



ROLE OF BATS IN THE EMERGENCE OF VIRAL ZONOOSES

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Abstract

Bats, both insectivorous and frugivorous, play a major role in wide range of ecosystems across the globe, mainly in depleting the insect population especially the pests as well as through the dispersal of seeds and pollination of many varieties of plants. Bats are the only flying mammal and have a widespread geographical distribution, occurring in all continents, except Antarctica (Moratelli and Calisher, 2015).

Bats are considered as the second most abundant mammals in the world, next to rodents, with around 1300 species (IUCN, 2010). This total comprises almost one fifth of the world's mammalian species, with more than 175 genera arranged in 20 families (Simmons, 2005; Wilson and Reeder, 2005). Most of the bats roost together in large colonies and have unique ability to travel long distances (Turmelle and Olival, 2009). Caves, underneath trees and canopy of thick vegetation, abandoned human dwellings etc. are the favourite aggregating sites of colonial bats (Kunz and Pierson, 1994). Despite their important positive role in ecosystem, bats have also been linked to the

incidence of many zoonotic diseases. The bats have been reported to carry many of deadly viruses in their secretions and excretions, thereby serving as a zoonotic pool for emerging infections. Bats host more zoonotic viruses per species than do rodents and most of the resulting zoonoses have been high-profile spillover incidents of extreme human pathogenicity (Dobson, 2005).

Bats as a reservoir of zoonoses

The role of bats in the spread of zoonoses remained a neglected arena. The cases of many emerging zoonotic diseases such as Rabies, Ebola, Severe acute respiratory syndrome (SARS) corona virus, Nipah, Hendra, Middle-East respiratory syndrome (MERS) etc., have been reported to be linked with bats and drew the attention of scientific community about the role of bats as a reservoir as well as source of these infections. As reported, zoonotic viruses from more than 15 virus families have been identified in at least 200 species in 12 families of bats around the world (Calisher *et al.*, 2006).

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Various aspects of bat life history and ecology including fly range, dependency on torpor and/or hibernation, long life span, and gregarious social structure are likely to influence bat's roles as reservoir for these pathogens. During their flight, bats are hypothesized to show an increase in the metabolic rate and body temperature, which is comparable to the fever response and thereby, limits the replication of infectious agents up to harmful level and makes them a reservoir for the harbouring pathogens (Calisher *et al.*, 2006).

Some species of bats can migrate to large distances as much as 41,000 km (McGuire *et al.*, 2013). Their long flight ranges allow them to disseminate and acquire pathogens over a wide geographical range. Bats live in large colonies or roosts (sometimes in the millions) and they also enjoy prolonged longevity for their body size. Many species of small temperate bats of the suborder Microchiroptera have longevity more than 25 years. The little brown bat, with the greatest documented longevity of 35 years, weighs only about 7 grams (Austad, 2005; Calisher *et al.*, 2006). Their remarkable longevity may lead to the maintenance of viruses for an extended period of time and, therefore, makes them a suitable reservoir for pathogens and provides them many opportunities to transmit these pathogens to other species (Barret, 2011).

As similar to other mammals, bats also share many of the physiological and immunological traits with humans. Moreover, the shared ecology of bats with humans in many activities like roosting in human-made constructions, feeding or hanging on fruit trees or flying around light poles to feed on insects in urban and rural areas, increases the chances of spillover of zoonotic pathogens (Brook and Dobson, 2005).

Brief overview of role of bats in emergence of important zoonotic diseases

The emergence of zoonotic diseases is a multi-dimensional event, involving many of the anthropologic factors like habitat destructions, change in land use patterns, change in human demography and behavior; and the increase in encroachment to the wild life. These changes depict a number of ecological effects, including human-domestic/farm animals-wild life conflicts, thus facilitating the spill-over and transfer of novel pathogens into susceptible hosts. An overview of the emergence and major outbreaks of important bat-borne viral zoonoses in time-scale has been depicted in Fig 1.

The details of important bat-borne viral zoonoses are discussed below

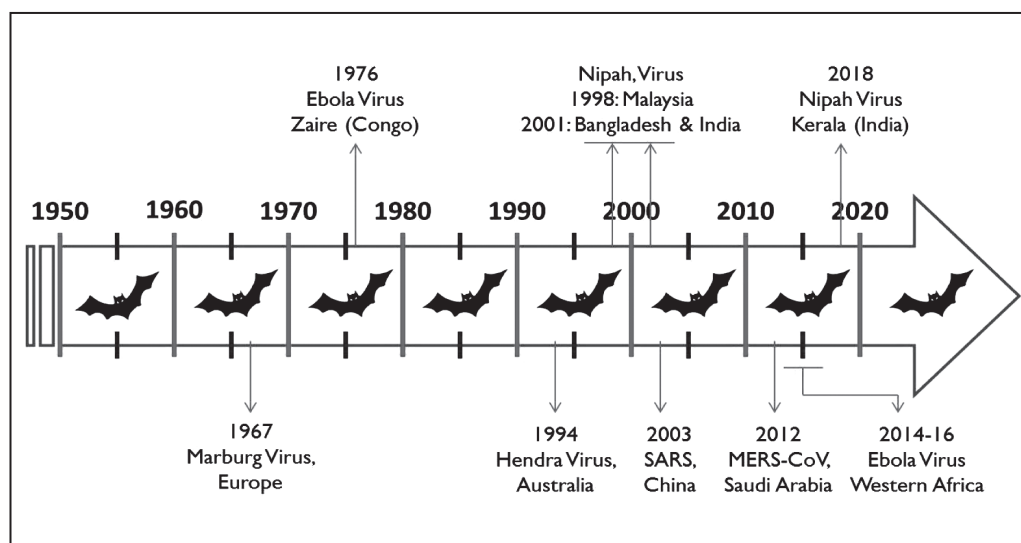


Fig. 1: Emergence and outbreaks of bat-borne viral zoonoses

1. Nipah and Hendra viral infections

The Nipah virus belongs to the family *Paramyxoviridae* under the genus *Henipavirus* which also contains Hendra virus. Both, Nipah and Hendra viruses belong to CDC 'category C' pathogen and have bats as a reservoir host (CDC, 2014).

The first outbreak of Nipah was reported during 1998 in Malaysia, where the virus was isolated from a fatal human case in Sungai Nipah, Malaysia; therefore the virus has been named as Nipah (Field *et al.*, 2001). The epidemiology of the outbreak is correlated with the slash-and-burn of forest area of Borneo and Sumatra as well as due to ecological effect of El Nino, which eventually led to mass exodus of fruit bats which later settled to orchid plantation nearby intensively farmed piggery (Chua *et al.*, 2002). The pigs became infected with virus and depicted "barking pig syndrome". The rapid transportation of infected pigs to five states of Malaysia and Singapore resulted in 265 human cases with 105 deaths (Parashar *et al.*, 2000). The infection also spread to other domestic animal species like dogs and cats which again may act as source of infection for humans (Chua, 2003). Finally, the outbreak had been contained by employing various public health measures including culling of more than 1 million pigs (Lam, 2003).

The second major outbreak of Nipah virus was observed during 2001 in Meherpur area of Bangladesh but it could not be investigated until 2003, when another cluster of febrile illnesses with neurologic features occurred in adjoining villages in Naogaon district resulting in 08 deaths (Hsu *et al.*, 2004). At the same time, the outbreak was also reported in Siliguri, India (adjoining area to Bangladesh). The primary route of infection in these outbreaks was found to be bat-to-human transmission linked to the consumption of contaminated date palm sap (Hsu *et al.*, 2004). Epidemiological studies have found evidence for Nipah virus infection in multiple flying fox species, such as the island flying fox (*Pteropus hypomelanus*), the Malayan flying fox (*Pteropus vampyrus*), the Indian flying fox (*Pteropus giganteus*) and Lyle's flying fox (*Pteropus lylei*)

(Yob *et al.*, 2001). Reports of person to person transmission in hospital settings as nosocomial transmission have also been documented from these outbreaks (Hsu *et al.*, 2004).

The most recent Nipah outbreak in Kerala has been promptly reported with the diagnosis of index cases on 17th May, 2018 in Kozhikode district. Later, the transmission of disease has been observed from person-to-person and to health care workers. The source of infection has been traced back to frugivorous bats. However, the robust efforts of public health system of Kerala managed to contain the outbreak within a short period with 16 casualties (The Hindu, July 4th, 2018).

Even though the geographical distribution of the frugivorous bats is even found in other South-East Asian countries, the disease is now limited to Malaysia, Bangladesh and India highlighting the complexity of the ecology of the disease with anthropogenic activities.

The flying foxes have also been linked with the first reported outbreak of Hendra virus in Brisbane, Australia in 1994. During the outbreak, horses were the sole species affected with Hendra virus. The infected horses developed high fever, respiratory and neurological symptoms following exposure to *Pteropus* bats nearby horse farms (Baldock *et al.*, 1996). The virus showed the transmission from horses to humans which is reported to claim 04 lives out of 07 cases in multiple outbreaks (Mahalingam *et al.*, 2012). However, human-to-human transmission was not observed in the outbreaks of the virus (Playford *et al.*, 2010).

2. Rabies

Rabies is considered as the most fatal zoonoses with nearly 100% fatality rate in infected individuals. The bites of rabid dogs and wild mammals like raccoons, skunks and foxes etc., are considered as the main route of rabies transmission in Asia and Africa (Baer, 2017). However, in United States, bats have been reported as a main source of bitten and non-bitten form of rabies which results in one to four human deaths annually (Barrett, 2011). Bites

as well as aerosolization of bat saliva, urine or faeces have been implicated as a source of infection to humans (Constantine, 2009).

Rabies virus (RABV), Lagos bat virus (LBV), Duvenhage virus (DUVV), European bat lyssaviruses type 1 and 2, Australian bat lyssavirus (ABLV), Aravan virus (ARAV), Khujand virus (KHUV), and Irkut virus (IRKV) are some of the bat borne viruses of Rhabdoviridae, many of which can cause a fatal human illness indistinguishable from classic rabies (Hanlon *et al.*, 2005).

The bats have been linked to the overwintering and constant shedding of lyssa viruses (Sulkin and Allen, 1974). Even the highly pathogenic rabies virus has been detected in apparently healthy bats (Davis *et al.*, 2012). Spill over of bat borne lyssa viruses to other mammals which could serve as source of infection to humans facilitate bats to serve as a zoonotic pool of virus. The danger of viral transmission from bats to other reservoir species such as foxes and jackals emerges as a setback to the canine rabies eradication programmes (McQuiston *et al.*, 2001).

3. Filoviruses

Ebola and Marburg viruses are among the most deadly viruses known to humankind. The transmission of these filoviruses to humans is believed to occur mainly through human-wildlife interface such as in 'bushmeat' activities (the capture and slaughtering of wild animals, including non-human primates) and subsequent transmission occurs between person to person by direct contact with infected blood or body fluids (Leroy *et al.*, 2009). The recent data indicated that bats could be the potential natural hosts of Ebola and Marburg viruses in Africa (Leroy *et al.*, 2005).

(a) Marburg hemorrhagic fever

The African green monkeys associated with the first outbreak of Marburg virus in Europe during 1967, were suspected to have encountered fruit bats on the shores of Lake Victoria before shipment from Uganda (Smith *et al.*, 1982)

It has also been reported that roosting of large numbers of bats (*Rousettus aegyptiacus*) were associated with the Marburg virus outbreak among the workers in Goroumbwa Mine in Durba, Democratic Republic of the Congo during 1998-2000 (Bausch *et al.*, 2006; Swanepoel *et al.*, 2007). Further, the genetic analysis demonstrated that the Marburg virus isolated from the infected mine workers was highly similar to those circulating in the *R. aegyptiacus* population (Towner *et al.*, 2009).

(b) Ebola hemorrhagic Fever

Ever since the first reported outbreak of Ebola haemorrhagic fever in 1976, the scientists were pondering the mystery of source of Ebola virus. The deadly viral haemorrhagic fever though earlier was linked to primates as the source of infection, the further scientific and circumstantial evidence proved the role of 'flying foxes' as the reservoir of infection (Feldmann, and Geisbert, 2011). The maintenance of Ebola virus in enzootic cycle is in the fruit bats of the *Pteropodidae* family from which the infection spills over to primates, which represents an epizootic transmission cycle of virus. The primates become seriously ill due to the viral infection and close proximity to these primate cases can serve as source of infection to humans (Groseth *et al.*, 2007). The virus then can cause massive deaths and fatalities in humans and is involved in person-person transmission especially in the community settings through close contact with secretions and/or the fomites of the infected person. The direct transmission of the Ebola virus from bat caves to tourists has also been reported (Smith *et al.*, 1982; Johnson *et al.*, 1996).

The largest global epidemic of Ebola virus occurred in West African countries during 2014-2016 which later expanded to the Central part of Africa. The health crisis shattered the social and economic security of the afflicted nations which were already fighting against poverty and other disease burdens. The most severely affected countries were Guinea, Liberia and Sierra Leone, which have weak health systems, lack basic infrastructural resources, and have only recently emerged from long periods of conflict and instability (WHO, 2016).

As on March 30, 2016, out of a total of 28,610 suspected cases of Ebola in these countries, 15,221 were laboratory confirmed cases and 11,308 were dead (WHO, 2016).

4. Severe acute respiratory syndrome coronavirus (SARS-CoV)

Severe acute respiratory syndrome coronavirus emerged in late 2002 and represents the first public health emergency of 21st century (Berger *et al.*, 2004). The index case was detected in Guangdong province of China in late 2002. Later, SARS wreaked havoc among the global public health agencies through its potential for rapid spread. As of early 2003, 8422 people were infected in 30 countries with 916 deaths and a case fatality ratio of 11% (WHO, 2003). Albeit, palm civets were shown to be infected with SARS virus in live animal markets and restaurants in the Guangdong province in southern China, extensive epidemiological and surveillance studies demonstrated that civets were probably an amplifying and/or adaptation host and that the true reservoir of the SARS and SARS-like coronaviruses were bats of the genus *Rhinolophus* (Horse shoe bats) (Li *et al.*, 2005).

5. Middle East respiratory syndrome coronavirus (MERS-CoV)

Since the first reported outbreak in 2012, the MERS-CoV poses a great public health threat, however, most of the infections have occurred in Middle Eastern countries on the Arabian Peninsula but the large epidemic potential can't be ruled out (Assiri *et al.*, 2013). On the basis of phylogenetic analysis, it is believed that MERS-CoV, like many other coronaviruses, originated in bats (De Benedictis *et al.*, 2014). This hypothesis was further supported when a polymerase chain reaction fragment with a sequence which was identical to that of a human MERS-CoV isolate was detected in the Egyptian tomb bat (*Taphozous perforates*) in Saudi Arabia (Memish *et al.*, 2013).

To date (May, 2018), a total of 2,220 laboratory-confirmed cases of MERS-CoV have been reported in the Middle East, Europe and Africa, including 790 associated deaths

with a case-fatality rate of 35.6 %; however, the majority of these cases were reported from Saudi Arabia (1844 cases, including 716 related deaths with a case-fatality rate of 38.8 %) (ProMed-mail, 2018).

Other bat-borne viruses

In addition to the major bat-borne zoonotic viruses, there have been a large number of previously unknown viruses discovered in the last decades. Many of these viruses have known zoonotic transmission (e.g., Menangle virus in Australia and the related Tioman and Melaka viruses in Malaysia, and other related bat reoviruses) (Chua *et al.*, 2007; Kohl *et al.*, 2012). Bat viruses related to known human pathogens have also been detected in large numbers (e.g., bat lyssaviruses, parainfluenza viruses, Hantaviruses, hepaciviruses and pegiviruses) (Li *et al.*, 2010). The public health threat potential of these viruses are yet to be unraveled, however, it would be prudent to keep a close surveillance on their potential spillover.

Prevention and control of bat borne zoonoses

The complexity of control of bat borne diseases lies in their abundance and widespread geographical location. Epidemiological investigation of the zoonotic diseases that may be linked to bats relies on efficient surveillance of free-ranging bat population. The fluctuation in the disease incidence and prevalence rate of bat-borne zoonoses has been linked to the fluctuations and migrations of the bat population (Hayman *et al.*, 2013).

Owing to the huge diversity of bats, in terms of number of species within the order and in terms of abundance, they can serve as reservoir for many new emerging viruses. The main control strategy for these emerging diseases depends on the early detection of viruses based on the efficient surveillance of bat population. Except for the European and African bat Lyssa viruses; there is little surveillance machinery established for other bat borne viruses (Barrett, 2011).

Minimizing the contact of livestock

with bats through improved farm biosecurity measures; rapid detection of disease in human and animals through early warning systems; and awareness among at-risk groups can serve as an effective and feasible control strategy. The wide spread global distribution of the free living bats makes it impossible to vaccinate the entire population, hence other measures to prevent spill over of infections from this important zoonotic pool must be considered. Sustainable land use pattern by avoiding the encroachment of human and domestic animals to the potential risk areas of the reservoirs and avoidance of risky behavior such as handling of wild bat or keeping bats as pets can play important role in prevention of these bat-borne zoonoses. Contact exclusion with bats in humans can be achieved through awareness programs on avoiding the bat handlings and use of safe techniques along with personal protective equipments (PPE) in cases of emergency. Vaccination of high risk groups is an efficient control strategy. But, pre- and post- exposure vaccinations are prevalent only for *Lyssa* viruses. The high risk groups of people such as veterinarians, forest guards, recreational and campestrial workers receive pre-exposure vaccination for bat borne rabies (Barrett, 2011).

Early detection and rapid response is the main key to contain many of these outbreaks. The medical and veterinary professionals along with ecologists should come together in a spirit of 'one-health' approach for tackling these deadly pathogens.

Conclusion

The increasing trend of bat-borne zoonotic virus emergence in the last few decades demonstrated the role that the 'One-Health approach' has played in almost every aspect of outbreak investigation, control and prevention of emerging zoonoses. It is imperative that health workers, veterinarians, forest officers and ecologist at every level and in every nation should work in collaboration to further nurture and maximize the benefits of One Health practices, which seems to be the most effective weapon in our future fight against emerging and re-emerging zoonotic diseases.

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