Review Article

Indian J Med Res 145, May 2017, pp 601-610
DOI: 10.4103/ijmr.IJMR_1871_15

Quick Response Code:

A mini-review of Bunyaviruses recorded in India

Pragya D. Yadav, Gouri Y. Chaubal, Anita M. Shete & Devendra T. Mourya

Maximum Containment Laboratory, ICMR-National Institute of Virology, Pune, India

Received December 1, 2015

Newly emerging and re-emerging viral infections are of major public health concern. *Bunyaviridae* family of viruses comprises a large group of animal viruses. Clinical symptoms exhibited by persons infected by viruses belonging to this family vary from mild-to-severe diseases *i.e.*, febrile illness, encephalitis, haemorrhagic fever and acute respiratory illness. Several arthropods-borne viruses have been discovered and classified at serological level in India in the past. Some of these are highly pathogenic as the recent emergence and spread of Crimean-Congo haemorrhagic fever virus and presence of antibodies against *Hantavirus* in humans in India have provided evidences that it may become one of the emerging diseases in this country. For many of the discovered viruses, we still need to study their relevance to human and animal health. Chittoor virus, a variant of Batai virus; Ganjam virus, an Asian variant of Nairobi sheep disease virus; tick-borne viruses such as Bhanja, Palma and mosquito-borne viruses such as Sathuperi, Thimiri, Umbre and Ingwavuma viruses have been identified as the members of this family. As Bunyaviruses are three segmented RNA viruses, they can reassort the segments into genetically distinct viruses in target cells. This ability is believed to play a major role in evolution, pathogenesis and epidemiology of the viruses. Here, we provide a comprehensive overview of discovery, emergence and distribution of Bunyaviruses in India.

Key words Animal virus - arthropods - Bunyavirus - CCHF - RNA virus - zoonosis

Introduction

Globally, emerging viral infections constitute a major public health challenge. About 350 viruses, most of which are arthropod borne, are classified in the *Bunyaviridae* family. *Bunyaviridae* is one of the largest families of animal viruses. Individuals infected by different Bunyaviruses exhibit a range of mild-to-severe diseases *i.e.*, febrile illness, encephalitis, haemorrhagic fever and acute respiratory illness. Earlier, many Bunyaviruses have been isolated and characterized at the serological level in India, for example, Ingwavuma virus (INGV), Thottapalayam virus (TPMV), Umbre (UMB), sandfly fever virus (SFV), Nairobi sheep disease virus/Ganjam virus (GANV), *etc*[1-4]. There is a need to understand the members of this family at molecular level which may help to understand their disease profile in nature.

Bunyavirus is named after Bunyamwera, Uganda, where the virus was first found in mosquitoes[5]. The particles of *Bunyaviridae* family of viruses are spherical and of 80-120 nm in diameter. These have a common genetic organization of three segmented negative-stranded RNA (S, M and L segments). These are subdivided into five genera on the basis of

antigenic, genetic and ecological relatedness. Except for the genus *Tospovirus* which is pathogenic in plants, *Orthobunyavirus*, *Hantavirus*, *Nairovirus* and *Phlebovirus* genera consist of enzootic viruses and some of these cause zoonotic diseases in humans. Of the more than 537 known arboviruses, more than 350 known viruses belong to these four genera. About 174 of these are listed under the genus *Orthobunyavirus* and include about half of the nearly 60 viruses of the family *Bunyaviridae* causing human diseases. Humans act as accidental dead-end hosts for these viruses in a zoonotic transmission cycle that alternates between arthropods and mammals (mostly rodents)[6,7].

Chittoor virus (CHITV)/Batai virus (BATV)

Chittoor virus (CHITV) was first isolated in 1957 from *Anopheles barbirostris* collected from Brahmanpalli, Chittoor district, Andhra Pradesh, India[8]. Subsequently, several isolates of this virus were obtained from *Anopheles* and *Culex* mosquitoes as well as from a piglet in India[9,10]. This virus was placed in Bunyamwera group based on serological characterization[11]. It was found to be antigenically related to Calovo virus and Batai virus (BATV) isolated from Slovakia and Malaysia, respectively[12]. Repeated isolations of CHITV and seroprevalence in several States suggest that the virus has been circulating in India for a many years[13]. However, this virus has not caused any outbreak or exhibited any disease symptoms involving humans. Its ability to replicate in vertebrates and mosquitoes may be the cause of concern for public health as it is related to severe fever with thrombocytopenia. A reassortant between Ngari virus and BATV was found to be associated with febrile human illness in Sudan[14]. This emphasizes that, though BATV on its own may not cause human or animal disease, it has the potential to cause febrile illness after reassortment with other viruses of the Bunyamwera group.

CHITV was isolated from *Anopheles* mosquitoes (*An. barbirostris* and *An. subpictus* from Andhra Pradesh and Karnataka, respectively), *Culex* mosquitoes (*Cx. tritaeniorhynchus* and *Cx. pseudovishnui* from Karnataka) and swine (*Sus scrofa* from Karnataka)[15]. A phylogenetic study based on S, M and L segments of CHITV isolated from India showed that a genetically uniform strain of CHITV is circulating in India, despite being isolated from different hosts *i.e.*, mosquitoes and pigs. Moreover, the strains isolated in the 1960s and 1980s have not changed genetically, indicating the conserved nature of the virus even after several years of circulation in nature[16].

A novel BATV NM/12 strain was isolated from bovine serum collected in inner Mongolia, China, and based on the L segment, it was found to be most closely related to the Chittoor strain[17].

Umbre virus (UMBV)

Umbre virus (UMBV) was first isolated in 1955 from *Cx. vishnui* group of mosquitoes, collected at Umbre, in Kolar district of Maharashtra, India[18,19], and was classified as *Orthobunyavirus* (Turlock serogroup which includes three other viruses, namely, M'opoko virus from Africa, Lednice virus from Europe and Turlock virus from America; *https://wwwn.cdc.gov/arbocat/VirusDetails.aspx?ID=499&SID=5*). Even though UMB virus is classified as a Bunyavirus, it cross-reacts by complement fixation (CF) and haemagglutinin inhibition (HI) assays with Barmah forest virus, an alpha virus from Australia[18]. Eight isolates obtained from *Culex* mosquitoes were characterized based on partial glycoprotein (G2) gene. The differences within these isolates at nucleotide and amino acid levels were 26 and 17 per cent, respectively. Phylogenetic analysis of 345 bp of glycoprotein gene G2, of UMBV and other Orthobunyaviruses, showed six distinct lineages, namely, Bunyamwera, Simbu, California encephalitis, Group C, Kaeng Khoi (KK) and UMBV. On comparing partial M gene, four lineages, excluding Group C viruses and Simbu group of viruses, were seen suggesting that UMBV represents a distinct group within the genus *Orthobunyavirus*[19]. UMBV has so far not been isolated from humans or animals and it is not known whether it causes any disease in humans or animals.

Kaikalur virus

This virus was isolated from a mosquito pool comprising 100 *Cx. tritaeniorhynchus* collected in a cattle shed at Kaikalur town, Krishna district, Andhra Pradesh, in 1971[20]. The virus belongs to Simbu group and is closely related to Shuni virus isolated in Nigeria by CF and neutralization tests. In 2008, it was shown by Yamakawa *et al*[21], that Aino virus isolated from Japan was closely related to Kaikalur virus. Aino and Kaikalur viruses were found to be indistinguishable by CF or neutralization tests[22]. These results indicate a broader global distribution pattern of the virus. Although Aino virus is known to cause developmental disorders in foetus of ruminants[23,24], the pathogenic potential of Kaikalur virus to humans and animals is not reported.

Thimiri virus

This was isolated from North Arcot district (currently named Vellore district), Tamil Nadu, in 1962 from *Ardeola grayii*, paddy bird[25]. Based on serology and sequencing data of partial S gene, though this virus was found to belong to Simbu serogroup of arboviruses[26], it was not closely related to other Simbu viruses and was placed in its own complex. Thimiri virus is associated with birds in south India, Egypt and midges in Australia[27]. The pathogenic potential of Kaikalur virus to humans and animals is not known.

Sathuperi virus (SATV)

This virus was isolated from a pool of *Cx. vishnui* in 1957 from a place called Sathuperi village, North Arcot district, Tamil Nadu, India[27]. This virus has been registered in the International Arboviruses catalogue and has been shown to belong to Simbu group[28]. Sathuperi virus (SATV) was also identified in Japan in 1999, isolated from cattle and *Culicoides* biting midges[29]. During an outbreak investigation of ruminants in Northern Europe caused by Schmallenberg virus, sequencing of genomic RNA segments of the virus showed that the M gene RNA of Schmallenberg virus was very similar to SATV. Phylogenetic analysis further indicated that Schmallenberg virus is a reassortant, with the M gene RNA segment from SATV[29]. Human disease caused by SATV virus is not known so far.

Ingwavuma virus

In India, INGV was isolated in 1963 from a paddy bird *A. grayii* (Sykes) (from Balagodu village) in Shimoga district in the then Mysore state (at present Karnataka) of South India[1]. The isolations from pig were made from Tumkur district, whereas the isolations from humans were made from Kolar district in Karnataka State. However, no studies have been done to understand its epidemiology in this country[1]. Human disease caused by INGV is not known so far.

INGV belongs to Simbu serogroup in genus *Orthobunyavirus*. It was first isolated in 1959 on the banks of 'Ingwavuma river' near the village of Ndumu, South Africa, from a passerine bird *Hyphanturgus* (*Ploceus*) *ocularis* and from mosquitoes such as *Ae. circumluteolus*, *Cx. guiarti*, *Cx. neavei* and *Cx. vishnui*[30]. Later on, its presence was recorded from several countries in Africa and Asia[1,31-33]. Pigs are considered to be the natural vertebrate host in Thailand, but isolations from wild birds in Africa and India suggested a natural bird-mosquito cycle also[27].

In spite of many reports of INGV worldwide, complete genome sequence of INGV is not available till date. No information is available about the disease caused, natural cycle of the virus or its molecular characterization. The study of virus pathology and its role in involvement in human disease is needed.

Phylogenetic study of nucleocapsid gene and glycoprotein gene of four viral isolates from India showed that Simbu viruses have evolved into at least five lineages and INGV from India had been clustered into third lineage[16].

Ganjam virus (GANV)

Ganjam virus was initially isolated from adult *Haemaphysalis intermedia* and *H. wellingtoni* ticks and *Cx. vishnui* mosquitoes collected from goats in Ganjam district, Odisha, Shimoga district, Karnataka, and Vellore, North Arcot district, Tamil Nadu, respectively[34]. The presence of GANV was again reported in 1977 during an investigation of acute febrile illness shown by fever, anorexia and lumbar paralysis of sheep in Chittoor district of Andhra Pradesh, India[35]. GANV was isolated from adult *H. intermedia* and *R. hemaphysaloides* ticks infecting domestic animals in some villages near Pune, Maharashtra, between 2000 and 2002[35].

Based on the documented evidence of isolation of GANV from ticks, mosquitoes, sheep and humans, it can be stated that the virus is prevalent in different parts of India. In addition, GANV antibodies were detected in sheep and goat serum samples in Verrapuram during an episode of febrile illness in 1994[36]. Neutralizing antibodies for the virus were found in human samples based on serological surveys conducted in Tamil Nadu and Jammu and Kashmir. Human laboratory-acquired infection of GANV with febrile illness, abdominal pain, back pain, headache, nausea, vomiting and conjunctival infection has been reported[36].

The genome S RNA segment of Nairobi sheep disease virus (NSD) and GANVs has been shown to differ by only 10.1 and 3.3 per cent at the nucleotide and amino acid levels, respectively. Therefore, GANV may be an Asian variant of NSD virus. Further, GANV and NSD are more closely related than other characterized *Nairoviruses,* no evidence of reassortment was found[37].

Crimean-Congo haemorrhagic fever (CCHF) virus

CCHF virus causes severe acute febrile illness and haemorrhagic fever with an overall case fatality of 9-50 per cent. It belongs to family *Bunyaviridae* and genus

Nairovirus. CCHF was first detected in the Crimean peninsula in the mid-1940s[38]. It was first isolated from a patient in Kisangani, the Democratic Republic of Congo, in 1956[38]. Direct exposure to blood or other secretions resulting in person-to-person transmission and instances of nosocomial transmission has been documented. *Ixodid* ticks, particularly those belonging to the genus *Hyalomma,* are known vectors of CCHF. The virus is capable of persisting in the tick throughout its life cycle by transstadial transmission. It can also be passed onto the offspring by transovarial transmission[38]. Cattle and goats play an important role in the natural cycle of the virus. CCHFV replicates to high titres in the lung, liver, spleen and reticuloendothelial system in other organs in these animals. Unlike humans, it generally causes only subclinical disease in cattle. Human infections show high levels of viral replication occurring in all major organs, including the liver accompanied by haemorrhagic manifestations[38].

Although CCHF had been detected in neighbouring countries such as Pakistan and China, it was confirmed for the first time in India in 2011[39]. Nosocomial human infections with haemorrhagic manifestations were reported from a tertiary care hospital in Ahmadabad, Gujarat, in 2011[39]. Domestic animals from Kolat and Ahmadabad were also found to be positive for anti-CCHF IgG antibodies. The possible sources of CCHFV infection were virus-infected *Hyalomma* ticks and livestock at the rural residence of the index case. In addition, a retrospective sample analysis showed the prevalence of CCHFV in Gujarat and Rajasthan before this outbreak[40]. So far, there is no evidence of circulation of multiple strains of the virus in the country. Though the 2011 outbreak may not have resulted from a very recent introduction, the probability of a recent re-introduction from any of the neighbouring countries during thoroughfare of livestock needs to be considered[41].

In addition, a CCHF case was also confirmed from Sirohi, Rajasthan State, in 2014, and during 2015, a nosocomial outbreak was recorded in a private hospital of Rajasthan which affected nursing staff. This indicated that trade of livestock and consequent movements of domestic animals infested with infected ticks may be the reason for the spread of CCHFV to newer areas[42]. Further, a cross-sectional serosurvey of CCHFV in livestock from 22 States and one Union Territory reported that this virus was widespread in the livestock population of India[43]. With the increasing spread of CCHFV to newer regions of the country, it becomes imperative to conduct regular surveillance programmes for human and animals. Increased awareness about the disease and its spread among at-risk population such as abattoir workers, people working in proximity with livestock and medical personnel working in CCHF-endemic areas is needed.

Bhanja virus (BHAV)

Bhanja virus (BHAV) was first isolated from a pool of ticks *H. intermedia* collected from a goat displaying lumbar paralysis in Bhanjanagar (district Ganjam, Odisha, India) in 1954. It was named based on the region of the isolation[44]. BHAV causes fever and symptoms indicating the central nervous system affection in young ruminants (lambs, kids, and calves). Bhanja virus has been isolated in India, various parts of Africa, former USSR and Europe[45]. Metastriate ticks of the genera *Haemaphysalis, Dermacentor, Hyalomma, Rhipicephalus, Boophilus* and *Amblyomma* transmit this arbovirus. Sheep, goat, cattle, African hedgehog *Atelerix albiventris* and African ground squirrel *Xerus erythropus* are vertebrate hosts of BHAV. It is so far not known to cause disease in humans. The complete genome sequence of BHAV has helped in phylogenetically placing the virus in the genus *Phlebovirus* in the *Bunyaviridae* family[45].

Sandfly fever virus (SFV)

The activity of SFV in India was suspected for many years on the basis of clinical diagnosis. Twenty isolates of this virus were obtained from India out of which 11 were identified as Naples and nine as Sicilian type, from human serum samples and wild caught sandflies[46]. The disease is usually self-limiting. However, sometimes, neurological involvement resulting in morbidity is seen[47]. New antigenically distinct serotypes have been identified from Europe, Southeast Asia, central Asia and Africa[48].

Malsoor virus (MV)

Malsoor virus (MV) was isolated from Mahabaleshwar, Maharashtra, from bats belonging to *Rousettus* species. Malsoor is the first *Phlebovirus* to be isolated from *Rousettus* bat species. So far, this virus is not known to cause human infections. The virus infects several different mammalian cell types[49].

Experimental studies showed pan cytotrophic property of the virus for different mammalian and insect cell lines *in vitro*. High-resolution transmission electron microscopy studies have been carried out to characterize the fine structure and morphogenesis of

this novel *Phlebovirus*[50]. Detailed ultrastructural studies on MV particles showed heterogeneous morphology. Majority of the virions (80%) were round, having well-defined envelope projections (6±1 nm) with an average size of 70 nm. A subclass of virions (15%) showed pleomorphism. Interestingly, the envelope projections on the virions were tightly packed and not fragile to staining. Virus-infected cells showed several interesting features not commonly reported for Bunyaviruses. These included frequent detection of multiple inclusion bodies, distinct cytoplasmic membrane-associated virus replication sites and presence of autophagy[50]. Recently, a human serosurvey was conducted in Mahabaleshwar region (the region from which the virus was first isolated), Maharashtra State, India to detect the presence of anti-Malsoor IgG antibodies, and all the tested samples were found to be negative for the same (NIV unpublished data).

Hantavirus

Hantavirus are a family of rodent-borne viruses (roboviruses) and are responsible for haemorrhagic fever with renal syndrome in Europe and Asia and *Hantavirus* cardiopulmonary syndrome in America. *Hantavirus* cases have not been reported from India[51-53]. A pilot study from south India conducted with serum samples obtained from individuals with acute febrile illness and voluntary blood donors indicated 14.7 per cent of samples positive for anti-*Hantavirus* IgM antibodies[54,55]. This indicated that *Hantavirus* infections may be present in population and further studies need to be conducted to understand its seroprevalence. In another study, the presence of *Hantavirus*-specific IgG antibodies was evaluated in 661 individuals. The individuals included tribal population, warehouse workers, patients with chronic renal disease and voluntary blood donors. Nearly 74 per cent of the tested samples were positive for anti-*Hantavirus* IgG antibodies[56]. These reports are an indication of *Hantavirus* prevalence in the country, and further studies need to be conducted to assess the threat of the disease.

Thottapalayam virus (TPMV)

TPMV (family *Bunyaviridae* and genus *Hantavirus*) was isolated from an Asian house shrew (*Suncus murinus*) in Tamil Nadu, India[2]. In fact, this was the first *Hantavirus* to be isolated in cell culture. Except TPMV, all other known *Hantavirus* members have been isolated or detected in murid rodents. Whether the shrew (*S. murinus*) is a primary reservoir or a 'spillover' host infected through contact with a primary host is not known. TPMV has also been reported from Nepal[57] and China[58].

The complete genome sequence analyses of S, M and L segments has confirmed that TPMV is a distinct virus in all the three segments compared to other *Hantavirus* members. Phylogenetic tree of all the three segments showed that this virus was unique compared to other rodent-borne *Hantavirus* members (*Sigmodontinae, Muridae* and *Arvicolinae*)[59].

Many shrew-borne *Hantavirus* members have been reported from different parts of the world, suggesting that shrews may play a greater role in the ecology and transmission of zoonotic diseases[60]. Virus sequences were obtained from two Asian house shrews captured in Indonesia[60]. In addition, anti-TPMV antibodies were detected from a febrile patient from Thailand[60]. In the light of recent reports of *Hantavirus* seropositivity, careful surveillance of TPMV is required in different States of India to ascertain whether this virus is involved in causing diseases in humans. The proximity of Asian house shrews with human habitation may result in TPMV infection in humans.

Kaisodi virus

The Kaisodi virus was isolated from ectoparasite of birds *H. turturis, H. spinigera* and *H. wellingtoni*[61]. This virus was isolated from Kyasanur forest disease (KFD)-affected area (Mysore, Karnataka State). Some cross-reactivity has been observed between Kaisodi and Malayan viruses isolated from *Ixodes granulatus*[61]. CF and HI tests confirmed it to be an Arbovirus. No human disease is known so far.

Wanowrie virus (WAN)

Wanowrie (WAN) virus is an ungrouped Arbovirus having morphogenetic characteristics in common with Bunyavirus. It was isolated for the first time in 1955 from a pool of four adult ticks; *Hyalomma marginatum isacci* collected from sheep at Wanowrie, near Pune, Maharashtra[62], and was subsequently isolated from a human sample. Isolation of the virus was also reported from the human brain suspension at the Virus Research Centre, Pune, in 1966[62].

No haemagglutinin was produced, but the virus was sensitive to sodium deoxycholate. Wanowrie virus was pathogenic in suckling mice by the intracerebral and intraperitoneal routes but produced only occasional deaths in adult mice inoculated intracerebrally. The virus was pathogenic for seven day old chick embryos

and produced cytopathic effects in Baby Hamster Kidney 21 cell line cultures, but no cytopathic effect or evidence of virus multiplication was elicited in an *Ae. albopictus* larval cell line. Wanowrie virus had no serological relationship to a very large variety of arboviruses. Only two of the 116 goat serum samples had evidence of neutralizing antibodies against the virus; no antibodies were detected in sheep, cow and buffalo serum[62]. A brief summary of all Bunyaviruses isolated in India is given in the Table. The Figure shows the places from where these Bunyaviruses were first isolated.

Conclusion

With advanced knowledge and technologies, many viruses have been identified and placed taxonomically in family *Bunyaviridae*. Under proactive research, the presence of CCHF and MV was detected from humans and animals, respectively[43]. Several Bunyaviruses are known worldwide for causing severe infections, diseases and mortality in humans and animals. Many of these cause severe economic loss (CCHFV, Rift Valley fever virus, SFTS virus, La Crosse encephalitis virus, *etc*.). In India, though many Bunyaviruses do not cause

Table. A brief summary of various Bunyaviruses isolated in India

Name of virus	Genus	Year of isolation in India	Place of isolation	Host	Pathogenicity
Chittoor/Batai	*Orthobunyavirus*	1957	Brahmanpally, Andhra Pradesh	*Anopheles* and *Culex* mosquitoes, swine	No known disease in humans or animals
Umbre	*Orthobunyavirus*	1955	Kolar, Karnataka	*Culex* mosquitoes	No known disease in humans or animals
Kaikalur	*Orthobunyavirus*	1971	Krishna district, Andhra Pradesh	*Culex* mosquitoes	No known disease in humans or animals
Thimiri	*Orthobunyavirus*	1962	Arcot district, Tamil Nadu	*Ardeola grayii*: Paddy bird	No known disease in humans or animals
Sathuperi	*Orthobunyavirus*	1957	North Arcot district, Tamil Nadu	*Culex* mosquitoes	No known disease in humans or animals
Ingwavuma	*Orthobunyavirus*	1963	Shimoga district, Karnataka	*A. grayii*: Paddy bird	No known disease in humans or animals
Ganjam	*Nairovirus*	1954	Ganjam district, Odisha	*Haemaphysalis* ticks	Febrile illness, characterized by fever, anorexia and lumbar paralysis in sheep. Abdominal pain, back pain, headache, nausea, vomiting, conjunctival infection in humans
Crimean-Congo haemorrhagic fever	*Nairovirus*	2011	Ahmedabad district, Gujarat	*Hyalomma* ticks, cattle, sheep, goat, humans	Severe acute febrile illness with haemorrhagic manifestations. Fatality rate of 9-50 per cent in humans. No known disease in cattle, sheep and goat
Bhanja	*Phlebovirus*	1954	Ganjam district, Odisha	*Haemaphysalis* ticks, sheep, goat, cattle, African hedgehog, African ground squirrel	Lumbar paralysis, fever and symptoms indicating central nervous system affection in sheep, goats and cattle
Sandfly fever	*Phlebovirus*	1976	Aurangabad district, Maharashtra	*Phlebotomus* species, humans	Neurologic involvement in severe cases, otherwise self-limiting disease in humans
Malsoor	*Phlebovirus*	2010	Mahabaleshwar district, Maharashtra	*Rousettus* bats	No known disease in humans or animals

Contd...

Name of virus	Genus	Year of isolation in India	Place of isolation	Host	Pathogenicity
Thottapalayam	*Hantavirus*	1964	Vellore district, Tamil Nadu	*Suncus murinus*: Asian house shrew	No known disease in humans or animals
Hantavirus	*Hantavirus*	2005		Antibodies found in human samples	Haemorrhagic fever with renal syndrome and cardiopulmonary syndrome
Kaisodi	Uncharacterized	1957	Kyasanur forest, Karnataka	Ectoparasite of birds such as *Haemaphysalis turturis*, *H. spinigera* and *H. wellingtoni*	No known disease in humans or animals
Wanowrie	Uncharacterized	1955	Pune district, Maharashtra	*Hyalomma* ticks	No known disease in humans or animals

Source: Refs 1, 2, 8, 18, 20, 25, 28, 34, 39, 44, 46, 49, 61-63

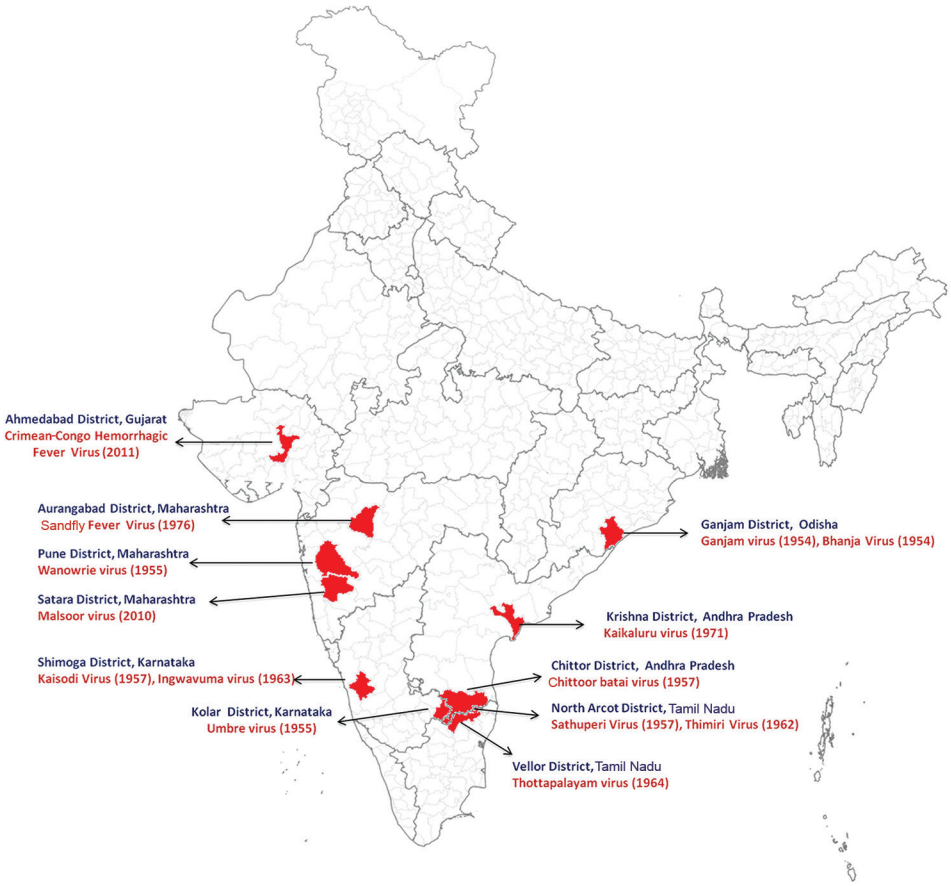

Figure. Places from where the Bunyaviruses were first isolated in India. *Source*: Refs 1, 2, 8, 20, 25, 28, 34, 39, 44, 46, 49, 61-63.

disease in humans or animals, their genetic similarity to other disease-causing viruses of the same family is of concern, especially in case of formation of reassortant viruses. On the other side of the spectrum are diseases such as CCHF and sandfly fever which cause severe disease in humans. The clinical signs and symptoms

of CCHF are very similar to other viral haemorrhagic fevers such as Omsk haemorrhagic fever, dengue and KFD[38]. Therefore, proximity to livestock, presence of ticks or travel to endemic regions are factors which play a role in suspecting CCHFV infection. With the CCHF, it is necessary to understand bunyavirus prevalence in India.

Most of the viruses described have been discovered during the 1960s/1970s. With better understanding of biosafety concerns, the work regarding discovery and identification of newer viruses began after the establishment of biosafety level three laboratory (BSL3) at the National Institute of Virology (NIV), Pune, in 2005[63]. Viruses such as CCHFV and MV have been identified in India after the establishment of BSL3 and BSL4. Further systematic searches for identification of viruses are ongoing and are necessary for understanding the emerging infectious diseases and identification of disease hot spots. A special emphasis needs to be laid on exploring animal, bird, arthropod and human viruses.

The current review is an attempt to concisely present information about various Bunyaviruses that were isolated from various insects, birds and animals and are circulating in the country. This information would help in preparedness in case of emergence of novel infections. Timely action could also be taken in case infections from these viruses are seen in either human or animal population. The available information will help not only in making new diagnostic tools but also in monitoring the emergence of diseases.

***Conflicts of Interest*:** None.

References

1. Pavri KM, Sheikh BH, Singh KRP, Rajagopalan PK, Casals J. Balagodu virus, a new arbovirus isolated from *Ardeola grayii* (Sykes) in Mysore State, South India. *Indian J Med Res* 1969; *57* : 758-64.
2. Carey DE, Reuben R, Panicker KN, Shope RE, Myers RM. Thottapalayam virus: A presumptive arbovirus isolated from a shrew in India. *Indian J Med Res* 1971; *59* : 1758-60.
3. Dandawate CN, Rajagopalan PK, Pavri KM, Work TH. Virus isolations from mosquitoes collected in North Arcot district, Madras state, and Chittoor district, Andhra Pradesh between November 1955 and October 1957. *Indian J Med Res* 1969; *57* : 1420-6.
4. Dandawate CN, Shah KV. Ganjam virus: A new arbovirus isolated from ticks *Haemaphysalis intermedia* Warburton and Nuttall, 1909 in Orissa, India. *Indian J Med Res* 1969; *57* : 799-804.
5. Smithburn KC, Haddow AJ, Mahaffy AF. A neurotropic virus isolated from *Aedes* mosquitoes caught in the Semliki forest. *Am J Trop Med Hyg* 1946; *26* : 189-208.
6. Elliott RM. Emerging viruses: The Bunyaviridae. *Mol Med* 1997; *3* : 572-7.
7. Weidmann M, Rudaz V, Marcio R, Nunes T, Vasconcelos PFC, Hufert FT. Rapid detection of human pathogenic orthobunyaviruses. *J Clin Virol* 2003; *41* : 3299-305.
8. Singh KR, Pavri KM. Isolation of Chittoor virus from mosquitoes and demonstration of serological conversions in sera of domestic animals at Manjri, Poona, India. *Indian J Med Res* 1966; *54* : 220-4.
9. Geevarghese G, Prasanna NY, Jacob PG, Hanumaiah H, Bhat HR. Isolation of Batai virus from sentinel domestic pig from Kolar district in Karnataka State, India. *Acta Virol* 1994; *38* : 239-40.
10. Singh KRP, Pavri KM. Isolation of Chittoor virus from mosquitoes and demonstration of serological conversions in sera of domestic animals at Manjri, Poona, India. *Indian J Med Res* 1966; *54* : 220-4.
11. Casals J, Whitman L. A new antigenic group of arthropod-borne viruses: The Bunyamwera group. *Am J Trop Med Hyg* 1960; *9* : 73-7.
12. Bardos V, Cupkova E. The Calovo virus - The second virus isolated from mosquitoes in Czechoslovakia. *J Hyg Epidemiol Microbiol Immunol* 1962; *6* : 186-92.
13. Pavri KM, Sheikh BH. Distribution of antibodies reacting with Chittoor virus in humans and domestic ungulates of India. *Indian J Med Res* 1966; *54* : 225-8.
14. Briese T, Bird B, Kapoor V, Nichol ST, Lipkin WI. Batai and Ngari viruses: M segment reassortment and association with severe febrile disease outbreaks in East Africa. *J Virol* 2006; *80* : 5627-30.
15. Sudeep AB. *Culex gelidus*: An emerging mosquito vector with potential to transmit multiple virus infections. *J Vector Borne Dis* 2014; *51* : 251-8.
16. Yadav PD, Sudeep AB, Mishra AC, Mourya DT. Molecular characterization of Chittoor (Batai) virus isolates from India. *Indian J Med Res* 2012; *136* : 792-8.
17. Liu H, Shao XQ, Hu B, Zhao JJ, Zhang L, Zhang HL, *et al.* Isolation and complete nucleotide sequence of a Batai virus strain in Inner Mongolia, China. *Virol J* 2014; *11* : 138.
18. Dalgarno L, Short NJ, Hardy CM, Bell JR, Strauss JH, Marshall ID. Characterization of Barmah forest virus: An alphavirus with some unusual properties. *Virology* 1984; *133* : 416-26.
19. Yadav PD, Mishra AC, Mourya DT. Molecular characterization of Umbre virus (*Bunyaviridae*). *Virol J* 2008; *5* : 115.
20. Rodrigues FM, Singh PB, Dandawate CN, Soman RS, Bhatt PN. Kaikalur virus - A new arthropod-borne virus belonging to the Simbu group isolated in India from *Culex tritaeniorhynchus* (Giles). *Indian J Med Res* 1977; *66* : 719-25.

21. Yamakawa M, Yanase T, Kato T, Tsuda T. Molecular epidemiological analyses of the teratogenic Aino virus based on the sequences of a small RNA segment. *Vet Microbiol* 2008; *129* : 40-7.
22. Kinney RM, Calisher CH. Antigenic relationships among Simbu serogroup (Bunyaviridae) viruses. *Am J Trop Med Hyg* 1981; *30* : 1307-18.
23. Parsonson IM, Della-Porta AJ, Snowdon WA. Developmental disorders of the fetus in some arthropod-borne virus infections. *Am J Trop Med Hyg* 1981; *30* : 660-73.
24. Tsuda T, Yoshida K, Ohashi S, Yanase T, Sueyoshi M, Kamimura S, *et al.* Arthrogryposis, hydranencephaly and cerebellar hypoplasia syndrome in neonatal calves resulting from intrauterine infection with Aino virus. *Vet Res* 2004; *35* : 531-8.
25. Carey DE, Reuben R, George S, Shope RE, Myers RM. Kammavanpettai, Kannamangalam, Sembalam and Thimiri viruses: Four unrelated new agents isolated from birds in India. *Indian J Med Res* 1971; *59* : 1708-11.
26. Saeed MF, Li L, Wang H, Weaver SC, Barrett AD. Phylogeny of the Simbu serogroup of the genus Bunyavirus. *J Gen Virol* 2001; *82* (Pt 9) : 2173-81.
27. Beran GW, editor. *Handbook of Zoonoses*, 2nd ed., Sec. B. Boca Raton, FL: Viral Zoonoses; New York: CRC Press; 1994.
28. Pinheiro FP, Travassos da Rosa APA, Travassos da Rosa JF, Ishak R, Freitas RB, Gomes ML, *et al.* Oropouche virus. I. A review of clinical, epidemiological, and ecological findings. *Am J Trop Med Hyg* 1981; *30* : 149-60.
29. Yanase T, Kato T, Aizawa M, Shuto Y, Shirafuji H, Yamakawa M, *et al.* Genetic reassortment between Sathuperi and Shamonda viruses of the genus Orthobunyavirus in nature: Implications for their genetic relationship to Schmallenberg virus. *Arch Virol* 2012; *157* : 1611-6.
30. Büchen-Osmond C, editor. Ingwavuma strain SA An 4165 isolate. In: *ICTVdB - The universal virus database*, Ver. 4. New York, USA: Columbia University; 2006. Available from: *http://www.ictvdb.mirror.ac.cn/ICTVdB/index.htm*, accessed on February 10, 2016.
31. Top FH Jr., Kraivapan C, Grossman RA, Rozmiarek H, Edelman R, Gould DJ. Ingwavuma virus in Thailand. Infection of domestic pigs. *Am J Trop Med Hyg* 1974; *23* : 251-7.
32. Hubálek Z. An annotated checklist of pathogenic microorganisms associated with migratory birds. *J Wildl Dis* 2004; *40* : 639-59.
33. Converse JD, Tan RI, Rachman IT, Lee VH, Shope RE. Ingwavuma virus (Simbu group) from *Culex* and *Mansonia* mosquitoes (*Diptera*: *Culicidae*) in Indonesia. *J Med Entomol* 1985; *22* : 339-42.
34. Dandawate CN, Work TH, Webb JK, Shah KV. Isolation of Ganjam virus from a human case of febrile illness: A report of a laboratory infection and serological survey of human sera from three different states of India. *Indian J Med Res* 1969; *57* : 975-82.
35. Joshi MV, Geevarghese G, Joshi GD, Ghodke YS, Mourya DT, Mishra AC. Isolation of Ganjam virus from ticks collected off domestic animals around Pune, Maharashtra, India. *J Med Entomol* 2005; *42* : 204-6.
36. Banerjee K. Emerging viral infections with special reference to India. *Indian J Med Res* 1996; *103* : 177-200.
37. Yadav PD, Vincent MJ, Khristova M, Kale C, Nichol ST, Mishra AC, *et al.* Genomic analysis reveals Nairobi sheep disease virus to be highly diverse and present in both Africa, and in India in the form of the Ganjam virus variant. *Infect Genet Evol* 2011; *11* : 1111-20.
38. Ergönül O. Crimean-Congo haemorrhagic fever. *Lancet Infect Dis* 2006; *6* : 203-14.
39. Mishra AC, Mehta M, Mourya DT, Gandhi S. Crimean-Congo haemorrhagic fever in India. *Lancet* 2011; *378* : 372.
40. Mourya DT, Yadav PD, Shete AM, Gurav YK, Raut CG, Jadi RS, *et al.* Detection, isolation and confirmation of Crimean-Congo hemorrhagic fever virus in human, ticks and animals in Ahmadabad, India, 2010-2011. *PLoS Negl Trop Dis* 2012; *6* : e1653.
41. Yadav PD, Cherian SS, Zawar D, Kokate P, Gunjikar R, Jadhav S, *et al.* Genetic characterization and molecular clock analyses of the Crimean-Congo hemorrhagic fever virus from human and ticks in India, 2010-2011. *Infect Genet Evol* 2013; *14* : 223-31.
42. Makwana D, Yadav PD, Kelaiya A, Mourya DT. First confirmed case of Crimean-Congo haemorrhagic fever from Sirohi district in Rajasthan State, India. *Indian J Med Res* 2015; *142* : 489-91.
43. Mourya DT, Yadav PD, Shete AM, Sathe PS, Sarkale PC, Pattnaik B, *et al.* Cross-sectional Serosurvey of Crimean-Congo Hemorrhagic Fever Virus IgG in Livestock, India, 2013-2014. *Emerg Infect Dis* 2015; *21* : 1837-9.
44. Shah KV, Work TH. Bhanja virus: A new arbovirus from ticks *Haemaphysalis intermedia* Warburton and Nuttall, 1909, in Orissa, India. *Indian J Med Res* 1969; *57* : 793-8.
45. Dilcher M, Alves MJ, Finkeisen D, Hufert F, Weidmann M. Genetic characterization of Bhanja virus and Palma virus, two tick-borne phleboviruses. *Virus Genes* 2012; *45* : 311-5.
46. Goverdhan MK, Dhanda V, Modi GB, Bhatt PN, Bhagwat RB, Dandawate CN, *et al.* Isolation of *Phlebotomus* (Sandfly) fever virus from sandflies and humans during the same season in Aurangabad District, Maharashtra State, India. *Indian J Med Res* 1976; *64* : 57-63.
47. Kocak Tufan Z, Weidmann M, Bulut C, Kinikli S, Hufert FT, Dobler G, *et al.* Clinical and laboratory findings of a sandfly fever Turkey Virus outbreak in Ankara. *J Infect* 2011; *63* : 375-81.
48. Tufan ZK, Tasyaran MA, Guven T. Sandfly fever: A mini review. *Virol Mycol* 2013; *2* : 1.
49. Mourya DT, Yadav PD, Basu A, Shete A, Patil DY, Zawar D, *et al.* Malsoor virus, a novel bat phlebovirus, is closely related to severe fever with thrombocytopenia syndrome virus and heartland virus. *J Virol* 2014; *88* : 3605-9.

50. Basu A, Yadav PD, Prasad S. Ultrastructure and morphogenesis of malsoor virus: A novel phlebovirus genetically related to the severe fever with thrombocytopenia virus. *J Hum Virol Retrovirol* 2015; *2* : 26.

51. Sandmann S, Meisel H, Razanskiene A, Wolbert A, Pohl B, Krüger DH, *et al.* Detection of human *Hantavirus* infections in Lithuania. *Infection* 2005; *33* : 66-72.

52. Lundkvist A, Niklasson B. Hemorrhagic fever with renal syndrome and other *Hantavirus* infections. *Rev Med Virol* 1994; *4* : 177-84.

53. Kruger DH, Rainer U, Lundkvist Å. *Hantavirus* infections and their prevention. *Microbes Infect* 2001; *3* : 1129-44.

54. Chandy S, Mitra S, Sathish N, Vijayakumar TS, Abraham OC, Jesudason MV, *et al.* A pilot study for serological evidence of *Hantavirus* infection in human population in South India. *Indian J Med Res* 2005; *122* : 211-5.

55. Clement J, Maes P, Muthusethupathi M, Nainan G, Ranst M. First evidence of fatal hantavirus nephropathy in India, mimicking leptospirosis. *Nephrol Dial Transplant* 2006; *21* : 826-7.

56. Chandy S, Yoshimatsu K, Ulrich RG, Mertens M, Okumura M, Rajendran P, *et al.* Seroepidemiological study on *Hantavirus* infections in India. *Trans R Soc Trop Med Hyg* 2008; *102* : 70-4.

57. Kang HJ, Kadjo B, Dubey S, Jacquet F, Yanagihara R. Molecular evolution of Azagny virus, a newfound *Hantavirus* harbored by the West African pygmy shrew (*Crocidura obscurior*) in Côte d'Ivoire. *Virol J* 2011; *8* : 373.

58. Lin XD, Zhou RH, Fan FN, Ying XH, Sun XY, Wang W, *et al.* Biodiversity and evolution of Imjin virus and Thottapalayam virus in Crocidurinae shrews in Zhejiang Province, China. *Virus Res* 2014; *189* : 114-20.

59. Yadav PD, Vincent MJ, Nichol ST. Thottapalayam virus is genetically distant to the rodent-borne Hantaviruses, consistent with its isolation from the Asian house shrew (Suncus murinus). *Virol J* 2007; *4* : 80.

60. Okumura M, Yoshimatsu K, Kumperasart S, Nakamura I, Ogino M, Taruishi M, *et al.* Development of serological assays for Thottapalayam virus, an insectivore-borne *Hantavirus*. *Clin Vaccine Immunol* 2007; *14* : 173-81.

61. Pavri KM, Casals J. Kaisodi virus, new agent isolation from *Haemaphysalis spinigera* in Mysore state, South India. *Indian J Med Res* 1966; *15* : 961-3.

62. Dandawate CN, Shah KV, D'Lima LV. Wanowrie virus: A new arbovirus isolated from *Hyalomma marginatum* isaaci. *Indian J Med Res* 1970; *58* : 985-9.

63. Mourya DT, Yadav PD, Majumdar TD, Chauhan DS, Katoch VM. Establishment of Biosafety Level-3 (BSL-3) laboratory: Important criteria to consider while designing, constructing, commissioning & operating the facility in Indian setting. *Indian J Med Res* 2014; *140* : 171-83.

Reprint requests: Dr Devendra T. Mourya, Microbial Containment Complex, ICMR-National Institute of Virology, Sus Road, Pashan, Pune 411 021, Maharashtra, India
e-mail: directorniv@gmail.com