

## A Review of Studies on Bovine Immunodeficiency Virus (BIV) in Asia

Ahmad Mohammed <sup>1</sup>, Asaad Jassim <sup>2</sup>, Khalefa Ali Mansour <sup>3</sup>, Saad Hashim Al-Husseiny, <sup>4</sup>

<sup>1</sup>-Veterinary teaching hospital in Babylon, Babylon, Iraq

<sup>2,3,4</sup>College of Veterinary Medicine, University of Al-Qadisiyah, Iraq

<https://orcid.org/0000-0001-9135-7256><sup>3</sup> , <https://orcid.org/0000-0002-0966-9515><sup>4</sup>

**Submitted:** November 9, 2025

**Revised:** December 02, 2025

**Accepted:** December 02, 2025

**Correspondence:**

Asaad Jassim

[assad.abid@qu.edu.iq](mailto:assad.abid@qu.edu.iq)

Khalefa Ali Mansour

[Khalefa.mansour@qu.edu.iq](mailto:Khalefa.mansour@qu.edu.iq)

Saad Hashim Al-Husseiny

[Saad.ghmeiss@qu.edu.iq](mailto:Saad.ghmeiss@qu.edu.iq)

**Abstract** Bovine Immunodeficiency Virus (BIV) is a widespread but often overlooked infectious agent in cattle. The first isolation of virus occurred in Louisiana, USA, in 1969, from a Holstein cow exhibiting lymphocytosis, weakness, and neurological symptoms, and has been recognized as the prototype lentivirus of cattle. It is known for its slow replication, long term persistence and immunosuppressive activity. Although infections are often mild or unapparent, BIV can cause immune alterations such as lymphoid hyperplasia, lymphocyte dysfunction, and decreased CD4/CD8 ratio, which make the host more susceptible to secondary infections.

Epidemiological observations from Asia have revealed the presence of Bovine Immunodeficiency Virus (BIV) in several countries, including Japan, Korea, Iran, Turkey, Cambodia, Pakistan, and India. Reported seroprevalence varies considerably from about 20 - 35% in Japan and Korea respectively, about 26% in Cambodia, and between 10% and 28% in Iran. Molecular investigations in India and Turkey have confirmed the detection of parvoviral DNA in native cattle populations

**Keywords:** Immunodeficiency, Asia, Cattle, Lentivirus

©Authors, 2025, College of Veterinary Medicine, University of Al-Qadisiyah. This is an open access article under the CC BY 4.0 license (<http://creativecommons.org/licenses/by/4.0/>).

**Introduction** Asia is the largest continent on earth, occupying almost 30 % of the planet's total land and home to around 60% of the world's population. Asia possesses the world's largest livestock population, accounting for more than 40% of the global total. The continent hosts a considerable share of the world's livestock particularly cattle and buffaloes (1).

Bovine Immunodeficiency Virus (BIV) is a lentivirus belonging to the family Retroviridae, subfamily Orthoretrovirinae, and genus Lentivirus. It shares structural and biological similarities with other animal and human lentiviruses such as Human Immunodeficiency Virus (HIV), Feline Immunodeficiency Virus (FIV), and Equine Infectious Anemia Virus (EIAV) (2). The virus was first isolated in 1969 from cattle with persistent lymphocytosis in the United States and was later classified as a bovine lentivirus based on its morphology, genomic organization, and replication kinetics (3). Since then, serological and molecular evidence of BIV infection has been reported in several countries in Asia including Japan, Korea, Iran, Turkey, Cambodia and Pakistan, confirming that

the virus has a global but often underestimated distribution (4).

The virus mainly targets monocytes, macrophages, and lymphocytes, leading to a lifelong persistent infection that is typical of lentiviruses. Although clinical signs are rarely overt, experimental infections have demonstrated immunopathological changes such as lymphocyte depletion, monocyte dysfunction, and general immune suppression (5). The virus has been shown to interfere with normal cytokine signaling, particularly by altering interleukin and interferon responses, leading to a gradual deterioration of immune competence. Recent immunological studies have revealed that BIV can modulate T-cell activation pathways and inhibit antigen presentation, which contributes to immune evasion and long-term persistence (6). Moreover, BIV can cause oxidative stress and apoptosis in infected cells, these mechanisms similar to other lentiviral infections (7). From both an epidemiological and economic standpoint, BIV infection mainly causes losses due to its immunosuppressive effects. Cattle infected with BIV become more vulnerable to secondary infections such as mastitis, pneumonia, metritis, and enteric

disorders, which reduced of milk production, fertility, and growth performance (8). Co-infection studies have shown that BIV frequently occurs alongside Bovine Leukemia Virus (BLV), Bovine Viral Diarrhea Virus (BVDV), and Brucella spp., where it appears to exacerbate disease severity and prolong viral shedding (9,10). The immunosuppressive environment caused by BIV may also compromise vaccine efficacy, highlighting its potential as an immunomodulatory cofactor in mixed infections. Recent epidemiological surveys conducted in Iran and Japan demonstrated that although BIV prevalence remains relatively low, the virus persists in both dairy and beef herds, emphasizing the need for continuous surveillance (7,11). Molecular research has greatly deepened the understanding of the genetic diversity and evolutionary patterns of the virus. Early comparative studies reported approximately 40–45% nucleotide similarity between BIV and other lentiviruses such as HIV and FIV; however, these estimates are based on limited gene regions (mainly gag and pol) and older sequencing data. More recent whole-genome comparisons are recommended for accurate evaluation. Phylogenetic analyses suggest that Bovine immunodeficiency virus isolates from Asia, particularly Japan, Korea, and Iran, are closely related to North American strains, implying intercontinental dissemination likely facilitated by international cattle trade (12,13,14). Most sequencing studies have been revealed genetic variation in the env and pol regions, with some mutations potentially affecting viral infectivity and replication efficiency (11).

Yilmaz et al., (15) mentioned that early serological methods, including ELISA and Western blot assays, were effective for detecting antibodies, efficiency was limited due to issues of cross-reactivity and relatively low sensitivity, these limitations, recombinant capsid-based ELISA systems and single-chain variable fragment (scFv)-based immunoassays have been developed, yield great diagnostic precision and reliability (16). Yamamoto et al., (11) reported that molecular analyses, particularly PCR and real-time PCR, now play a central role in BIV detection. The most recent major advancement were the development of a multiplex real-time PCR assay capable of simultaneously detecting both bovine immunodeficiency and bovine leukemia viruses, the significantly enhances diagnostic efficiency in large-scale surveillance programs. These developments improve diagnostic accuracy and support molecular characterization of circulating strains, helping to track viral evolution. Although research has advance, BIV still doesn't get enough attention in cattle health

programs around the world. There is no vaccine or specific treatment for virus. Prevention depend on biosecurity practice, routine testing, and the culling or isolation of infected animals (17). Since the infection is often subclinical and progresses slowly, the virus can persist in herds undetected for years, serving as a silent reservoir. Ongoing studies on how BIV replication, immune modulation, and latency is essential for designing effective control strategies. Because BIV is very similar to HIV in its genetic and biological features, it serves as a useful model for studying how lentiviruses work and how the immune system responds to them (6).

Bovine immunodeficiency virus is an immunosuppressive and persistence infection in cattle. Although the clinical signs are rare, the virus can impair immune function, enhance susceptibility to other diseases, and reduced productivity, and giving it both veterinary and economic importance (11). The objectives of this paper are to provide a comprehensive overview of the Bovine Immunodeficiency Virus (BIV), focusing on its economic and health significance in cattle production and productivity. The paper aims to describe the characteristics and pathogenic potential of BIV as a Lentivirus, and to summarize current knowledge about its epidemiology and global distribution specially in Asian. It also highlight the lack research on BIV infection in Iraq and stresses the need for effective diagnostic, preventive, and control measures, along with further studies to determine its presence and impact on Iraqi cattle.

#### Classification of the Virus

According to the most recent report by International Committee on Taxonomy of Viruses published by (18) that the bovine immunodeficiency virus is classified within the family of Retroviridae, subfamily Orthoretrovirinae, and genus Lentivirus. The virus is considered a complex retrovirus because, in addition to the three major structural open reading frames (gag, pol, and env), it possesses accessory genes such as vif and tat that are essential for replication in non-dividing cells. This genetic composition distinguishes lentiviruses from the simple retroviruses like Alpharetrovirus and Gammaretrovirus, which lack these additional genes(19).

As this is a review paper, it is recommended to include illustrative images such as electron micrographs or structural diagrams of BIV to support the morphological description and improve the overall quality of the manuscript. The virion contains a conical capsid enclosing two identical copies of positive-sense single-stranded RNA, along with three

key enzymes reverse transcriptase (RT), integrase (IN), and protease (PR) that mediate reverse transcription, integration into the host genome, and maturation of viral particles. The viral envelope, derived from the host cell membrane during budding, contains surface (SU) and transmembrane (TM) glycoproteins responsible for host cell attachment and entry (20,21).

### Epidemiology

Bovine Immunodeficiency Virus (BIV) is a lentivirus of the family Retroviridae, first identified in 1969 in Louisiana, USA, from a Holstein cow showing lymphocytosis, weakness, and neurological signs. The strain, known as R-29, became the prototype for all subsequent research (3).

Reported infection rates vary from very low levels in Europe and Oceania (1–5%) to moderate prevalence in the Americas (5–30%), and higher rates in parts of Asia (20–35%) and Africa (approximately 11%), as summarized from several regional surveys (7,22,23,24,25,26).

### The Occurrence of BIV Infection

The global distribution of BIV is linked to cattle trade and animal movement, with molecular studies revealing more than 98% genetic identity between strains from Asia, Africa, and the Americas. This genetic stability indicates a long-standing, silent global spread with minimal viral evolution (27,28).

### The Spread of BIV in Asia

An experimental infection of calves with Bovine Immunodeficiency Virus (BIV) evaluated immune cell responses and the virus's pathogenic potential. The animals exhibited both lymphocyte and monocyte impairment without severe clinical symptoms. This experiment illustrated that BIV has the ability to suppress the immune system even without causing obvious disease., laying the groundwork for future pathogenesis research (29).

This research was the first to report BIV infection in Japan, Examining dairy cattle in Hokkaido using ELISA and Western blot tests. About 20% of the tested animals were seropositive, confirming the presence of BIV antibodies in Japanese herds. No clinical abnormalities were found, suggesting a mild or latent infection. The authors stressed the need for long-term studies to assess viral persistence and possible effects on productivity(30).

A follow-up investigation in Hokkaido expanded they conducted serological surveillance and achieved the first successful field isolation of BIV in Asia. The study confirmed 24–28% seropositivity and isolated viral strains genetically related to North American lineages. The findings showed active viral circulation and offered molecular evidence of BIV in Japanese

cattle, suggesting that imported animals may have introduced the virus to the region(5).

This nationwide study in South Korea investigated the prevalence of antibodies against BIV in dairy and beef cattle herds using the ELISA test. The researchers tested blood serum samples from herds in various provinces to assess how widely the animals had been exposed to the virus.. They found seroprevalence rates of 35% in dairy cattle and 33% in beef cattle, This indicates that BIV was widely spread among cattle in Korea. No obvious clinical symptoms were observed with the infection, suggesting that the virus was circulating subclinically (31).

The study examined the occurrence of BIV and BLV in draught cattle and water buffaloes in Cambodia using ELISA. The results showed that 26.3% of cattle and 16.7% of buffaloes tested positive for BIV antibodies, in these study represented the first report of BIV infection in Southeast Asia. The authors suggested that poor sanitary and management practices could facilitate viral transmission(25).

A serological survey conducted in Pakistan tested cattle and buffaloes for BIV and BLV antibodies. The results showed that 22% of cattle and 14% of buffaloes were infected with BIV, confirming the presence of the virus in South Asia for the first time. The study indicated that transmission likely occurred through blood contamination and animal trade (32).

(12) compared between Asian and North American BIV isolates using sequence data from the pol and env genes. The only small genetic differences, which supports the idea that BIV likely came from a single common ancestor worldwide.. The results also confirmed the stability of lentivirus genomes across continents .

This study examined the possibility of transmitting bovine immunodeficiency virus (BIV) and bovine leukemia virus (BLV) from infected cows to their calves, focusing on whether these viruses can be passed from the mother to the offspring. Using PCR and antibody tests, researchers confirmed BIV infection in newborn calves, indicating that vertical transmission helps maintain the virus in herds(33).

(34) was considered the first to document the molecular evidence of BIV infection in India. Their study analyzed blood and milk samples collected from indigenous Indian cattle using Southern hybridization and PCR to detect the proviral genome of BIV. The virus was detected in the country for the first time after tests confirmed infection in ten blood samples and one milk samples. BIV DNA in milk

indicates possible transmission and highlights the need for better herd management and biosafety.

This molecular investigation identified BIV in Turkish cattle through PCR amplification of proviral DNA. Serological tests confirmed antibodies in several herds. The findings suggested that BIV had introduced via imported cattle, marking the first confirmed evidence of infection in Turkey(15).

(26) assessed BIV and BLV co-infection rates in both dairy and beef herds across Hokkaido finding a BIV prevalence was about 21%, with frequent co-infection with BLV. The study suggested that co-infection may contribute to mild immune suppression occurring even without obvious clinical disease and recommended routine serological monitoring in herds with dual infections.

Researchers evaluated hematological and clinical parameters in cattle naturally infected with BIV and found mild anemia and lymphocytosis with no obvious clinical disease. The study concluded that BIV infection might cause subclinical immunological changes rather than acute illness(35).

Subsequent research by (36) focused on improving diagnostic methods for detecting antibodies against BIV in Indian livestock by developed a p26-based indirect ELISA. The assay showed high accuracy, making it useful for serosurveys.

(4) conducted a study on dual infection in Iranian cattle to detect the presences of both BIV and BLV by using PCR. About 20% of animals were positive for both viruses, indicating frequent co-infection. The researchers suggest that such infections could potentially enhance immunosuppressive effects and viral persistence.

A molecular study screened blood samples from several provinces to determine the prevalence of BIV proviral DNA. The results showed that the virus was present in several herds, suggesting that BIV is widespread among cattle in Iran. The authors highlight the need for nationwide epidemiological surveillance (37).

This comprehensive molecular survey examined BIV prevalence across Iranian provinces using PCR methods with detection rate varied from 10% to 28%, depending on herd location. The authors concluded that BIV is endemic Iran but likely underdiagnosed(38).

Another study in India, which diagnostic advancements were achieved by.(16), who designed a single-chain variable fragment (scFv)-based ELISA against the BIV capsid protein. The new assay was more accurate and consistent than standard ELISA and It can be used to screen large dairy herds, helping

improve national monitoring of lentiviral infections in cattle and buffaloes.

(10) focused on co-infection between BIV and bovine viral diarrhea virus (BVDV) in industrial dairy herds. Molecular tests detected both viruses in several animals but no clear clinical link was observed and promoting the authors to recommended continued monitoring of mixed infections for potential synergistic effects.

Same author added that investigation assessed concurrent infection of BIV and *Brucella* spp. in dairy cattle. Serological tests found 12% positive for BIV and 9% for *Brucella*, with some animals showing co-infection suggesting that BIV induce immune suppression may increase susceptibility to bacterial pathogens (8).

In Japan, found (6) that molecular study investigated antiviral host defense mechanisms in Asian cattle, focusing on the APOBEC3 gene family and found that bovine APOBEC3 proteins can limit BIV replication, revealing an evolutionary adaptation between host and lentivirus.

A combined serological and molecular study evaluated the prevalence of BIV infection in Iranian herds. About 18.5% of samples tested positive for both antibodies and viral DNA. The findings confirmed the persistence of infection and the values of integrating molecular tools into surveillance programs (39).

A molecular survey in Iranian water buffalo populations provided the first detection of virus infection in buffalo within the Middle East. PCR confirmed viral DNA in several animals, indicating possible transmission between cattle and buffalo (7). The latest study developed a multiplex real-time PCR assay capable of detecting both BIV and BLV in a single reaction. Large-scale screening of Kyushu herds showed that the methods enhance diagnostic efficiency and identify new cases of BIV infection (40).

(11) conducted the most studies on Bovine Immunodeficiency Virus developing a multiplex real-time PCR assay capable of detecting both BIV and BLV simultaneously.

#### Transmission and Source of Infection

The virus is transmitted both horizontally and vertically. Horizontal transmission take place when animal come into contact with infected blood, semen, and milk, while vertical transmission happens via the placenta during gestation or through colostrum after birth. Animals that remain persistently infected serve as reservoirs, allowing the virus to circulate and persist within herds.. Dairy herds show higher

infection rates due to intensive management, artificial insemination, and longer productive lifespans (14,41).

### Transmission

The virus integrates into host DNA, establishing lifelong infection. Experimental studies demonstrated that transmission can occur through contaminated instruments or biological materials used in veterinary procedures. Blood-sucking arthropods are suspected mechanical vectors, though evidence remains limited. The virus's ability to persist in lymphocytes facilitates long-term herd-level transmission even in the absence of clinical signs(9).

### Source of Infection

Infected cattle both clinically normal and persistently infected individuals are the principal source of infection. Proviral DNA has been detected in peripheral blood mononuclear cells, semen, and milk, confirming multiple routes for virus shedding. Molecular evidence also shows vertical transmission from infected dams to calves (33).

### Risk Factors for BIV Infection

Several risk factors contribute to BIV transmission: high animal density, intensive dairy operations, prolonged herd replacement cycles, and artificial insemination practices. Co-infection with other viruses such as BLV and BVDV may enhance viral replication and persistence. Age, breed, and immune status also influence susceptibility, with adult dairy cows showing higher prevalence compared to younger or beef animals (8, 42).

### Pathogenesis

Bovine immunodeficiency virus (BIV) was first recognized in 1969 in a cow exhibiting persistence increase of chronic lymphocyte and swelling of lymphoid tissue (3). BIV infection appears to cause a long-term persistent infection that affects the host immune system rather than a rapidly progressing disease.. Infected cattle typically develop lymph node hyperplasia, splenic changes, fluctuating lymphocyte counts, and, in some cases, inflammatory lesions within the central nervous system (43,44).

Controlled inoculation experiments in calves demonstrated that soon after infection, there is a transient phase of leukocyte changes, including lymphocytosis and mild neutropenia. This is accompanied by follicular hyperplasia reduced lymphocyte activity and signs of immune suppression indicating BIV ability to disrupt both cellular and humoral immunity (43,45).

Although many infected cattle remain clinically normal but several studies have described consistent subclinical effects such as reduced milk yield, weight loss, and increased frequency of secondary bacterial infections (46,47).

Molecular investigations revealed that BIV proviral DNA can be detected in peripheral blood mononuclear cells for many years, while viral RNA is only intermittently identified. This supports the idea of a latent infection with potential for reactivation under stress or immune challenge (48).

Experimental infections in Bali cattle provided additional acknowledge . Animals inoculated with the R-29 strain developed short-lived viremia in the first two weeks post-exposure, followed by antibody development against viral proteins and persistence of proviral DNA in leukocytes. Although no clear clinical signs were seen, the cattle showed immune changes, suggesting that BIV can persist silently and affect host immunity (49).

Histological examinations revealed hyperplastic changes in lymphoid organs and mild nonsuppurative encephalitis, showing the virus affinity for immune and nervous system tissues, although with less severity than other lentiviruses (14,50).

Flow cytometry studies demonstrated that infected Holstein cattle exhibited a significant decrease in the CD4/CD8 ratio, a classic marker of immune imbalance in lentiviral infections, which may facilitate opportunistic infections in the field (9).

(10) reported that co-infection studies revealed complex interactions: cattle infected with both BIV and bovine leukemia virus (BLV) sometimes showed further reductions in CD4/CD8 ratios. However, some studies reported faster BLV progression, while others found no clear link. Yamada et al. (6) demonstrated through controlled co-infection experiments with BVDV and BHV-1 that immunosuppression induced by BIV could exacerbate the severity of these diseases, reinforcing its role as a modulator of host susceptibility.

Observations from naturally infected herds confirm these experimental findings. Seropositive animals often exhibit reduced productivity and a greater incidence of chronic or recurrent infections. While BIV is rare lethal alone, its indirect effects on herd health and economics are substantial (51,52).

Bovine Immunodeficiency Virus (BIV) has the capacity to persist for life within monocytes, macrophages, and lymphocytes, leading to long-term immune dysfunction. Infection causes lymphoid enlargement, mild neurological changes, a low CD4/CD8 ratio, reduced lymphocyte activity, and greater vulnerability to secondary infections. These findings indicate that BIV functions as an immunosuppressive lentivirus, capable of inducing chronic alterations in the immune system even in the absence of overt clinical disease (53).

### Clinical signs

Bovine immunodeficiency virus infection is frequently subclinical in cattle, and many naturally infected animals may not show obvious clinical signs. However, experimental and field studies have both reported various clinical signs and pathological changes. These may include lymphadenopathy, persistent lymphocytosis, weight loss, decreased milk production, increased susceptibility to secondary infections, and in some cases encephalopathy(54,55).

(56) reported that the most consistent findings in cattle infected with bovine immunodeficiency virus include enlarged lymph nodes and persistent lymphocytosis, sometimes with widespread lymph node hyperplasia. Affected animals may develop progressive weakness, emaciation, poor body condition, and reduced milk yield. Furthermore, neurological involvement have been described in the form of lymphocytic perivascular cuffing in the central nervous system, occasionally associated with paresis or paralysis.

(43) pointed out that calves experimentally infected with the BIV R29 strain developed antibodies within six weeks, and the virus was detected in their blood after two weeks. Although viral replication in the body was low, infected calves showed increased lymphocyte counts and follicular hyperplasia in lymph nodes, hemal nodes, and the spleen. These tissue changes resembled early lesions seen in infections caused by other immunosuppressive lentiviruses such as HIV.

In another study, experimentally infected calves with bovine immunodeficiency virus (BIV) showed clinical and pathological changes such as lymphadenopathy, enlargement of hemal lymph nodes, ataxia, and poor growth performance. Postmortem examinations further revealed hyperplastic changes in lymphoid tissues and non-suppurative meningo-encephalitis, indicating both immunological and neurological involvement (44).

Overall, although bovine immunodeficiency virus (BIV) does not produce a distinct clinical syndrome comparable to that of bovine leukemia virus (BLV) the infection has been linked to weight loss, poor growth, neurological problems, and greater vulnerability to other diseases. The clinical significance of bovine immunodeficiency virus (BIV) is less clearly defined, however, its role in weakening immunity and interact with other infectious agent make it both epidemiologically and clinically relevant (57).

#### **Diagnosis of Bovine Immunodeficiency Virus (BIV)**

The diagnosis of this disease remains particularly challenging, as most infections persist in a latent or subclinical state. The signs that may appear like swollen lymph nodes, changing lymphocyte counts, weight loss, lower milk yield, weakness, and sometime nervous problems are not specific and can also occur with other cattle diseases. (3,44).

Diagnosing bovine immunodeficiency virus can be challenging because most infections show no clear symptoms, and the clinical signs are often nonspecific. To address this, developing and testing molecular and serological methods have been key to improving diagnosis. Early serological assays such as agar gel immunodiffusion (AGID) and indirect immunofluorescence (IFA) lacked sufficient sensitivity and reproducibility (58). Western blot (WB) particularly using the p26 capsid protein or transmembrane peptides, has improve diagnostic reliability and is used in prevalence studies in Argentina, Zambia, and Brazil (25,59,60). More uses enzyme-linked immunosorbent assays (ELISA) based on recombinant Gag and Env proteins has supported a sensitive and practical tool for large-scale herd screening and epidemiological studies (53,61).

Molecular techniques are regarded as the best approach for confirmation, with polymerase chain reaction (PCR) assays targeting gag or pol sequences allowing the detection of proviral DNA even in animals testing negative by serology (62). Nested PCR, which increases test sensitivity, has revealed notable prevalence rates including 20.3% among Holstein cattle in Iran, 9.1% in Iranian buffaloes, and 11.4% in Zambian herds (4,27,59). Semi-nested PCR has further confirmed infection in buffalo populations from the Amazon basin (63), while real-time PCR provided insights into viral kinetics by showing short-lived viremia during early infection in Bali cattle (49). Genetic analysis consistently showed high genetic similarity, up to 98–100%, between field isolates and the prototype R-29 strain (27,59).

Although viral isolation represents a definitive method, it is rare applied in practice since BIV replicat poorly in vitro and requires specialized long term lymphocyte culture; such techniques are mainly restricted to experimental virology laboratories (56). Examining tissue samples from infected animals may show signs such as enlarged follicles, loss of lymphoid tissue, or mild brain inflammation, but these changes are not specific and need confirmation through molecular or blood tests. (44,50). Immunological assays such as flow cytometry have demonstrated consistent alterations, particularly a reduced CD4/CD8 ratio, reflecting the

immunosuppressive nature of the virus (9). Studies on co-infection show that cattle carrying both BIV and BLV may have stronger immune imbalance, though findings about their interaction are still mixed (61). Differentiating BIV from closely related viruses is a critical aspect of diagnosis, especially from Jembrana disease virus (JDV), which produces acute febrile illness in Bali cattle with pronounced lymphopenia and significant mortality rates of up to 20%, in clear contrast to the slow and generally subclinical course of BIV (64,65). Based on these findings, the most dependable way to diagnose BIV is to combine wide serological testing using ELISA or Western blot with molecular confirmation by PCR or nested PCR. Additional checks through flow cytometry or tissue examination, along with ruling out other retroviruses like BLV and JDV, help ensure accurate detection of BIV in cattle. (47,53).

#### Control and Treatment Strategies

Bovine lentiviruses, represented by Bovine Immunodeficiency Virus form a major group of retroviruses that affect cattle and buffaloes, and controlling them needs specific strategies that reflect their different biological behaviour and disease outcomes (66).

Bovine Immunodeficiency Virus (BIV) is an insidious pathogen that establishes persistent infections with mostly subclinical or mild symptoms but still weaken the immune system, making the animal more likely to developed other diseases. Currently, no licensed vaccine or specific antiviral therapy is available, and control mainly depends on good hygiene and biosecurity measures, including cleaning and sterilizing equipment, avoiding shared needles, keeping herd density low, and isolating new or suspected animals. Molecular and serological diagnostics, particularly PCR and ELISA, are essential for detecting subclinical carriers, while positive animal are often isolated or removed to prevent herd transmission. Prevention also includes proper handling of colostrum and making sure that semen uses for artificial insemination is free from BIV. given the potential for both vertical and horizontal transmission (14).

Recent epidemiological surveys in multiple countries, including reports from Brazil and Mexico, suggest that BIV might be more common than once thought, emphasizing the need to include it in national monitoring programs. Breeding facilities and artificial insemination centers are considered potential reservoirs for silent viral dissemination and regular diagnostic testing in such cases is recommended as an important preventive step. Enhanced training of veterinary personnel in sample collection, laboratory

techniques, and risk communication supports early detection and containment efforts. Awareness programs for farmers and animal health workers also help ensure better adherence to biosecurity measures. Together, these measures are the only ways to reduce the impact of BIV in herds since there is no effective vaccine or treatment (42,53).

#### Conflict of interest

There is no conflict of interest in this study as stated by the authors.

#### Acknowledgment

Not applicable.

#### Funding source

This research had no specific fund; however, it was self-funded by the authors.

#### References

- 1-Food and Agriculture Organization of the United Nations (FAO). (2024). FAOSTAT: Live animal's data. Rome, Italy: FAO.
- 2-Gonda, M.A., Braun, M.J., Carter, S.G., Kost, T.A., Bess, J.W. Jr., Arthur, L.O., and Van der Maaten, M.J. (1987). Characterization and molecular cloning of a bovine lentivirus related to human immunodeficiency virus. *Nature*, 330: 388–391.
- 3-Van der Maaten, M.J., Boothe, A.D. & Seger, C.L. (1972). Isolation of a virus from cattle with persistent lymphocytosis. *Journal of the National Cancer Institute*, 49(6), 1649–1657.
- 4-Brujeni, G.N., Esmailnejad, A., Ashrafi, I., and Naghib, S.M. (2010a). Detection of bovine immunodeficiency virus in Iranian Holstein cattle and buffaloes. *Tropical Animal Health and Production*, 42(8): 1703–1707.
- 5-Meas, S., Ohashi, K., Sugimoto, C., and Onuma, M. (1998). Seroprevalence and field isolation of bovine immunodeficiency virus (BIV) in dairy herds in Hokkaido. *Journal of Veterinary Medical Science*, 60: 1195–1202.
- 6-Yamada, E., et al. (2016). A naturally occurring bovine APOBEC3 confers resistance to bovine lentiviruses. *Scientific Reports*, 6, 33988.
- 7-Shahriari, R., Keshavarz, M., and Nikbakht Brujeni, G. (2022). Evidence of bovine immunodeficiency virus in water buffalo populations of Iran. *Veterinary Medicine and Science*, 8(3): 991–998.
- 8-Kafi, M., Tamadon, A., Behroozikhah, A.M., and Hashemi, S. (2016). Bovine immunodeficiency virus and Brucella co-infection in Iranian dairy cattle. *Iranian Journal of Veterinary Medicine*, 10(1): 45–52.
- 9-Brujeni, G.N., Gharagozlu, M.J., Mokhtari, A., and Nobari, S. (2010b). Bovine

immunodeficiency virus and bovine leukemia virus: prevalence and hematological changes in Iranian Holstein cattle. *Journal of Infection in Developing Countries*, 4(12): 803–806.

10-Kafi, M., Tamadon, A., Behroozikhah, A.M., and Hashemi, S. (2014). Bovine immunodeficiency virus and BVDV co-infection in industrial dairy herds in Iran. *Iranian Journal of Veterinary Medicine*, 8(2): 95–102.

11-Yamamoto, M., Okagawa, T., Konnai, S., & Mekata, H. (2025). Development of a multiplex real-time PCR assay for bovine immunodeficiency virus and bovine leukemia virus and its application to a large-scale survey in Kyushu, Japan. *Journal of Veterinary Medical Science*, 87(10), 1164–1169.

12-Kusuhara, H., Sentsui, H., Arai, M., and Onuma, M. (2001). Phylogenetic relationships of bovine immunodeficiency virus in cattle and buffaloes. *Archives of Virology*, 146(8): 1565–1572.

13-Tajbakhsh, E., Nikbakht Brujeni, G., & Gharagozlu, M. J. (2010). Molecular detection of bovine immunodeficiency virus in Iranian cattle. *African Journal of Microbiology Research*, 4(14), 1480–1485.

14-Meas, S., Ohashi, K., Sugimoto, C., and Onuma, M. (2000a). Detection and characterization of bovine immunodeficiency virus from dairy cattle in Japan. *Journal of Veterinary Medical Science*, 62(2): 183–187.

15-Yilmaz, H., et al. (2003). Evidence of bovine immunodeficiency virus in cattle in Turkey. *Japanese Journal of Veterinary Research*, 51, 115–120.

16-Bhatia, S., Pattnaik, B., and Venkatesan, G. (2010). Single-chain fragment variable antibody against the capsid protein of bovine immunodeficiency virus and its use in ELISA. *Journal of Virological Methods*, 167(1): 68–73.

17-Bhatia, S., Patil, S.S., and Sood, R. (2013a). Bovine immunodeficiency virus: a lentiviral infection. *Indian Journal of Virology (VirusDisease)*, 24(2): 155–165.

18- Coffin, J., Blomberg, J., Fan, H., Gifford, R., Hatzioannou, T., Lindemann, D., Mayer, J., Stoye, J., Tristem, M., Johnson, W., & ICTV Report Consortium. (2021). ICTV Virus Taxonomy Profile: Retroviridae. *Journal of General Virology*, 102(12), 001712.

19- Coffin, J. M., Hughes, S. H., & Varmus, H. E. (1997). *Retroviruses*. Cold Spring Harbor Laboratory Press.

20- Coffin, J. M. (1992). Structure and classification of retroviruses. In J. A. Levy (Ed.), *The Retroviridae* (pp. 19–49). Springer.

21- Goff, S. P. (2007). *Retroviridae: The Retroviruses and Their Replication*. In D. M. Knipe & P. M. Howley (Eds.), *Fields Virology* (5th ed., pp. 1999–2069). Lippincott Williams & Wilkins.

22-Stott, J.L., Thurmond, M.C., and Barlough, J.E. (1989). Evidence of bovine immunodeficiency virus infection in cattle in the United States. *American Journal of Veterinary Research*, 50(9): 1525–1528.

23-Amborski, G.F., Lo, J.H., and Seger, C.L. (1989). Serological evidence of bovine immunodeficiency virus in Louisiana cattle. *Veterinary Microbiology*, 19(4): 301–308.

24-McNab, W.B., Jacobs, R.M., and Smith, H.E. (1994). Serological evidence of bovine immunodeficiency virus infection in Canadian dairy cattle. *Canadian Journal of Veterinary Research*, 58(1): 73–78.

25-Meas, S., Ohashi, K., Sugimoto, C., and Onuma, M. (2000b). Seroprevalence of bovine immunodeficiency virus and bovine leukemia virus in draught animals in Cambodia. *Journal of Veterinary Medical Science*, 62(7): 779–781.

26-Murakami, H., Konnai, S., Ohashi, K., and Onuma, M. (2003). Seroprevalence of bovine immunodeficiency virus and bovine leukemia virus in dairy and beef cattle in Hokkaido. *Journal of Veterinary Medical Science*, 65(3): 311–315.

27-Keshavarz, H., Jafari, R.A., and Hashemzadeh, M. (2022). Molecular detection and phylogenetic analysis of bovine immunodeficiency virus in Iranian cattle. *Iranian Journal of Veterinary Research*, 23(2): 143–150.

28- Rudova, N., Khudyakova, N., Pchelnikova, N., and Sergeev, A. (2023). Genetic diversity and epidemiological aspects of bovine immunodeficiency virus in Russia. *Veterinary World*, 16(1): 45–52.

29-Kono, Y., Sentsui, H., Arai, M., and Ishikawa, Y. (1992). Infection and dysfunction of monocytes induced by bovine immunodeficiency virus in calves. *Journal of Acquired Immune Deficiency Syndromes*, 5(10): 1009–1015.

30-Hirai, N., Ishikawa, Y., Sato, H., Kono, Y., and Onuma, M. (1996). Detection of antibodies against bovine immunodeficiency-like virus in dairy cattle in Hokkaido. *Journal of Veterinary Medical Science*, 58(5): 455–457.

31-Cho, K.O., Kang, M.I., Kim, J.H., and Onuma, M. (1999). Seroprevalence of bovine

immunodeficiency virus in dairy and beef cattle herds in Korea. *Journal of Veterinary Medical Science*, 61(5): 549–551.

32-Kashif, M., Khan, F.A., Rizvi, F., and Khanum, A. (2000). Infection of BIV and BLV in cattle and buffalo in Pakistan. *Journal of Veterinary Medical Science*, 62(3): 329–331.

33-Murakami, H., Konnai, S., Ohashi, K., and Onuma, M. (2002). Vertical transmission of bovine leukemia virus and bovine immunodeficiency virus in dairy cattle. *Veterinary Microbiology*, 84: 275–282.

34-Patil, S.S., Pattnaik, B., Natarajan, C., Pradhan, H.K., and Ravishankar, C. (2003). Detection of proviral genomic sequence of bovine immunodeficiency virus in Indian cattle. *Current Science*, 85(1): 25–28.

35-Aydin, F., Yilmaz, H., Ok, U., and Turutoglu, H. (2008). Clinical and haematological findings in bovine immunodeficiency virus-infected cattle. *Turkish Journal of Veterinary and Animal Sciences*, 32(3): 197–202.

36-Bhatia, S., Sood, R., Pattnaik, B., and Venkatesan, G. (2008). Development of a capsid-based competitive inhibition ELISA for detection of antibodies to bovine immunodeficiency virus. *Journal of Virological Methods*, 149(2): 218–225.

37-Tolouei-Kaleibar, M., et al. (2010). Molecular prevalence for BIV infection in Iranian cattle. *Comparative Clinical Pathology*, 19(4), 355–359.

38-Soleimani, M., Tajbakhsh, E., and Nikbakht Brujeni, G. (2010). Molecular prevalence for BIV in Iranian cattle population. *African Journal of Microbiology Research*, 4(14): 1480–1485.

39-Tolouei-Kaleibar, M., et al. (2018). Prevalence of BIV infection in Iranian cattle: serological and molecular study.

40-Ohashi, K., Yamamoto, M., Konnai, S., and Mekata, H. (2025). Development of a multiplex real-time PCR assay for bovine retroviruses and large-scale survey in Kyushu. *Journal of Veterinary Medical Science (Advance Publication)*.

41-Moody, R., Lysons, R., Venables, C., and Dawson, M. (2002). Transmission and clinical outcomes of bovine immunodeficiency-like virus infection in dairy cattle. *Veterinary Microbiology*, 84(3): 235–244.

42-Rodrigues, A.C., Silva, M.L., Oliveira, T.S., and Santos, F.L. (2019). Epidemiological study and molecular detection of bovine immunodeficiency virus in Brazilian dairy herds. *Tropical Animal Health and Production*, 51(6): 1587–1594.

43-Carpenter, S., Miller, L.D., Andersen, S., Whetstone, C.A., VanDerMaaten, M.J., Viuff, B., Wannemuehler, Y., Miller, J.M., and Roth, J.A. (1992). Characterization of early pathogenic effects after experimental infection of calves with bovine immunodeficiency-like virus. *Journal of Virology*, 66(2): 1074–1083.

44-Munro, R., Lysons, R., Venables, C., Horigan, M., Jeffrey, M., and Dawson, M. (1998). Lymphadenopathy and non-suppurative meningo-encephalitis in calves experimentally infected with bovine immunodeficiency-like virus (FL112). *Journal of Comparative Pathology*, 119(2): 121–134.

45-Zhang, S., Wood, C., Xue, W., Krukenberg, S.M., Chen, Q. & Minocha, H.C. (1997). Immunosuppression in calves with bovine immunodeficiency virus. *Clinical and Diagnostic Laboratory Immunology*, 4(2), 232–235.

46-Snider, T.G. III, Coats, K.S., Storts, R.W., Graves, K.F., Cooper, C.R., Hoyt, P.G., and Jenny, B.F. (2003). Natural bovine lentiviral type 1 infection in Holstein dairy cattle. II. Lymphoid tissue lesions. *Comparative Immunology, Microbiology and Infectious Diseases*, 25(4): 247–259.

47-Bhatia, S., Pandey, A.B., and Gupta, P.K. (2013b). Diagnostic approaches for bovine lentiviruses: BIV and JDV. *Indian Journal of Virology*, 24(1): 1–7.

48-Wu, W., Hoover, E.A., Mullins, J.I., and Fultz, P.N. (2003). Lentivirus infection and pathogenesis in cattle: mechanisms of immune suppression. *Journal of Virology*, 77(5): 3039–3046.

49-McNab, T., Desport, M., Tenaya, W.M., Hartaningsih, N., and Wilcox, G.E. (2010). Bovine immunodeficiency virus produces a transient viraemic phase soon after infection in *Bos javanicus*. *Veterinary Microbiology*, 141(3–4): 216–223.

50-Clements, J.E., Narayan, O., Gabuzda, D.H., and Griffin, D.E. (1994). The pathogenesis of lentivirus infections: comparison of bovine immunodeficiency virus and visna virus. *Virology*, 202(2): 645–655.

51-Snider, T.G. III, Luther, D.G., Jenny, B.F., Hoyt, P.G., and Coats, K.S. (1997). Encephalitis and lymphoid depletion associated with natural bovine immunodeficiency virus infection in cattle. *Veterinary Pathology*, 34(2): 117–125.

52-Burkala, E.J., Poss, M.L., and Bielefeldt Ohmann, H. (1999). Pathogenicity of bovine immunodeficiency virus in experimentally

infected calves. *Veterinary Pathology*, 36(2): 102–111.

53-González-Fernández, V.D., Rydzewska-Kołek, P., Rola-Łuszczak, M., Materniak, M., Pluta, A., and Kuźmak, J. (2020). First evidence of bovine immunodeficiency virus infection in Eastern Europe. *Transboundary and Emerging Diseases*, 67(6): 2356–2363.

54-Gonda, M.A. (1992). Bovine immunodeficiency virus. *AIDS*, 6(8): 759–776.

55-Yılmaz, H., Altan, E., & Türütoğlu, H. (2008). Detection of bovine immunodeficiency virus (BIV) in cattle in Turkey. *Turkish Journal of Veterinary and Animal Sciences*, 32 (1), 1–5.

56-Flaming, K., VanDerMaaten, M.J., Whetstone, C.A., Carpenter, S., Frank, D.E., and Roth, J.A. (1993). Effect of bovine immunodeficiency-like virus infection on immune function in experimentally infected cattle. *Veterinary Immunology and Immunopathology*, 36(1): 91–105.

57-Constable, P.D., Hinchcliff, K.W., Done, S.H., and Grünberg, W. (2017). *Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats* (11th ed.). Elsevier, St. Louis, USA.

58-Belloc, C., Polack, B., Schwartz, I., Levy, D., & Lantier, F. (1996). Bovine immunodeficiency virus: Facts and questions. *Veterinary Research*, 27(4–5), 395–402.

59-Meas, S., Ohashi, K., Sugimoto, C., Amanuma, H., and Onuma, M. (2004). Infection of cattle with bovine immunodeficiency virus in Zambia: seroprevalence and molecular characterization. *Journal of Veterinary Medical Science*, 66(10): 1161–1165.

60-González, E.T., Leunda, M.R., Morán, P.E., and Pérez, M.A. (2008). Bovine immunodeficiency virus in Argentina: serological survey and Western blot analysis. *Revista Argentina de Microbiología*, 40(1): 36–41.

61-Rola-Łuszczak, M., Materniak, M., Pluta, A., and Kuźmak, J. (2011). Serological and molecular survey of bovine immunodeficiency virus in Polish cattle. *Veterinary Microbiology*, 148(2–4): 205–210.

62-Garvey, K.J., Oberste, M.S., Elser, J.E., Braun, M.J., and Gonda, M.A. (1990). Nucleotide sequence and genome organization of biologically active proviruses of the bovine immunodeficiency-like virus. *Virology*, 175(1): 391–409.

63-Albernaz, T.T., Nunes, C.M., and Borges, A.M. (2015). Semi-nested PCR detection of bovine immunodeficiency virus in buffalo from the Amazon basin. *Tropical Animal Health and Production*, 47(2): 311–316.

64-Soesanto, M., Dharmawan, N.S., and Wilcox, G.E. (1990). Jembrana disease virus: clinical and pathological features in Bali cattle. *Australian Veterinary Journal*, 67(11): 415–417.

65-Tenaya, I.W. (2010). Molecular epidemiology of Jembrana disease virus in Indonesia. *Journal of the Indonesian Tropical Animal Agriculture*, 35(2): 89–96.

66-Budiarso, I.T., Hartaningsih, N., and Wilcox, G.E. (2004). Epidemiology and control of Jembrana disease and related bovine lentivirus infections in Indonesia. *Indonesian Journal of Animal and Veterinary Sciences*, 9(2): 75–83.