagos bat virus (LBV; genotype 2), Mokola virus (MOKV; genotype 3), and Duvenhage virus (DUVV; genotype 4) have not yet been reported beyond Africa (Ogunkoya et al., 2003). Even though classical rabies infection of bats the causal agents have only been known to cause infection only in land mammals in Africa (Mebatsion et al., 1992). In contrast, Mokola virus have never been isolated form bats except from different terrestrial animals (Nel et al., 2000). Duvenhage and LBV have majorly been reported in bats with occasional isolation in land animals (Mebatsion et al., 1992). In the African continent, RABV has been reported to be a major cause of zoonosis. There are few reports of human cases of rabies due to Mokola and Duvenhage viruses while LBV has never been associated with human cases (Nel et al., 2000; Carter and Wise, 2005).

Lagos bat virus was isolated from fruit bats in Nigeria for the first time in 1956 (Boulger and Porterfield, 1958), but it was not recognized as a rabies related virus until 1970 (Shope et al., 1970).

The rabies virus and Mokola virus are related in terms of morphology and serology (Aghomo et al., 1990). It was first isolated in Ibadan, Nigeria, in 1968 from shrews. However, antigenically, while rabies virus is most distantly related to Mokola virus, it is most closely related to Australian bat Lysavirus (Constantine, 2009). The distant relationship can be illustrated by the fact that standard rabies post vaccination provides protects poorly against Mokola virus (Bishop et al., 2003).

However, when preformed antibodies and vaccines specific for the different viruses are not available, it is more beneficial to use standard rabies immunoglobulin and vaccines (Bishop et al., 2003). A number of unvaccinated dogs in Nigeria have been reported to have Lysavirus antibodies (Ogunkoya et al., 2003; Dzikwi et al., 2010) which is indicative that dogs in Nigeria may maintain rabies and other Lysaviruses. Rabies is and may remain endemic and neglected in Nigeria because of it's under reportage and under diagnosis.

Epidemiologically, rabies has 2 cycles which are the urban and sylvatic. Lyssavirus genotypes 1-3. The rabies virus (RABV), Mokola virus (MOKV) and Lagos bat virus (LBV) have been reported in Nigeria (Dzikwi et al., 2010).

Occurrence of rabies

Epidemiologically, there are two cycles of rabies which are the urban and sylvatic (wildlife). The major reservoir host of urban rabies are dogs although in Africa, Middle East, Latin America and Asia few sylvatic cases of rabies have been reported (Hanlon et al., 2005). In the United States of America, Canada and Europe urban rabies have been literarily eliminated leaving only wildlife cycle of the disease (Constantine, 2009). Wild Carnivores play an important role as vector in sylvatic rabies. This cycle usually reverts to urban cycle due to frequent contact between rabid wild carnivores and stray dogs/domestic animals (**Figure 1**).

There is increasing incidence of urban and sylvatic rabies in Africa, this is of great concern to Public Health and conservation of endangered species especially carnivores (Macdonald, 1993; Blanton et al., 2009). Often one or up to three wildlife species are responsible in any ecosystem. In most part of the world rabid animals are identified every month of the year but the epizootic can be seasonal (Blanton et al., 2009). Therefore, in-contact humans and pets are always at risk of rabies. However, there were reported cases of dog bites that resulted to human fatality, without the dog showing the clinical signs of rabies (Ogunkoya et al., 2003; Ajayi et al., 2006; Okonko et al., 2010).

All mammalian species can exhibit susceptibility to rabies virus only very few species serves as important reservoirs of the disease. In North America and Europe, the wolf and dog were very important in the maintenance of the disease among populations until the twentieth century when the red fox emerged as the important maintenance host of the disease (Wilsmore et al., 2006).

There are other species of wildlife that have been incriminated in the epidemiology these include the raccoon which is reported to be the reservoir host in Northern Europe while skunks and raccoons are involved in North America (Weber and Fresard, 2004). The rate of diagnosis of rabies in bats is on the increase (Artois et al., 2001; Fooks, 2004). This is no more limited to well established hosts like vampire bats in Central and South America but is now inclusive of insect and fruit eating bats all over the world, over 1,200 species of bats identified with about 140 rabies variants (Artois et al., 2011). Fifty percent of human diagnosed rabies cases in the United States are vaariants from bats (Wilsmore et al., 2006). The main host that maintains and transmits rabies to other animal (including wildlife) and man in Nigeria is the dog (Dzikwi et al., 2010).

Reservoirs of rabies viruses

Bats: Rabies virus transmitted to human are increasingly being done by bats, over 140 variants have been identified in insectivorous bats. Transmission of rabies virus can occur from bat bites that may be small and insignificant (Krebs et al., 2005; CDC, 2008). Due to this man and other animals' contact with bats should be limited, they should only be handled by trained and vaccinated persons and should not be kept as pets (CDC, 2008). Terrestrial animals inflict more visible wounds from bites compared to bats which makes the assessment of the risk of contracting rabies from bat encounter to be difficult (Fooks, 2004; Artois et al., 2011). Any animal bitten or scratched by bat should be regarded as exposed (CDC, 2010).

Wild terrestrial carnivores: Wildlife species of special concern in Nigeria include Jackals and mongooses (Dzikwi et al., 2010). Wildlife such as several species of bats, coyotes, foxes racoons and skunks account for the occurrence of most of the rabies cases in USA (Krebs et al., 2005, Blanton et al., 2009). The clinical signs exhibited by wildlife is not well documented therefore scratches and bites from wildlife and their crosses should be taken as possible rabies exposure (CDC, 2008).

Other wild animals: Squirrels, chipmunks, rats, mice, hamsters, guinea pigs, gerbils, rabbits and hares are not usually infected with rabies (Wu et al., 2009). Crosses of wildlife and other domestic animals are regarded as wild animals (NASPHV, 2007). Due to the fact that the duration of time of shedding of rabies virus in wild animal crosses is unknown their bite in human should be followed by rabies testing of the hybrid animal, euthanasia or vaccination which should be discontinued if the animals involved are not positive for rabies (CDC, 2008).

Domestic dogs and cattle: In the United States, because of good stray animal control programme and improved canine vaccination cases of rabies in dogs have drastically reduced (Krebs et al., 2005). In many developing countries including Nigeria, the major reservoir and vector of rabies are dogs (CDC, 2008; Dzikwi et al., 2010). They infect human, domestic animals and wildlife (Ogunkoya et al., 1990; Awoyomi et al., 2007). Dogs still represent the major hazard to public health in relation to rabies worldwide (Velasco-Villa et al., 2008). Cattle cannot support rabies independently therefore the disease occur in the specie usually as a spill-over host acting as sentinel hosts for rabies (and Vos, 2005).

Transmission

This occurs when an infected host's saliva passes to an animal that is not infected (Milius et al., 2004; Ehizibolo et al., 2011). The most common transmission mode is through bite and infected saliva, other routes include the eyes, mouth, nose mucous membrane, corneal transplantation and aerosol transmission (Milius et al., 2004). In most developing regions of the world, dogs are still the chief host of rabies and account for the majority of deaths that occur due to human rabies all over the world (WHO, 2008). Although animals like horses, deer and cattle can be infected with rabies and transmit to other animals and human this seldom occur (WHO, 2008).

Concerns of spread of urban rabies to wildlife in specific countries

Nigeria: There are concerns that there could be spread of urban rabies, through apparently healthy dogs, to wildlife. Such spread typically occurs through infected hunting dogs; the domestic dog may also be re-infected when exposed to infected wildlife (Ogunkoya et al., 2003). There are heightened public campaigns and vaccination programme which are expected to lead to significant reduction in incidence of urban rabies.

Europe: Red fox emerged as a new wildlife major host in Europe after the elimination of rabies in dogs. The disease thereafter spread westward towards Western and Central Europe within a few years. In France and Northern Italy, however, foxes were treated with oral rabies vaccine which halted the spread of the disease (Wandeler, 2004; Potapov et al., 2012).

North America: As in Europe, wildlife rabies began to emerge after canine rabies was successfully eliminated in the United States and Canada. Since 1980s, wildlife have accounted for >90% of rabid animals in the US (ASE, 2008; Okonko et al., 2010).

Pathology

In all warm blooded animals rabies virus causes acute encephalitis with fatality rate of almost 100%. The pathology of the disease is therefore that of myelitis and encephalitis. The entire Central Nervous System will be infiltrated with plasma cells, polymorphonuclear leukocytes, and lymphocytes. The hippocampus, purkinje cells and pyramidal cells of the cerebellum characteristically contain cytoplasmic eosinophils called inclusion bodies or Negri bodies. These areas represent regions of active viral replication (Kashyap et al., 2004).

Prevention of rabies

Wildlife have been established to be sources of different zoonosis, moderating wildlife management programmes such as culling, conservation, feeding, translocation and fencing of wildlife natural habitants could be useful in the prevention of rabies. Therefore, control programmes employed in wildlife curb the spread of rabies, eliminate and prevent the spread of the disease in enzootic areas (Gortazar et al., 2007; Kock et al., 2010). Prevention of rabies is relatively straightforward and consists of a primary strategy aimed at avoiding interactions with possibly rabid animals. For the at-risk group, primary vaccination and secondary defense after an exposure has occurred is the key (Ratzan, 2006; Aiyedun and Olugasa, 2012).

Pre-exposure vaccines are usually administered to animals while post-exposure vaccines are given as treatment to humans. Pre-exposure inoculations may be recommended in high risk group of people (Bishop et al., 2003). Post exposure vaccines are usually more expensive but have been used with good degree of success. Treatment of clinically infected man and animals usually produces no positive result (Wilsmore et al., 2006). Oral Rabies Vaccine (ORV) may be used successfully in controlling wildlife rabies. Efforts should be intensified so as to make them more available and affordable for wider use in wildlife populations (Blanton et al., 2009). ORV uses oral bait targeting rabies wildlife reservoir hosts which releases the attenuated rabies virus after ingestion of the vaccine too produce immune response (Hanlon et al., 2005). The rabies vaccines in use presently protect against many Lyssaviruses with studies showing that it will protect against all known rabies strains (Fekadu et al., 1988, Carter and Wise, 2005). Vaccines have been used successfully against rabies all over the world conferring about 3 years immunity. The threshold immunity is antiboby level of 0.5 IU/mL and above though protection have not been fully equated to antibody response (Wilsmore et al., 2006; WHO, 2010).

CONCLUSION

Control of rabies in the urban and in the wild require an extensive awareness creation through education, information and communications disseminated through mass media, radio and television programs. Educational tools like publications, handbills, leaflets, posters and other short messages in different dialects on the risks, dangers, and roles of the wildlife in rabies transmission are critical. We recommend human capacity building in this field for further research on collaborative studies among the medics and veterinarians for rapid detection of this disease in the hosts both in the urban and rural settings where the incidences of this deadly disease are frequently reported. Government needs to support the veterinarians to ensure the anti-rabies vaccines for humans and animals are readily available and vaccination subsidies are considered for the animal keepers and other professional at risks. Empowerment of the stakeholders at the grassroots level is paramount through training of personnel, task force on routine anti rabies vaccination for dogs and wild animals. Border control strategies should be expanded to cover active rabies surveillance in the zoological gardens, wildlife parks, museums and tourist for wildlife reserves. The roles of the veterinarians

in synergies with the medics on the ground of one-health are paramount in the control and complete eradication of rabies.

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CONFLICT OF INTEREST

The authors declare no conflict of interests.

AUTHORS' CONTRIBUTION

JOA initiated the work, the initial draft and literature review; OOO made the necessary corrections over the entire manuscript and serves as our contact fellow. IDO overhauled the overall manuscript to give it the present outlook.

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