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Popular Article

Schmallenberg Virus Disease- An Emerging Arbovirus Infection in Ruminants

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Abstract:

Emerging infectious diseases, such as the Schmallenberg virus (SBV) within the Orthobunyavirus genus of the Peribunyaviridae family, are causing concern due to their potential spread to new hosts and regions. SBV was first identified in Germany in 2011 and has since spread across Europe, affecting various wild and domestic ruminants. The virus, transmitted by arthropods like *Culicoides* species, has been linked to severe clinical signs such as fever, diarrhea, and congenital malformations in offspring. While vertical transmission plays a significant role in the spread of SBV, zoonotic potential has not been confirmed. Diagnostic methods involve serological, histopathological, and molecular analyses, with various cell lines supporting viral culture. Controlling vector populations, implementing vaccination strategies, and monitoring vector dynamics are crucial steps in preventing and controlling SBV outbreaks. Several vaccine candidates, including inactivated, genetically modified live, DNA, virus-vectored, and recombinant subunit vaccines, show promise in mitigating the impact of SBV on ruminant populations.

Keywords: Schmallenberg virus (SBV), Simbu serogroup, *Culicoides*, vaccines, CPT-Tert cells, HEK cells, arthrogryposis, hydranencephaly, micromyelia

Introduction:

New or unidentified infections, those that are spreading to new hosts and geographic areas, and those that are reemerging are all referred to as emerging infectious diseases. Within the family Peribunyaviridae, the genus Orthobunyavirus contains the Schmallenberg virus (SBV). It was found in Schmallenberg, Germany, in 2011 and has since spread throughout Europe, hence its name. Additional epidemiological research has connected SBV to wild ruminants including deer, mouflons, and bison, despite the fact that it was initially

identified in sheep, goats, and cattle. The virus was discovered in dairy cattle that had fever; diarrhea and decreased milk production, as well as in lambs, youngsters, and calves that were deformed. SBV affects ruminants, same like the Simbu serogroup's genetically related viruses. This teratogenic virus known as SBV was spread by arthropods i.e. Biting midges/ No see urms/ *Culicoides* spp. and afflicted domestic ruminants and is a negative-sense RNA virus that is enveloped and has three genomic segments: the large (L), medium (M), and small (S) segments. Similar to other viruses in the Bunyavirales order, SBV nonstructural protein has been shown to be a major virulence factor that suppresses host cell mRNA synthesis and type I interferon production in mammalian cells, thereby improving viral replication. Most countries confirmed SBV infection within a year or two of the virus's initial introduction, demonstrating how quickly SBV spread throughout Europe.

Aetiology And Epidemiology:

Schmallenberg virus (SBV) is an enveloped, negative-sense, segmented, single-stranded RNA virus. The virus is morphologically similar to other bunyaviruses and is visible as a membrane-enveloped particle approximately 100 nm in diameter. The membrane encased the three parts genetic information. Preliminary classification and phylogenetic analysis SBV as a member of the genus Orthobunyavirus closely related to the family Bunyaviridae, Akabanevirus, Ainhoavirus, and Shamondavirus. All these viruses belong to the subgroup Simbu serogroup previously unnoticed in Europe. Like the Akabane virus, another Simbu serogroup virus, SBV can infect fetuses during a vulnerable time and result in deadly congenital defects in pregnancy stage. Three single-stranded, negative-sense RNA segments make up the genome of the genus Orthobunyavirus. These segments are referred to as large (L), medium (M), and small (S) segments based on their respective sizes. The two surface glycoproteins (Gn and Gc) and the other non-structural protein (NSm) are encoded by the M RNA segment, while the RNA-dependent RNA polymerase is encoded by the L RNA segment. Neutralizing antibodies can recognize the Gn and Gc proteins, which function as antigenic determinants. The nucleocapsid protein (N) and non-structural protein (NSs), which are encoded by the S RNA segment, are involved in complement fixation and host cell innate immune response modulation. When SBV was first characterized, it was discovered that the N gene was most closely related to Shamonda virus, while the M- and L-segment sequences most closely matched those of Aino and Akabane viruses. Subsequent research showed that SBV is a reassortant, containing the S and L RNA segments from Shamonda virus and the M RNA

segment from Sathuperi virus.

While the serological presence of SBV antibodies has been found in roe deer, red deer, alpaca (new-world camelids), mouflons, and water buffalo, SBV has been isolated or confirmed by PCR in cattle, sheep, goat, bison, roe deer, and red deer. There is currently no proof that this virus has zoonotic potential.

In Asia and Africa, bunyaviruses linked to human and animal diseases are frequently spread by insect vectors like mosquitoes and biting flies (*Culicoides* spp.). It was immediately clear that Culicoides species contribute to the spread of SBV after it was discovered. SBV genomic sequences were found in biting flies, specifically in the Ceratopogonidae family's *Culicoides obsoletus* species group. It was also demonstrated that several Culicoides species, including *Culicoides dewulfi, Culicoides chiopterus, Culicoides punctatus*, and others, tested positive for SBV genomic markers. SBV genomic markers were detected in *Culicoides* captured as early as the summer and fall of 2011 in Belgium, Italy, the Netherlands, and Denmark. Additionally, SBV spreads vertically through the placenta. Since SBV has been linked to congenital malformations in lambs, goat kids, and calves, vertical transmission from females to their offspring is especially significant. Bovine semen has been found to contain SBV. It's still unclear if semen that tests positive for SBV can spread the virus. It is extremely unlikely; nevertheless, that SBV can spread directly from one animal to another. Additionally, it doesn't seem like the virus spreads orally. Viral RNA was found in serum and blood samples for several days in naive cattle that were infected with SBV both subcutaneously and orally. In contrast, animals that were inoculated orally and uninfected controls showed no signs of viral RNA during the course of the study.

Clinical Signs and Pathology:

SBV infection has been linked to two clinical presentations. Firstly, there is fever (> 40 °C) is the result of an acute infection in adult cows. Anorexia, poor general health, a 50% reduction in milk production, and diarrhea follow the brief (one to six days) viraemic stage, which is followed by full recovery in two to three weeks. The vector-active season, which runs from April to November, is when these symptoms have been most frequently seen. Disease outbreaks typically last two to three weeks in the impacted herds. Although cases of diarrheal sheep in the UK and decreased milk production in milking sheep in the Netherlands have been documented, adult sheep and goats may not exhibit any overt clinical symptoms at the time of infection.

Another sign of SBV infection is abnormalities in animals that are either born alive or dead at term, stillbirths, or abortions after the dam becomes infected. This condition primarily affects sheep, but it can also affect

cattle and goats. The main clinical symptoms, which are comparable to those of an Akabane virus infection, are congenital malformations in fetuses and newborns. AHS, which includes stillbirth, premature birth, mummified fetuses, arthrogryposis, hydranencephaly, ataxia, paralysis, muscle atrophy, joint malformations, torticollis, kyphosis, scoliosis, behavioral abnormalities, and blindness, is the collective term for these congenital abnormalities. In lambs, goat kids, and calves, transplacental infection with SBV causes severe congenital malformations like arthrogryposis, malformations of the skull (macrocephaly, brachygnathia inferior), the vertebral column (kyphosis, lordosis, scoliosis, and torticollis), and the brain (hydranencephaly, porencephaly, cerebellar hypoplasia, and hypoplasia of the brain stem). Some animals have neurological symptoms like blindness, ataxia, recumbency, inability to suck, and convulsions even though they appear normal on the outside at birth. The timing of infection during pregnancy affects the fetal abnormalities.

At necropsy, the central nervous system (CNS) of young ruminants infected with SBV frequently exhibits cerebellar and cerebral hypoplasia, micromyelia, hydranencephaly, porencephaly, lissencephaly, hydrocephalus, and more. Glial nodules typically found in the mesencephalon and hippocampus of lambs and goats, lymphohistiocytic meningoencephalomyelitis, and neuronal degeneration and necrosis primarily found in the brain stem of calves are among the microscopic lesions. Lesions in the spinal cord are most likely the cause of the musculoskeletal abnormalities that show up in fetuses as arthrogryposis.

Diagnosis:

Clinical manifestations of disease, which differ by species, are the basis for clinical diagnosis. Blood and serum samples preserved with EDTA should be obtained from suspected acute infections in adults and brought to the lab in a chilled environment. Samples ought to be taken while the clinical infection is still in its acute phase, such as when there is fever, decreased milk production, or diarrhea. Newborn animals or suspected cases in aborted fetuses are sampled for histopathological, serological, and viral analyses as needed. While samples of brain tissue, preferably the cerebrum, cerebellum, and other brain stem components, as well as the spleen and blood, are taken from necropsy, live newborn pre-colostral blood, serum, and meconium should be taken and transported in a chilled or frozen state. Numerous cell lines originating from different animal species as well as humans can harbor the Schmallenberg virus. At 48 hours after infection, SBV reached titres of 10 PFU/ml in sheep choroid plexus (CPT-Tert) cells, bovine foetal aorta endothelial (BFAE) cells, human 293T, canine MDCK, and hamster BHK-21 and BSR cells. It

also caused cytopathic effect (CPE) in the majority of cell lines, with the exception of the BFAE cell. Sheep CPT-Tert cells were the best cell lines for SBV culture out of all of them. 72 hours after infection, well-defined plaques measuring about 3 mm in diameter were seen in these cells. Other methods have also been developed by scientists of various countries which includes *in situ* hybridization, immunoflourosecnce assay, virus neutralization tests, indirect ELISA, quantitative real time PCR. Adults with acute SBV infection do not exhibit any particular clinical symptoms. Bluetongue, epizootic hemorrhagic disease (EHD), foot and mouth disease (FMD), bovine viral diarrhea (BVD), border disease and other pestiviruses, bovine herpesviruses 1 and other herpesviruses, Rift Valley fever, bovine ephemeral fever, toxic substances, and other potential causes of high fever, diarrhea, milk reduction, and abortion should all be considered. However, other Orthobunyavirus infections, bluetongue, pestiviruses, genetic factors, and toxic substances should all be considered in the diagnosis of malformations in calves, lambs, and kids.

Prevention And Control:

The best method for forecasting future SBV outbreaks appears to be monitoring the dynamics of competent vectors and vector infection rates. Additionally, since vaccination, in particular, lowers SBV infection in ruminants, controlling insect populations and vaccinating replacement stocks are the two most crucial strategies for preventing SBV outbreaks. Controlling the Culicoides vectors could involve using techniques like applying pathogens and insecticides to areas where larvae develop, removing larval breeding grounds through environmental interventions, treating host animals or resting areas like animal housing with insecticides, keeping livestock in screened buildings, and luring and killing adult midges with repellents or host kairomones. The best solutions currently available involve treating livestock and animal housing with pyrethroid insecticide, reducing the number of local breeding sites, and using midge-proofed housing for viraemic or valuable animals.

The vaccines and vaccine candidates include-

1. **Inactivated Vaccines:** Bovilis SBV (MSD Animal Health), Zulvac SBV (Zoetis), SBVvax (Merial)
2. **Genetically Modified Live Vaccines:** Recombinant NSm and/or NSs deletion mutants
3. **DNA Vaccines:** SBV Gc (N-terminal), SBV Gn (ectodomain), SBV Gc (ectodomain 1 and 2)
4. **Virus Vectored Vaccines:** Modified Vaccinia Virus Ankara, Gc (N-terminal), Recombinant Equine Herpes Virus 1, Gc (N-terminal)
5. **Recombinant Subunit Vaccine:** Baculovirus-expressed Gc or Gc/Gn, Gc + Gn linked ectodomains,

HEK cells, Gc (N-terminal) of SBV and Akabane, HEK cells

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