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Battling bovine leukaemia virus: unravelling the zoonotic transmission - a one health perspective

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Abstract

Zoonotic diseases, which can be passed between humans and animals, represent serious public health challenges, often arising at the intersection of these populations. BLV, known for causing enzootic bovine leukosis has been observed in humans and in products derived from cattle. Although BLV is considered a possible risk factor for breast cancer in humans, the exact transmission route remains unclear. This article explores the genetic dynamics of BLV among humans, animals, and food items, highlighting its zoonotic potential and promoting implementing One Health strategies for efficient prevention and management.

Keywords: *blv; zoonotic diseases; enzootic bovine leukosis; cattle; one health approinfection.st cancer; climate change; genetic dynamics; blv in humans; blv genome; diagnosing blv infection*

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Evidence in Context

- Explores BLV as a potential breast cancer risk in humans, found in both humans and cattle products.
- Conducts molecular epidemiology to show genetic exchange between cattle, humans, and food.
- Reveals shared genetic sequences across species, indicating zoonotic transmission pathways.
- Discusses BLV's global prevalence and its economic impact on cattle productivity.
- Advocates for vaccine development and a One Health approach to control and prevent BLV.

To view Article

Introduction

Pathogens transmitted between animals and humans, leading to zoonotic diseases, have notable public health implications. These diseases frequently occur at the interface of human and animal populations, making it challenging to understand their transmission routes and prevent outbreaks. Addressing these complex zoonotic challenges requires the One Health approach, which combines human, animal, and environmental health efforts [1]. The Bovine Leukaemia Virus (BLV), a delta retrovirus, is accountable for the occurrence of enzootic bovine leukosis among cattle, and has been detected in both humans and food products originating from cattle [2]. Although it has been characterized as a possible contributing factor for the onset of breast cancer in human individuals, the mechanism of transmission remains uncertain [3]. The article examines the flow of BLV between animals, humans, and food products, illuminating its zoonotic potential and advocating for One Health policies in prevention and control efforts.

Bovine Leukaemia Virus (BLV) - A Zoonotic Concern

Enzootic bovine leukosis, a chronic lymphoproliferative disease affecting cattle herds, is caused by this virus. While the majority of infected cattle are asymptomatic carriers,

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Some eventually develop leukaemia and/or lymphoma due to persistent infection [2]. BLV is prevalent worldwide, with rates differing by region, and has a notable impact on North and Latin American countries. BLV has the ability to infect a variety of species, including cattle, buffaloes, sheep, goats, and alpacas, which is a noteworthy observation. The expansive range of hosts gives rise to apprehensions regarding the spread of BLV in populations where different species coexist, potentially aiding in the transfer of the virus between species [4,5]. The hypothesis of BLV crossing species barriers in natural environments is supported by its ability to infect multiple mammalian species, possibly due to shared receptors between species. This highlights the complexity of BLV transmission and the need for comprehensive One Health strategies in livestock production.

BLV in Humans: A Potential Zoonotic Link

Bovine leukemia virus (BLV) has been identified in the human population, as various studies have detected BLV gene segments, proteins, and antibodies across different regions of the globe [3,6]. Despite these findings, the mechanisms of BLV transmission in humans and its role in oncogenesis remain incompletely understood.

The transmission routes of Bovine Leukemia Virus (BLV) in cattle are comprehensively clarified, encompassing direct exposure to bodily secretions, iatrogenic interventions (e.g., vaccination, dehorning, insemination), and vertical transmission via lactation. However, the pathways of transmission from cattle to humans are less clear but are thought to involve consuming BLV-infected animal food products [7]. Figure 2 depicts the multiple transmission pathways of Bovine Leukemia Virus (BLV) from cattle to humans.

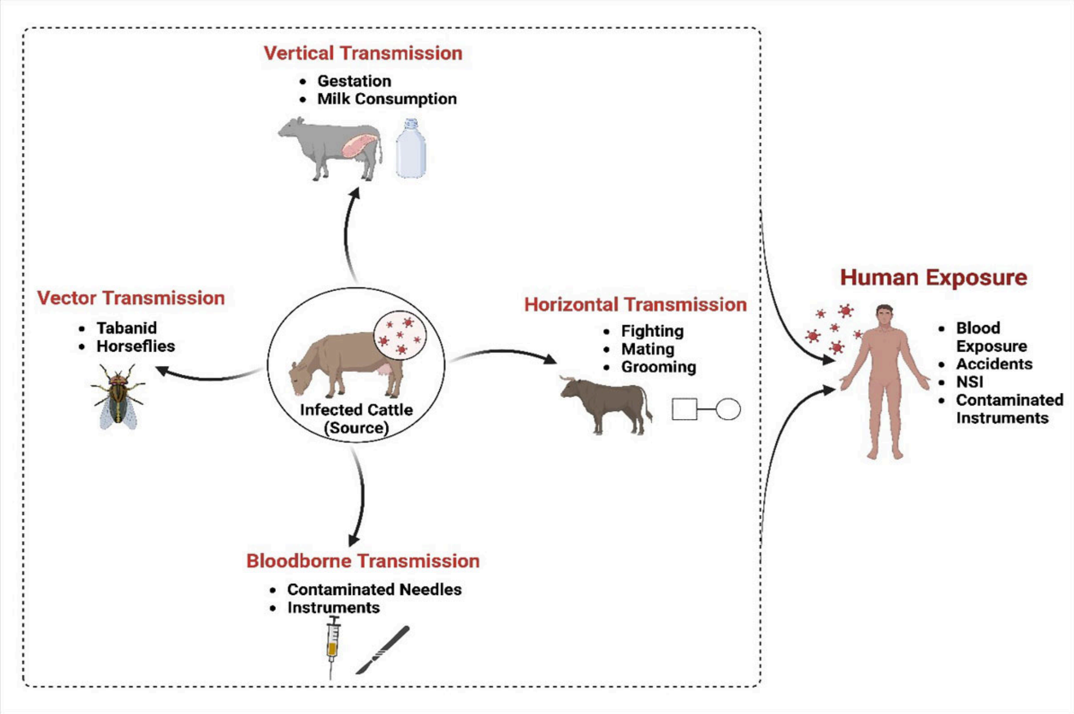

Figure 2 illustrates the various pathways of BLV transmission from cattle to humans.

Molecular Epidemiology Reveals Insights

This study conducted a comprehensive molecular epidemiology analysis to explore BLV transmission profiles when present in different sources, including cattle, humans, and food products. The sequences derived from these origins in Colombia were compared with the reference sequences identified in GenBank. Genetic flux patterns were identified through phylogenetic reconstruction and haplotype distribution analyses, and recombination events between viral isolates were examined. Results showed that the phylogenetic analysis did not identify specific branches for Colombian sequences or different sources. Thirty-one haplotypes were found, with several shared among all three sources, suggesting potential genetic flux between cattle, humans, and food products. Reticulation events, indicating genetic exchange, were detected among these sources during recombination analysis [8].

Understanding BLV: The Genome

BLV is a single-strand, diploid RNA virus consisting of a single strand, with a genome spanning 8714 nucleotides, and is structured with long terminal repeats (LTRs). The LTR regions located at the 5' and 3' ends play a crucial role by housing the regulatory sequences required for the activation of Tax protein. Encoded by the gag gene, the precursor Pr44 is responsible for generating non-glycosylated proteins upon cleavage. Within the pol gene lie the enzymes responsible for facilitating reverse transcription and integration of BLV proviral deoxyribonucleic acid (DNA), ultimately resulting in a persistent infection. Moreover, the env gene is responsible for the synthesis of glycoproteins that are vital for mediating viral entry into host cells and subsequent fusion with them.

Within the BLV genome's pX region are accessory and regulatory genes, including the oncogenic Tax protein, which trans-activates BLV provirus transcription. Other genes like rex, R3, and G4 contribute to viral regulation and tumorigenesis. BLV also produces RNA polymerase III-transcribed microRNAs (miRNAs) from both LTR regions and antisense transcripts from the 3'-LTR, playing key roles in its regulation and tumorigenic potential [9].

BLV Prevalence: A Global Perspective

BLV's origins trace back to Lithuania in 1871, and today, it is distributed globally with varying prevalence rates [10]. In the United States, BLV infects around 40-50% of the cattle population, causing annual economic losses of over USD 525 million from milk production alone. Japan, Canada, and Argentina also report high prevalence rates. contrast, several European countries, Australia, and some Middle Eastern nations have initiated successful BLV control programs, eradicating or significantly reducing the virus.

Egypt, like many countries, has reported BLV seropositivity in cattle. Egypt's dairy cattle have a prevalence rate of approximately 15.83%, while cattle, buffaloes, and camels show varying rates. BLV's prevalence is a global concern due to its potential implications for public health [2,6]. Figure 1 illustrates the global distribution of cases (top panel) and deaths (bottom panel) due to Enzootic Bovine Leukosis caused by Bovine Leukaemia Virus, as reported by the World Organisation for Animal Health (OIE-WAHIS) from 2005 to 2023 (up to November 21st).

Diagnosing BLV Infection

To manage BLV spread and mitigate economic losses, detecting the infection is vital. Serological testing techniques like agar gel immunodiffusion (AGID), radioimmunoprecipitation assay (RIA), and ELISA are widely used for their specificity and sensitivity in detecting antibodies produced due to BLV infection. Proviral DNA detection techniques, RT-PCR tests, offer a direct method to identify BLV proviral DNA in blood samples, known for their high specificity and sensitivity [2,11].

Challenges and Prospects for BLV Control

Efforts to control BLV have encountered significant challenges, primarily due to the absence of an effective vaccine. The most potent control strategy currently relies on testing and culling infected animals. However, this approach is impractical in areas with high BLV prevalence. To effectively combat BLV, several strategies and prospects should be considered:

Vaccine Development: Research into an effective BLV vaccine must continue, with the goal of stimulating a robust and lasting immune response in cattle.

Genomic Surveillance: Monitoring the genetic diversity of BLV genotypes is crucial. Different genotypes may have unique interactions with host organisms and varying leukaemogenic potential. Genomic surveillance helps identify new virus mutations.

Public Health Awareness: Understanding the potential risks of BLV transmission to humans through food products is vital. Public health policies should aim to reduce viral prevalence in cattle populations and ensure the safety of food products.

Improved Diagnostic Tools: Developing more efficient and cost-effective diagnostic tools can aid in early detection and containment of BLV.

International Collaboration: Collaborative efforts between countries can facilitate the exchange of knowledge and best practices in BLV control [11,12].

These findings offer new insights into BLV's zoonotic potential, indicating genetic exchange between cattle and humans. This genetic flux raises concerns about BLV transmission from animals to humans, especially through contaminated food products. Therefore, prevention and control strategies should be devised and enacted as part of One Health program policies [13].

Conclusion

BVL presents a complex zoonotic challenge, with evidence of genetic flux between cattle, humans, and food products. The molecular epidemiology analysis highlights the need for a One Health approach to understand and address the transmission pathways of BLV. This collaborative approach is vital for preventing zoonotic infections, safeguarding public health, and promoting the well-being of both animals and humans. As we gain a deeper understanding of BLV's transmission patterns, the implementation of effective prevention and control measures becomes increasingly critical in a One Health framework.

Table 1 shows the number of confirmed cases and deaths due to Enzootic Bovine Leukosis caused by Bovine Leukaemia Virus (BLV) as reported by the World Organisation for Animal Health (OIE-WAHIS).

Continent	Species	Cases	Deaths
Africa	Cattle	8942	25
Asia	Cattle	53642	45
Europe	Cattle	1116852	1400
Oceania	Cattle	26	0
South America	Cattle	24315	303
North America	Cattle	63545	101

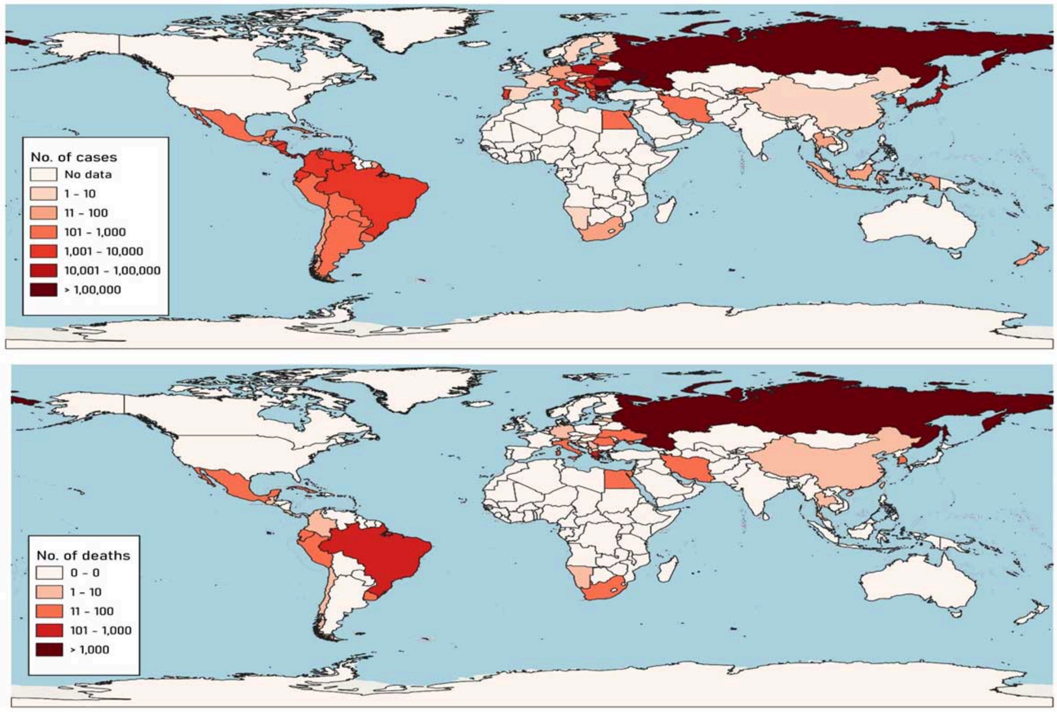

Figure 1 depicts the global distribution of cases (Top) and deaths (Bottom) due to Enzootic Bovine Leukosis caused by Bovine Leukaemia Virus as reported by World Organisation for Animal Health (OIE-WAHIS) from 2005-2023 (till 21st November).

Supporting information

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Ethical Considerations

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