

## Review Article

## Status of Bluetongue Disease in India: An Updated Systematic Review

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**Abstract:** Bluetongue (BT) is an infectious viral disease which affects a wide range of ruminants and was first reported in India in 1964. Bluetongue Virus (BTV) is devastating haemorrhagic viral disease of both wild and domestic ruminants, classified among category 'A' diseases notifiable to the World Organization of animal Health (OIE). The vector of the disease is biting midges of genus *Culicoides* (Diptera: Ceratopogonidae) and the disease is characterized by high morbidity and mortality resulting severe economic losses to sheep farmers. BTV distribution depends on the vector presence, and it is endemic in geographical regions located in latitude of approximately 40°–50° North and 35° South. Over the five decades after the first report of BT in 1964, most of the known serotypes of Bluetongue Virus (BTV) have been reported by detection of serotype specific antibodies and rarely by virus isolation from the fly. Although virus isolation and serotyping are the gold standards, rapid method based on the detection of the viral nucleic acid may be more suitable for India, yet for effective control of BT may be pertinent to introduce sentinel and vector traps systems for identification of the circulating serotypes and to evaluate herd immunity against them, so that relevant strains can be included in vaccine formulations. Recently, an inactivated pentavalent vaccine (BTV- 1, 2, 10, 16 and 23) is developed and commercialized in India.

**Keywords:** Bluetongue Virus, *Culicoides*, Diptera, Ceratopogonidae, Vaccine, Morbidity.

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## INTRODUCTION

Bluetongue (BT) is an insect-borne infectious viral disease of domestic and wild ruminants. It is caused by Bluetongue virus (BTV) and transmitted by *Culicoides* species (Mellor *et al.*, 1984; Rao *et al.*, 2016). The virus belongs to the genus *Orbivirus* of the family *Reoviridae* (Pringle 1999; Ranjan *et al.*, 2015). Sheep are considered as the most susceptible hosts for Bluetongue, whereas cattle, buffalo and goats serve as reservoirs. The disease is a vector borne viral disease of ruminants such as sheep, goat, cattle, buffalo, white-tailed deer, antelope, sambar and camelid species such as camels and llamas (Prasad *et al.*, 2009; Maheshwari, 2012) mainly transmitted by midges of the genus *Culicoides* (Diptera: Ceratopogonidae).

Bluetongue Virus is highly diverse, there are more than two dozen serotypes, and virus can reassort to form new variants. The virus is endemic in a broad, worldwide from tropical to subtropical zones with approximately 35° S to 40°N; however, outbreaks also

occur outside this area, antiviral may persist long-term if the climate and vectors are suitable (Walton, 2004). In India, first outbreak of Bluetongue in sheep and goats from Maharashtra state was reported by Sapre in 1964 (Sapre, 1964; Rao *et al.*, 2016). After the initial report of Bluetongue in Maharashtra, the disease was reported in exotic sheep, namely Southdown, Rambouillet, Russian Merino and Corriedale between 1967 and 1970. Severe BT was also reported in the Dorset breed in Andhra Pradesh in 1974. However, the native sheep maintained in close proximity did not present any symptoms. During 1981, in Southern India, the disease was widely spread and many outbreaks were reported between 1986 and 1995 demonstrated by Sreenivasulu (Sreenivasulu, 2004). In Northern India, an outbreak of Bluetongue was reported from Dehradun, Uttarakhand (that time Uttar Pradesh), in that more than 60 goats died and have observed prevalence of Bluetongue Virus antibody in sheep, goat and cattle in different regions, ranges from 34.78 to 48.71% (Joardar *et al.*, 2009).

Due to its economic impact, BT is a World Organisation for Animal Health (OIE) listed multispecies disease (MacLachlan and Osburn, 2006; Gunn *et al.*, 2008; OIE, 2008; Rushton and Lyons, 2015). BTV infection causes severe direct economic losses due to high morbidity, mortality, stillbirths, and abortions, foetal abnormalities, less birth weight in young ones, reduced milk yield and fertility rate, weight loss, early culling as well as meat and fleece losses. Indirect losses are due to trade restrictions imposed on ruminant animal movement, their germplasm and animal products, and expenditure for vaccination, diagnosis, vector control and treatment of clinically pretentious animals (MacLachlan and Osburn, 2006; Gunn *et al.*, 2008; Rushton and Lyons, 2015; Piniar, Brugger, *et al.*, 2015; Piniar, Lebl, *et al.*, 2015; Grewar, 2016; Gethmann *et al.*, 2020). It was estimated that BTV outbreaks caused economic losses of approximately US dollars (US\$) 3 billion in 1996 worldwide (Tabachnick, 2004). The total cost for prevention of incursion of BTV-8 into Scotland was estimated to be approximately Euro (€) 141 million over the 5-year period between 2009 and 2013 (Gunn *et al.*, 2008). In the US livestock industries, BTV caused losses of US \$144 million annually due to trade restrictions and diagnosis for assessing BTV status (Hoar *et al.*, 2003).

Recent studies on vectors indicated that *Culicoides oxystoma* and *C. imicola* were found to be mostly responsible for transmission of BTV (Maheshwari 2012; Archana *et al.* 2016). Other alternative routes of spread are venereal transmission through semen (Bowen and Howard 1984; Kirschvink *et al.* 2009), contact and oral transmission (Menziez *et al.* 2008), *in utero* infection by transplacental transmission (Menziez *et al.* 2008), and mechanical vectors (Bouwknegt *et al.* 2010). BT outbreaks are highly seasonal, occur during the late summer and autumn. The BTV outbreaks occur throughout tropical,

subtropical and temperate regions of the world, wherever competent vector population exists for dissemination of the virus (Maheshwari 2012).

**Vector**

Maheshwari reported thirty valid species of biting midges and 29 species of *Culicoides* have uncertain systematic status. He has included eight new spp. of the fly (Maheshwari, 2012). Vasic provided detail on host preference by *Culicoides* vector and discussed nuisance value of the fly (Vasic *et al.*, 2019).

**Epidemiology**

Bluetongue in India is endemic to Tamil Nadu, Andhra Pradesh, Karnataka, Maharashtra, Gujarat, Rajasthan, Haryana, Uttarakhand, Uttar Pradesh, Himachal Pradesh and Jammu & Kashmir (Ramkumar *et al.*, 2020). In Tamil Nadu, 22 out of 23 districts were reported to be affected by the BTV (Bluetongue Virus). The reported cases of Bluetongue Virus among sheep and goats occur presumably in an epidemic form during the monsoon season. Although the history of reporting was not continuous, the number of outbreaks, attacks and deaths among ruminants reported is of great concern that needs immediate attention for the protection of livestock and economic growth. During 1997-98 from 12 districts in southern Tamil Nadu, outbreak of BT in sheep and goats swept in an epizootic form leaving alarmingly 5,23,203 infected and 2,98,018 dead. Later the Bluetongue disease was reported from different states including Uttar Pradesh, Himachal Pradesh, Haryana, Karnataka, Maharashtra, Tamil Nadu, Madhya Pradesh, Gujarat, West Bengal and Andhra Pradesh (Table 1). Bluetongue outbreaks were most important in 1998 with case fatality rate of 18.65% and over all Bluetongue outbreaks with case fatality rate of 18.85%. The investigations made by different authors demonstrating BTV antibodies established the fact that BTV infection is present in cattle, buffaloes and goats in India.

**Table-1: Distribution of Bluetongue Virus serotypes reported from India**

State	Host species	Virus Isolation
Jammu and Kashmir	Sheep	18
Karnataka	Sheep	1,2,12,16,17,20
Uttar Pradesh	Sheep, Goat	9,18,23
Madhya Pradesh	Sheep	18
Andhra Pradesh	Sheep	2,3,9,10,16,21
Gujarat	Cattle, Camel and Sheep	6
Tamil Nadu	Sheep	1,3,16,23
Haryana	Sheep, Goat	1,4
Himachal Pradesh	Sheep	3,9,16,17
Maharashtra	Sheep	1.2.3.4.8.9.16.18.23

There are reports of 26 serotypes of BTV worldwide, of which 21 serotypes, of which 21 serotypes have been reported from India either on the basis of virus isolation or serology (Sreenivasulu, 2004). Seroprevalance of BT in ruminants in Kerala for the first time (Ravishankar, 2005). Although no

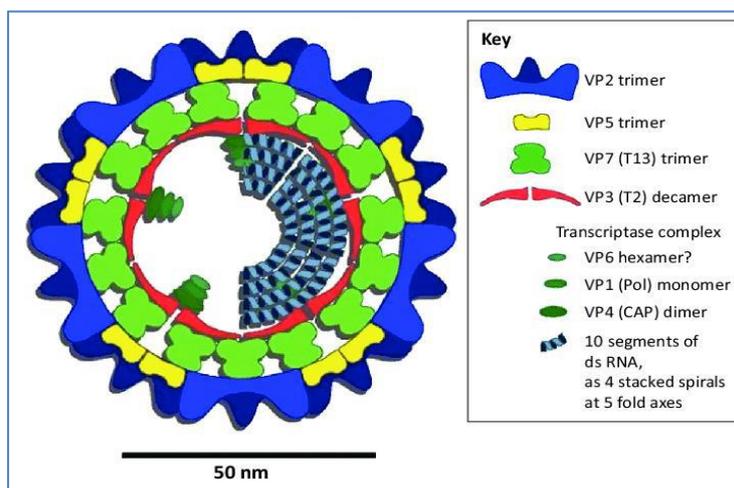
frequent outbreaks reported after 2006 in India as such, yet very few sporadic cases for the seroprevalance of Bluetongue among ruminants have been reported from Haryana, Tamil Nadu, Andhra Pradesh and Kerala. It has been stated that a few serotypes may be involved in causing outbreaks every year, the combination of

serotypes may change from year to year, therefore, it is important to identify the circulating serotype, so that relevant serotypes can be included in vaccine formation (Rao *et al.*, 2016).

**Bluetongue aetiology**

Bluetongue disease is caused by Bluetongue Virus (BTV) of the genus Orbivirus, placed under the subfamily Sedoreovirinae and family Reoviridae. Bluetongue is listed as a multispecies disease by Office International des Epizootics (OIE). BTV particle is ~65-80 nm diameters, non-enveloped with icosahedral symmetry. Viral genome consist of 10 discrete double-stranded (ds) RNA segments which codes for seven structural (VP1-VP7) and at least four non-structural (NS1-NS3/NS3A and NS4) proteins. The complete genome of BTV is ~19.2 kbp in length where the length of ds RNA segments varies from 3954-822 bp. The Bluetongue Virus with its 24 serotypes and high

antigenic variation among the serotypes created a nasty confusion in controlling the disease since last two decades. The outstanding techniques, amplification of DNA by a polymerase enzyme, invented by the Kary Mullis in 1983 n American scientist, provided a solution for most challenging problems of biology (Maheshwari, 2012). With this technique, BTV became one of the most well studied viruses at molecular level. According to USDA (2016), the numerous serotypes are the result of genetic shift (reassortment) and the drift (mutation) from alternating passage of BTV through ruminant and vectors. In India, at least 21 serotypes have been recognized based on serology and/or virus isolation. Till date, 13 serotypes namely BTV-1, 2, 3, 4, 6, 9, 10, 12, 16, 17, 18, 21 and 23 have been isolated by researchers involved in the All India Network Program on Bluetongue (AINP-BT) and other research laboratories (AINP-BT, 2012) . Following figure shows a schematic structure of BTV core particle (Fig. 1).



**Fig-1: Structure of bluetongue virus core particle**

Bluetongue is naturally transmitted by Culicoides species and consequently outbreaks depends on the presence of efficient midge vector and susceptible animals, conventionally believed to be transmitted only through the bite of infected vector and not by contact or through infected products. The following figure (Fig. 2a &b) shows the vector of Bluetongue disease and an infected sheep with Bluetongue Virus.



**Fig-2a: Culicoides: Vector of Bluetongue Disease**



**Fig-2b: Infected Sheep with Bluetongue Virus**

**History and morphology of btv**

The first official report of BTV infection was from the Cape Province of South Africa in the late 18<sup>th</sup> century, following import of fine-wool Merino sheep from Europe (Spreull, 1905). Initially, BT was called as ‘epizootic catarrh’ or ‘fever’ or ‘malarial catarrhal fever of sheep’ or ‘epizootic malignant

catarrhal fever of sheep', due to the erroneous belief that BT was caused by an intraerythrocytic parasite (Spreull, 1905). The English translated term 'Bluetongue' was first introduced by Spreull (1905) and derived from the Afrikaans word 'bloutong' or 'Blaauwtong', which was used by Afrikaans farmers after observing the cyanosis of tongue in clinically affected sheep (Spreull, 1905). After observing oral lesions, Afrikaans farmers also called the BT as 'Bekziekte', which means 'mouth sickness'. The disease was first reported in cattle in 1933 (Bekker *et al.* 1934), and the clinical signs were similar to that of foot-and-mouth disease. Hence, the disease was called as 'pseudofoot-and-mouth disease' or 'sore-mouth' or 'seer-beck'. BTV is a filterable virus and it was first time reported by Theiler in 1906 (Sperlova and Zendulkova, 2011). BTV serotype-4 was the first BTV to be identified in South Africa in 1906 (Coetzee *et al.*, 2012).

Before 1940s, occurrence of BT was restricted to South Africa (Coetzee *et al.*, 2012). The first outbreak of BTV, outside the African continent was reported in sheep from Cyprus (Eastern Mediterranean) in 1943, and BTV-3 was isolated from this outbreak (MacLachlan, 2004); however, there are some indications that BT had been there since 1924. Again, BTV-4 was isolated from Cyprus in 1969. Then, BTV was spread to Israel in 1943–44 (Sperlova and Zendulkova, 2011), and it was reported in Texas, USA in 1948 (Hardy and Price, 1952). Mckercher *et al.* (1953) isolated the BTV for the first time from the United States. The initial isolate was identified as BTV serotype-10, followed by BTV-11 in 1955, BTV-17 in 1962, and BTV-13 in 1967 (Barber, 1979). During 1956–57, a major epizootic occurred due to BTV-10 in Portugal and Spain (Iberian Peninsula), where 1, 79, 000 sheep died resulting in 75% mortality rate (Lopez and Botija, 1958).

Subsequently, BT was spread to Europe and then to North America, Middle East, and Asia (MacLachlan, 2004). In Germany, BTV was first time reported in late August 2006. In the Netherlands, BTV was first time reported in sheep on 17 August 2006 and little later time in goats and cattle in same year (Dercksen *et al.*, 2007). BTV was first recorded from Greece in 1998, and subsequently, it spread to Bulgaria, Turkey, Montenegro, Serbia, Macedonia, and Kosovo in 1999. BTV was also reported in Sicily, Sardinia, Italy, Corsica, Mallorca, and Menorca in 2000. BTV was first time reported in Croatia in 2001 and subsequently, it spread to Albania and Bosnia in 2002 (Sperlova and Zendulkova, 2011). In North America, BTV-1 was first isolated from white-tailed deer in Louisiana in 2004. BTV serotype-2 was first reported from Florida in 1982 and BTV-12 from Texas in 2008 (Schirtzinger *et al.*, 2018).

In the Indian sub-continent, BTV was first reported from Pakistan in 1959 (Sarwar, 1962). The

BTV-16 serotype was the first BTV isolated in Pakistan (Sarwar, 1962). Subsequently, first BT outbreak was reported amongst sheep and goats in Maharashtra state of India in 1964 (Sapre, 1964). In China, BTV was first isolated from Yunnan Province in 1979 (Sun *et al.*, 2016; Yang *et al.*, 2017). The first BTV outbreak was reported in Indonesia from Suffolk sheep imported from South Australia in 1981. The serological evidence of BTV was first reported from Malaysia in 1977 (Daniels *et al.*, 2004). BTV serotype-26 was first time isolated from Kuwait (Maan *et al.*, 2011). In Australia, BTV was first time reported from the Northern Territory in 1975 (St George *et al.*, 1978). BTV serotype-5 was first time isolated in cattle from Northern Territory in Australia in 2015. In South America, BTV was first time reported from Brazil in 1978 (Sperlova and Zendulkova, 2011).

Bluetongue virus is a non-enveloped linear and segmented double stranded ribonucleic acid (dsRNA) virus. The 10 segments of virus code for 10 proteins, seven structural proteins (VP1-VP7) and three non-structural proteins (NS1, NS2 NS3/NS3a) proteins. Two structural proteins VP2 and VP5 make up the icosahedral capsid of the virus. Serotype is primarily determined by VP2, the most variable of the BTV proteins, which interacts with the neutralizing antibodies. The geographical origin of the serotypes is reflected in the variable sequence of the segments that make up a specific serotype's genome, allowing further classification of serotypes into topotypes.

### Clinical symptoms

In severe cases there is an acute febrile response characterized by hyperaemia and congestion, leading to oedema of the face, eyelids and ears and haemorrhages & erosion of the mucous membranes. The tongue may show intense hyperaemia and become oedematous, protrude from the mouth and, in severe cases become cyanotic. Hyperaemia may extend to other parts of the body particularly the coronary band of the hoof, the groin, axilla and perineum. There is often severe muscle degeneration. Breaks in the wool may occur associated with pathology in the follicles. A reluctance to move is common and torticollis may occur in severe cases. In fatal cases the lungs may show interalveolar hyperaemia, severe alveolar oedema and the bronchial tree may be filled with froth. The thoracic cavity and pericardial sac may contain varying quantities of plasma-like fluid. Most cases show a distinctive hemorrhage near the base of the pulmonary artery.

### Control

The control strategy of Bluetongue is mainly through vaccination of animals, management practices as well as the control of the vector. Due to a large number of susceptible hosts and Bluetongue Virus serotypes, control of Bluetongue Virus is very difficult. It can be intended with keeping susceptible animals

away from *Culicoides* vector but all time this is not possible. Control of vector can be tried with pouring *Culicoides* insecticides, but it is expensive and does not attain complete freedom from the vector. Live attenuated vaccines, as well as inactivated vaccines, have been successfully used in China, South Africa, Europe and other countries and a genetically engineered Virus-Like Particle (VLPs) has also been projected as a next generation vaccine. However, prevalence of multiple serotypes within a limited geographical area and incidence of genetic and phenotypic drift during natural infection in vectors and hosts, ensuring neutralization-resistant phenotypic variants within a serotype making the circumstances further difficult. There is no current BTV vaccination in North India and the presence of large number of non-cross-protecting BTV serotypes circulating in the area and hence control of disease is difficult to achieve (Maan *et al.*, 2017).

#### Disclosure statement

The authors declare that there are no conflicts of interest.

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