



# Bovine Leukemia Perspectives and its Impact on Dairy



**Cristina Úsuga Monroy\***, José Julián Echeverri Zuluaga and Albeiro López Herrera

*Department of Animal Production, Faculty of Agricultural Sciences, National University of Colombia at Medellín, Colombia*

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**\*Corresponding author:** Cristina Úsuga Monroy, Department of Animal Production, Faculty of Agricultural Sciences, National University of Colombia at Medellín, Colombia, Tel: (57) 3137062484; Fax (57-4) 4309025; Email: cusugam@unal.edu.co

## Abstract

Livestock production is affected by several diseases caused by microorganisms such as viruses, bacteria or protozoa that reduce the efficiency and profitability of livestock enterprises by causing economic losses. The enzootic bovine leukemia (EBL) is a disease that affects cattle and especially those dedicated to milk production, is caused by the bovine leukemia virus (BLV). The EBL is one of the diseases of mandatory declaration for terrestrial animals according to the World Organization for Animal Health. The importance of this disease in the productive systems is due to the fact that currently there is no vaccine or treatment and therefore the eradication and control of this virus is based on early diagnosis. The use of different molecular or serological methodologies, not only allow to identify the prevalence in a herd, but also to understand more about the biology of the virus and to design strategies that allow to control the dispersion of the same through management practices that will be reflected in the increase of productive or reproductive parameters of the herd.

**Keywords:** Bovine leukemia; Diagnosis; Milk production; Immune system; Terrestrial animals; Animal Health; Lymphocytes; Etiology; Enzootic; Dairy farms; Cattle; Streptococcus; Pathogens; Livestock; Dairy Herds

**Abbreviations:** EBL: Enzootic Bovine Leukemia; BLV: Bovine Leukosis Virus; BIV: Bovine Immunodeficiency Virus; OIE: Organization of Animal Health; BoLA: Bovine Leukocyte Antigen;

## Introduction

Enzootic bovine leukemia (EBL) is a disease of viral origin caused by infection with bovine leukosis virus (BLV), characterized by affecting the immune system of cattle, specifically B lymphocytes. Bovines are usually clinically healthy and it is so much more difficult to control the disease. The EBL was reported for the first time in 1871 in Germany by Leisering, who described yellowish nodules in the spleen of the cattle which he called leukemia [1]. In-apparent infection is often accompanied (30-70%) by an increase in white blood cell count called persistent lymphocytosis. On the other hand, between 0.1 and 10% of cattle with more than 3 years of infection can present the tumor form of the disease or lymphosarcoma [2], this is characterized by the lack of control over the cell cycle of the lymphoid line (lymphocytes B). It has been shown that the herds infected with BLV had a lower milk production between 2.5 to 7% compared to the average production of the herd [3,4] and an increase in the rate of selective losses, as well as greater susceptibility to other diseases of infectious etiology such as mastitis [5], diarrhea and pneumonia [3].

## Distribution

The BLV is widely distributed in the world, probably migrated from Europe to America through infected cattle. Some

countries in Europe are free while others are in the process of eradication [6]. In countries like the United States of America where milk production plays an important role in the economy, a seroprevalence of 83.9% can be found (452 of 534 dairy farms sampled) according to the report presented by the Department of Agriculture (USDA) and the National Animal Health Monitoring System (NAHMS) in 2007 [7]. It is considered that in America the disease is enzootic; the molecular prevalence for BLV in Colombia is 44% of infection in Holstein cows [8], while other countries in South America have lower molecular prevalence such as Chile 27.9%, Bolivia 30.7% or Peru 42.3%. Countries such as Paraguay and Argentina have higher prevalence than those found in Colombia (54.7% and 77.4% respectively) [9].

## Transmission

The EBL is transmitted through two routes, horizontally through direct contact between an infected animal and an uninfected animal, the reuse of needles for vaccination processes, gloves during palpation [10] or dehorning [11] they help the spread of the virus. The virus can also be transmitted vertically from mother to calf within the uterus, which can be up to 26%. Colostrum is another vehicle for the BLV [12], in which the cells may be infected especially if the mothers are co-infected with the bovine immunodeficiency virus (BIV) [13].

## Diagnosis

Because there is no vaccine or treatment for bovine leukemia, the eradication and control of this disease is based on early diagnosis, separation and differential management of infected animals. Because of this, the specificity and sensitivity of the diagnostic test used is a critical point [14]. The samples of blood, milk, colostrum and semen have been used for the identification of BLV through serological and molecular techniques. Serological tests (AGID and ELISA) are the tests currently recommended by the Organization of Animal Health (OIE) for the diagnosis of infection. However, the methodologies that directly detect the virus are very important, such as PCR. It has been reported that PCR is a highly sensitive methodology for the direct diagnosis of BLV [15-17].

## Productive Impact

EBL generates costs for secondary treatments, repetition of vaccine doses [18] and indirect losses due to reproductive failures associated with secondary infections such as metritis [3] and reproductive parameters are affected so that infected cows have a greater interval between births and services by conception. Milk production can be reduced up to 7.67% with respect to the herd [19] and the compositional quality of milk is also affected as infected cows produce less amount of protein [20]. On the other hand, the somatic cell score is higher in infected cows because the BLV infection increases the susceptibility to other pathogens such as bacteria of the genus *Streptococcus*, which have been found more frequently (35.9%) in cows positive to BLV with respect to cows free of infection [21].

## Discussion

### Molecular and Serological Prevalence of BLV in Antioquia, Colombia

The evaluation of 1000 Holstein cattle of specialized dairy herds in the department of Antioquia has allowed to establish a molecular prevalence of 47.6%; while the serological prevalence was 54.6% [22]. The prevalence of EBL in the Antioquia region has been increasing during the last years, since for 1984 the Andean region presented seroprevalences of 29.9% [23] and today it is more than 50%. The place of origin of the animals is herds ( $X^2=777.6420$   $P<0.0001$ ), municipalities ( $X^2=500.5000$   $P<0.0001$ ) or subregion ( $X^2=29.2811$   $P<0.0001$ ) are related to the presence or absence of the disease [22]. The management practices within the herd, the production system, and the different iatrogenic practices such: dehorning, milking, vaccination [24], they can disperse viral particles in the herd and to promote the spread of the disease.

### Presence of Bovine Leukemia Virus in Milk Samples

Milk samples are an important alternative for the diagnosis of EBL in dairy herds, as it can be taken quickly and without causing any stress in animals. The evaluation through the ELISA assay in milk allowed to establish a seroprevalence of 79.69% in Holstein cattle from specialized dairy herds in the department of

Antioquia [22], this seroprevalence is as high as others found in Argentine herds of 82.5% [25]. It has been reported that the milk of infected cows has exosomes that contain BLV proteins that although "are not infectious", are transmitted by an alternative route different from the viral infection and have an important role in the elimination of BLV proteins by the cells infected [26]. In addition, colostrum and colostrum replacers [27] are another vehicle for infection with BLV [12]. It has been found that colostrum can have cells infected with BLV; especially if the mothers are co-infected with the bovine immunodeficiency virus (BIV) [13].

## Bovine Leukemia and Immune System

Bovine leukocyte antigen (BoLA) is membrane protein responsible for presenting antigenic peptides to lymphocytes and can alert on the presence of pathogens. The gene for this protein is highly polymorphic and has been associated with different diseases, because in some cases it could give resistance or susceptibility to the animal. 37 alleles for BoLA DRB 3.2 were identified in a population of 500 dairy Holstein cows specialized in the department of Antioquia (18). The most frequent alleles were BoLA DRB 3.2\*16 (12.8%), allele BoLA DRB 3.2\*8 (16.3%) and allele BoLA DRB 3.2\*22 (16.8%). Two alleles associated with resistance against EBL were found: allele BoLA DRB 3.2\*8 (OR=1.489,  $P<0.05$ ) and allele BoLA DRB 3.2\*12 (OR=3.897,  $P<0.10$ ), while allele BoLA DRB 3.2\*16 (OR=0.710,  $P<0.10$ ) was associated with susceptibility [28]. This information is of great importance for the producers since it is a beginning to develop selection plans, in which the animals are selected with the alleles of resistance or neutrality, thus avoiding the animals susceptible to this disease.

## Bovine Leucosis and Milk Production

From a population of 500 dairy Holstein cows specialized in the department of Antioquia, the presence of BLV was related to productive and reproductive parameters. The BLV was significantly associated with the characteristics: milk production and kilograms of fat ( $P<0.05$ ). No association was found between the BLV and the characteristics of kilograms of protein or somatic cell score ( $P>0.05$ ). It was found that infected animals produce 7.67% less milk but produce more fat (23.67Kg/lactation) than healthy animals [19]. The compositional quality of the milk and the hygienic quality (measured as somatic cell score) are two very important factors for the payment of the milk and therefore the economic losses caused by this virus are significant in the dairy systems. For example, costs for secondary treatment of subclinical infections are \$6406 USD and annual costs for control and management of bovine leukemia are \$1765 USD [29].

## Control Measures

There is no vaccine for this virus, the treatment for this disease is done through good practices with the use of needles, gloves or during milking; the discarding of infected animals also contributes to controlling the disease, in addition to continuing the research that generates more information about this patho-

gen. From dairy herds can reduce the number of positive cases to BLV that occur. The positive effect has been observed when implementing rigorous management procedures, such as: using milk from negative cows or colostrum replacers to feed the calves, using milk from infected cows only after freezing or heating, using chemical dehorning or cauterization, using disposable needles for each animal and if they are not disposable, sterilize them among animals, clean and disinfect each implement used during tattoos, use separate gloves for rectal examination, wash and disinfect all equipment used in assisting the calves, use separate paddocks for infected cows of non-infected, implement a program against flies. "These practices reduce the spread of the disease as much as possible" [30].

### Conclusion

Bovine leukemia is an important disease in the productive systems, as it silently affects the dairy herds, which leads to productive, reproductive and economic losses that involve not only small livestock, but also consumer health and food security of a region. It is important to continue the studies on the BLV and its effect on milk production systems, which will allow to expand the current panorama of this pathogen.

### Conflict of Interest

This manuscript was prepared and reviewed with the participation of all the authors, who declare that they have no conflict of interest that compromise the validity of the results.

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