Bovine Ephemeral Fever: Diagnostic Approaches and Associated Risk Factors

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Abstract

Bovine Ephemeral Fever, known as "three-day sickness," is a menace to cattle populations. It is mainly spread by vector transmission. The culicoides, biting midges and mosquitoes are principal vectors whose contribution to the dynamics of an outbreak with this disease is central, as reflected in various studies. Vector activity, and hence the incidence of BEF, is therefore greatly influenced by climatic factors such as shifts from drought to heavy rains. Major outbreaks are mostly associated with favorable environmental conditions. Influences of host factors, such as age, sex, species, and lactation stage, modulate susceptibility and severity. The highest levels of susceptibility are found in young cattle under three years old and those in the early stages of lactation. Though cattle show higher susceptibility than buffalo, recent investigations have established a possible role of wildlife as BEFV reservoirs. Successful design of mitigation and management strategies for BEF outbreaks depends on the complicated interaction of vectors, climate and host factors.

Keywords: Bovine Ephemeral Fever, Bovine Ephemeral Fever Risk Factors, Vectors

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Introduction

Bovine Ephemeral Fever (BEF) commonly named "Three days sickness" is a viral arthropod-borne disease of livestock animals, that primarily affects cattle (George & Standfast, 2019). The causative Bovine Ephemeral Fever Virus (BEFV), is characterized as a single-stranded RNA virus classified under the *Ephemerovirus* genus within the *Rhabdoviridae* family (Chaisirirat et al., 2018). The disease has a wide geographical spread, affecting regions from Africa to the Nile River, South Asia to the Middle East, Korea, Taiwan, and Southern Japan. It is particularly prevalent in humid and flat areas (Walker & Klement, 2015a).

The BEF exerts considerable economic influence, from mortality to trade repercussions within nations (Yang DaRam et al., 2018). The incubation period of disease is relatively short, usually ranges from about 36 to 48 hours (Akakpo, 2015). Interestingly, young calves, typically under 3 to 6 months of age, are generally less susceptible and often do not show any visible signs of illness. Mortality rates are generally low, usually less than 1% of the herd. In most instances, the disease often presents acutely (Constable et al., 2016). The disease causes a sudden, biphasic rise in body temperature. Severe cases can manifest with high fever, loss of appetite, depression, nasal discharge, and a stiff gait. A second peak in fever might occur, resulting in respiratory complications and potential secondary issues like pneumonia and arthritis. Recovery usually takes 5-6 days, but reduced milk yield and other complications may persist (Ashraf et al., 2023).

Viral Isolation and identifying its genome can be done using blood samples collected with anticoagulants. Although this method is costly, it yields results within three to four days (Akakpo, 2015). Traditional reverse transcription polymerase chain reaction (RT-PCR) is used for detection of viral genome (Zheng et al., 2011). Prevention strategies primarily aim at eliminating arthropod vectors and enhancing animal hygiene practices, though their effectiveness can vary, particularly in regions lacking robust vector control programs and where livestock management majorly relies on extensive or range-based practices (Akakpo, 2015).

This review seeks to provide a thorough overview of BEF by identifying the primary risk factors, including host-related, environmental, vector-related, and animal-specific factors. We will evaluate current literature, discuss implications for BEF control and prevention, and highlight knowledge gaps while proposing areas for future research.

1. Overview of Bovine Ephemeral Fever

1.1 Etiology

BEFV is a single-stranded RNA virus, a bullet-shaped virion of rhabdoviruses (Walker & Klement, 2015b). The virus's structural proteins enable it to evade the host's immune response. BEFV is primarily transmitted through arthropod vectors, such as biting midges and mosquitoes, which are prevalent in warm, humid environments (Burgess & Spradbrow, 1977). A complete understanding of the viral genome and its mode of transmission is essential for developing coping responses against them.

1.2 Clinical Signs

Clinical presentation of BEF-affected animals is usually typical. The description of these clinical signs is given in Table 1.

- Fever: One of the first signs observed is a sudden onset of high fever which is often biphasic and exceeding 104°F. The fever lasts only a short duration, typically two to three days (Burgess & Spradbrow, 1977).
- Lameness: One of the most important signs of this disease is lameness, particularly of hind legs. The animal is reluctant to move and therefore exposed to environmental and managemental diseases.(Tobin et al., 2020).
- Respiratory Distress: Some animals may experience respiratory system-related issues which mostly result in coinfection by other opportunistic microorganisms of the respiratory system (Liao et al., 1998).
- Recovery: While most animals recover within three days, some may experience lingering effects such as muscle weakness or paralysis, which can affect their productivity and overall health (Uren, 1989).

Table 1: Clinical Signs of Bovine Ephemeral Fever

Clinical Sign	Description
Fever	Sudden onset of high fever (up to 41°C) (Burgess & Spradbrow, 1977).
Lethargy	Reduced activity and feed intake, leading to weight loss (Burgess & Spradbrow, 1977)
Lameness	Stiffness and lameness due to muscle soreness (Tobin et al., 2020).
Respiratory Distress	Changes in heart rate and respiratory patterns (Liao et al., 1998).
Recovery	Most animals recover within three days, but some may have lingering effects (Uren, 1989).

2. Diagnostics of Bovine Ephemeral Fever

2.1 Clinical Diagnosis

The diagnosis of BEF mainly relies on the clinical signs of the animal and the history by the owner or manager. An overall clinical examination is required to assess the condition and to rule out the differential diagnosis (Bakhshesh & Abdollahi, 2015). Identifying these clinical signs and initiating an immediate response is essential for the veterinarian to cope with the disease.

2.2 Laboratory Diagnosis

Laboratory diagnosis is also essential for assessing the severity of the disease and the extent of damage it causes. It plays a significant role in the confirmation of outbreaks.

2.2.1 Serological Tests

Laboratory diagnostics are essential for confirming cases of BEF. The key serological tests include:

- Enzyme-Linked Immunosorbent Assay (ELISA): ELISA is one of the most widely used diagnostic tools for detecting antibodies in an animal using a serum sample (Zheng et al., 2009). This method is helpful in differentiating those animals that were vaccinated from those that have been naturally affected (Benevenia et al., 2024). Through the use of ELISA, veterinarians can develop an effective plan for immunization of a herd, and the overall immunity levels of the herd can also be accessed.
- Virus Neutralization Test (VNT): Another key serological test for the confirmation of virus is the VNT test which is often considered the golden standard serological test. It is a method used to evaluate the ability of antibodies to neutralize the virus. To perform it, serum samples from vaccinated animals or those with natural infections are taken and then these samples are mixed with a known amount of the virus. Then this mixture is incubated with susceptible cells. After the incubation period, the cells are examined for any signs of damage. If there are fewer signs of damage, it suggests a stronger immune (Whiteman et al., 2018). This method has not yet been used in the case of BEF.

2.2.2 Molecular Techniques

Advancements in molecular diagnostics have enhanced the ability to detect BEFV quickly and accurately. Key differentiating features are given in Table 2. Key techniques include:

- Reverse Transcription Polymerase Chain Reaction (RT-PCR): RT-PCR is a type of PCR technique that is employed to detect viral RNA in blood or tissue samples. These methods provide rapid and precise results (Niwa et al., 2015). However, one of the major drawbacks of this technique is that viruses with only samples from acute phases can be detected and temperature maintenance during the transportation of samples is essential otherwise the viral RNA can be destroyed (Vomelova et al., 2009).
- Lateral Flow Assays: Lateral Flow Assays (LFAs) play a crucial diagnostic tool in cattle. These tests are mostly simple, quick, and easy making them ideal for farmers and veterinarians working in the field. By detecting specific proteins (antigens) or immune responses (antibodies) associated with the virus (Koczula & Gallotta, 2016) LFAs help identify infected animals within minutes. This rapid detection is particularly important during outbreaks, allowing for swift action to manage and contain the disease (Sadeghi et al., 2021). But still, to date, no information regarding its use in BEF has been reported.

2.3 Differential Diagnosis

It is essential to differentiate BEF from other diseases that present with similar clinical signs. Important differential diagnoses include:

- Foot-and-mouth disease: Contagious disease and it mostly affects oral cavity, hooves along with high fever (Grubman & Baxt, 2004).
- Hemorrhagic Septicemia: Seasonal pattern and respiratory system involvement along with High fever (Shivachandra et al., 2011).
- Infectious bovine rhinotracheitis: Caused by a herpesvirus, this disease leads to respiratory distress and can be confused with BEF (Wyler et al., 1989).

Table 2: Diagnostic Tests for Bovine Ephemeral Fever (Jacobson et al., 1998; Wang et al., 2021; Tawheed et al., 2023)

Parameter	Clinical Diagnosis	Serological Diagnosis	Molecular Diagnosis
Basis of Diagnosis	Observation of clinical signs	Detection of specific antibodies or antigens	Detection of viral genetic material
Techniques Used	Physical examination, history, and signs analysis	ELISA, Virus Neutralization Test (VNT),	PCR, RT-PCR
Speed	Rapid (immediate observation)	Moderate (days to process and interpret)	Quick (a few hours for processing)
Specificity	Low (symptoms may overlap with other diseases)	Moderate to high (depends on test type)	High (specific to BEF virus)
Sensitivity	Low (may miss subclinical cases)	High (detects antibody or antigen levels)	Very high (detects minute quantities of virus)
Cost	Low	High	Moderate to high
Field Applicability	High (can be performed on-site)	Low (requires lab setup)	Low (requires specialized lab equipment)
Confirmatory Ability	Preliminary diagnosis	Supportive/indicative (with paired samples)	Confirmatory (detects pathogen directly)
Sample Required	Animal history and observation	Serum samples	Blood, tissues, or swabs
Drawbacks	Non-specific; cannot confirm diagnosis	False positives/negatives possible; timing matters	Requires expertise and infrastructure
Utility	Initial screening	Epidemiological studies; retrospective diagnosis	Definitive diagnosis

2.4 Diagnostic Sequence

The table below outlines the initial steps in the diagnostic workflow, including observing clinical signs and collecting samples, with a brief description of each step to guide the process as recommended by (Constable et al., 2016) as given in Table 3 .

Table 3: Methodolgy to diagnose a disease (Constable et al., 2016)

Step	Description
1	Observe clinical signs: fever, lameness, lethargy.
2	Collect samples: blood or tissue samples.
3	Perform serological tests: ELISA or VNT.
4	Conduct molecular testing: PCR for viral RNA detection.
5	Interpret results: confirm diagnosis based on clinical presentation and test outcomes.

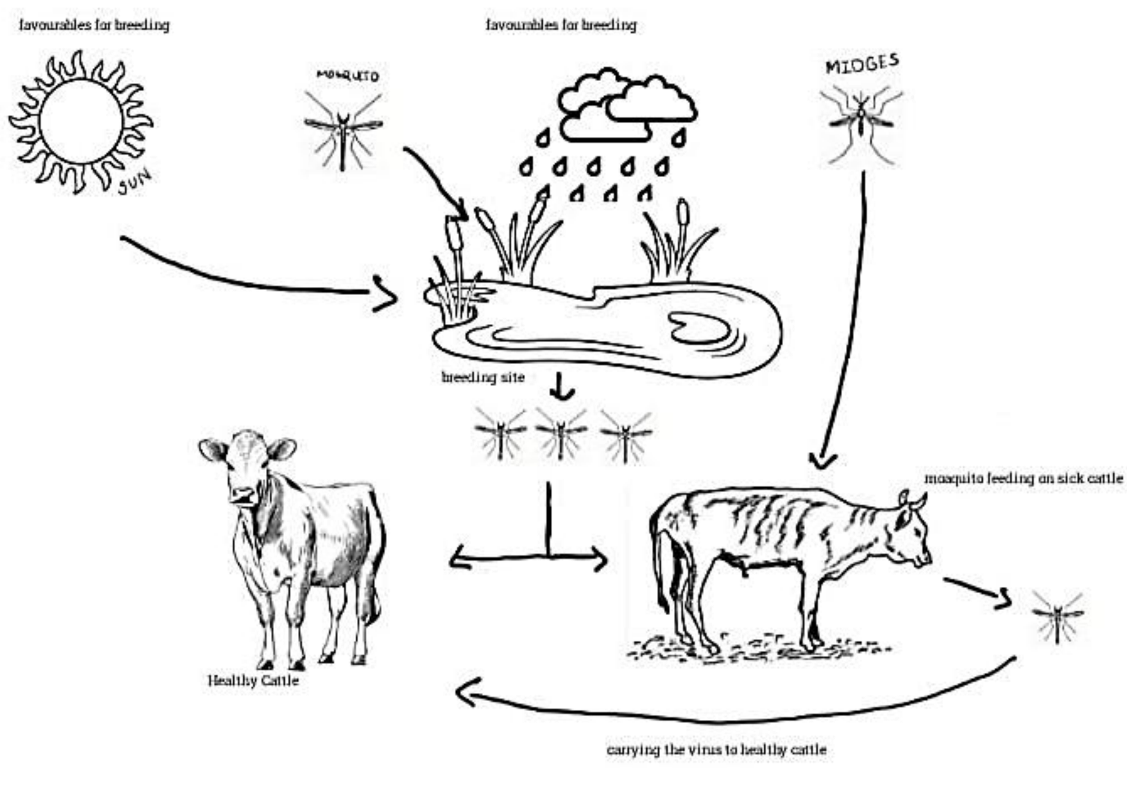

Fig. 3.1: Transmission of BEFV from sick to healthy cattle and risk factors that contribute for the life cycle of vector.

3. Risk Factors for Bovine Ephemeral Fever

3.1 Environmental Factors

Environmental conditions play a very significant role in the prevalence of BEF as they provide optimal conditions for vector proliferation and virus survival. Key factors include:

- Climate: The climate of a region significantly impacts the severity of Bovine Ephemeral Fever (BEF), as it influences the number of vectors responsible for spreading the disease. BEF is transmitted by mosquitoes and biting midges, which thrive in warm and humid conditions (Lee, 2019). During the rainy season, especially in regions with frequent rainfall, standing water provides ideal breeding grounds for mosquitoes, causing their populations to spike (Sellers & Infection, 1980). This increase in vector populations, like mosquitoes and midges heightens the risk of BEF spreading among cattle. In areas with consistent rainfall and humidity, these conditions create a perfect environment for these vectors to thrive all year long, leading to higher chances of outbreaks with higher intensity in such regions. Additionally, the rainy season brings its own set of challenges for livestock, sudden weather changes, overcrowding, poor nutrition, and damp conditions can weaken their immune systems and make them more susceptible to other diseases (White, 2008). In regions where rain is constant the climate not only plays a major role in increasing the number of disease-carrying vectors but also puts the health of the livestock at risk. That's why it's so important to keep an eye on both the environment and the health of the animals to manage BEF effectively (Zaghawa et al., 2016).
- Vectors: Vectors play a crucial role in how BEF spreads. These insects pick up the virus when they feed on the blood of infected cattle. Then, when they bite healthy animals, they pass the virus along. This is why BEF usually peaks during the rainy seasons it's all about the seasonal patterns of these vectors (Burgess & Spradbrow, 1977).

The activity and population of vectors are very much dependent on climatic conditions such as temperature, rainfall, and humidity, which provide them with an optimal environment for their breeding and ultimately increase in numbers (Githeko et al., 2000). BEF outbreaks are most often during high vector activity, usually during warm and wet seasons, which signifies the seasonal nature of the disease and its relation to vectors. Effective disease control strategies are therefore needed to manage the vector during harsh environmental conditions, the use of insecticides as control is one of the ways to control the spread of disease, other management practices for small farmholders should be implemented which include vaccination of animals, draining of stagnant water and use of immune boosters during harsh environmental conditions. Although vector control strategies may present some challenges, combining managemental flaws identification and their mitigations along with vaccination programs offers a very helpful strategy for reducing the incidence and the overall impact of BEF. Understanding the significant role of vector populations in BEF transmission is essential for developing sustainable control measures and limiting economic losses in affected regions.

- Geographic Distribution: BEF is endemic in tropical and subtropical regions around the world, Due to the favorable environment for vectors, such as biting midges (*Culicoides spp.*) and mosquitoes (*Culex spp.*, *Aedes spp.*), they are abundant in these regions (Lee, 2019). These vectors thrive in warm, humid climates, which is why BEF is commonly found in some specific parts of the world which include Africa, Asia, and Australia, as well as certain areas of the Middle East and South America (Walker & Klement, 2015b). All these regions have something in common and that is rainfall along with a humid climate which maybe present be present throughout the year or during some specific time of the year.

The disease is most prevalent in regions where these vector populations are dense and where climatic conditions favor their breeding. For example, South Asia, which includes countries like India, Pakistan, and Bangladesh, faces recurrent outbreaks of BEF (Lee, 2019), particularly during the monsoon season, when vector populations increase. Similarly, sub-Saharan Africa and parts of the Middle East, including Saudi Arabia (Zaghawa et al., 2016), Iran (Bakhshesh & Abdollahi, 2015), and Turkey (Tonbak et al., 2013), also report frequent BEF outbreaks (Venter et al., 2003) . In Australia, BEF is a significant concern for the cattle industry, particularly in the northern and coastal areas where vector populations are highest (Walker, 2005).

In addition to endemic regions, BEF has now also been reported from newly affected areas due to the movement of infected animals, global warming, and global trade. The spread of BEF to this new region where BEF was not reported earlier is thought to be because of the trade of animals carrying the virus with them (De La Rocque et al., 2011), but another important and more authentic reason is that the vectors carrying the virus have reached the region via trading vehicles or by winds (Hendrickx et al., 2008). As a result, the disease can emerge in regions outside of its historical geographic range, posing challenges for control and eliminating the disease. Thus, the geographic distribution of BEF is closely tied to the presence of suitable vectors and the environmental conditions that support their proliferation, making the disease a significant concern in areas with favorable climates for vector populations.

3.2 Management Factors

Management practices on farms can either increase or decrease the risk of BEF outbreaks:

- Animal Husbandry: Intensive farming practices can increase the case ratio of BEF, such as high stocking densities, which can facilitate the spread of BEF (Barker & Reisen, 2019). Farms with poor management are at higher risk of being affected by BEF outbreaks. Farms with no proper dung management and with the least hygienic farming practices are at greater risk of introducing and spreading the virus among cattle (Wilson et al., 2020). The reason is that with poor management animals can easily get stressed and become immunocompromised, on the other hand, an unhygienic environment acts as a breeding site for the vectors which resultantly makes the farm more prone to BEF.
- Control: Effective control measures for vectors and managemental issues should be addressed seriously, the use of insecticides in large-scale farms and the use of other traditional methods for small-scale farms can be useful. Other strategies include timely vaccination of animals against BEF, managing water, ensuring there is no stagnant waterbody within the farm, closing the drainage pipes, timely dung disposal, etc. Implementing these measures can significantly lower the risk of outbreaks

3.3 Herd Factors

Age and Immunity: Younger animals are more susceptible to BEF, particularly those under three years old (Ashraf et al., 2023). The exact reason for the higher susceptibility of this age group is still unknown but it is believed that due to lower immunity levels, this age group is more prone to BEF (Burgess & Spradbrow, 1977). Those animals that haven't faced any outbreak previously, those areas where the disease wasn't reported earlier or those animals that have moved from a disease-free region to an endemic area are at higher risk and are more susceptible to the disease (Wang et al., 2001). Age as a risk factor has shown almost a similar pattern throughout many research. Still detailed research is required to identify the factors that influence the susceptibility of young animals to BEF that will help develop strategies for controlling the disease for this particular age group

3.4 Sex

In this context of BEF, the sex of the animal does not have any direct or well-established relation with the disease. In most reports and research around the world, there is a mixed trend shown regarding the sex association with BEF but still, there are certain factors related to sex that can influence how the disease affects them (Nadeem et al., 2024). For example, those cows that are lactating or higher yielders or cows that are in late pregnancy are often under more stress as compared to those that are low yielders or nonlactating phase (Trevisi et al., 2012). This can weaken their immune systems and make them more vulnerable to infections like BEF. Hormonal changes in pregnant cows or those cows that are in their estrous cycles can also impact their immune response, which ultimately makes them more susceptible to infections (Hughes et al., 2014). Additionally, during mating seasons, in small-scale farming cattle are more likely to move between different herds or grazing areas, from there they can be exposed to vectors that spread BEF, further increasing the risk of infection.

3.5 Species

BEF mainly affects cattle and buffalo, with cattle being more susceptible to disease. Many studies have shown that cattle exhibit more severe clinical signs as compared to buffalo. In many countries, the trend was almost similar with cattle exhibiting higher serological rates as compared to buffalo (Nadeem et al., 2024). Another important study regarding species is that wildlife species have been found to harbor neutralizing antibodies to the BEF virus, suggesting they may act as reservoirs for the virus. Species such as buffalo, wildebeest, impala, and giraffe in Kenya have shown evidence of exposure to BEFV (Anderson et al., 1998). Additionally, recent data from the Republic of Korea indicates a 10.8% seroprevalence in cervid populations, supporting the idea that wildlife, including cervids, may play a role in the transmission dynamics of BEFV (Yeh et al., 2023). These findings highlight the complex host range and potential reservoirs of BEFV beyond just cattle.

3.4 Socioeconomic Factors

Socioeconomic factors greatly influence the management of BEF and its impact on livestock production:

- Economic Impact: The economic impact of BEF is very serious, mainly losses from milk production and decreased weight gain in cattle, to add to the cost the use of treatment and control measures strategies for controlling the disease also leaves a significant impact on farm economics (Lavon et al., 2023). The overall impact can significantly affect the profitability of livestock operations(Walker & Klement, 2015a).
- Awareness and Education: Educating farmers about BEF symptoms, prevention strategies, and control measures are essential for reducing outbreak risks. Increased awareness can lead to timely reporting of suspected cases, facilitating quicker interventions and better management of the disease.

Table 4: Risk Factors for Bovine Ephemeral Fever

Risk Factor	Description
Climate	Warm and humid conditions conducive to vector proliferation (Lee, 2019).
Geographic Distribution	Areas with high rainfall and humidity (Lee, 2019).
Animal Husbandry	Intensive farming practices, high stocking densities (Wilson et al., 2020)
Vector Control	Effective control measures for vectors (Burgess & Spradbrow, 1977)
Age and Immunity	Younger animals have lower immunity levels (Walker & Klement, 2015a) .
Previous Exposure	Herds with prior exposure may develop herd immunity (Aziz-Boaron et al. 2014)
Economic Impact	Loss of milk production, decreased weight gain, and treatment costs (Lavon et al., 2023).
Awareness and Education	Educating farmers about BEF symptoms, prevention and control.

Conclusion

Bovine Ephemeral Fever (BEF) is a serious threat to both cattle health and the economic stability of livestock farming, especially in areas where the disease is common. The virus spreads through blood-feeding insects like mosquitoes and biting midges, which can lead to outbreaks that cause significant financial losses. Financial losses are majorly due to reductions in production, increases in treatment costs, and loss of livestock. Early detection and diagnosis are necessary for minimizing the impact of outbreaks of BEF, as early intervention reduces the damage and losses caused by the outbreak.Effective surveillance systems are crucial for managing BEF in areas where it frequently occurs, with reliable diagnostic methods researchers can identify the most susceptible population among the natural hosts. These efforts make control more effectiveTo handle BEF effectively we need to develop a comprehensive approach by combining clinical and laboratory expertise of a veterinarian and microbiologist at the same time. Educating farmers, especially small farm holders about preventive measures such as vaccine, vector population and some major clinical signs is essential. By combining all these efforts not only the welfare of an animal can be enhanced but also the livelihood of farmers can improved who rely on cattle for their income.

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