

ASSOCIATION BETWEEN FELINE LEUKEMIA VIRUS (FELV) AND THE DEVELOPMENT OF NEOPLASMS: SYSTEMATIC REVIEW

**ASSOCIAÇÃO ENTRE O VÍRUS DA LEUCEMIA FELINA (FELV) E O
DESENVOLVIMENTO DE NEOPLASIAS: REVISÃO SISTEMÁTICA**

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ABSTRACT

Feline Leukemia Virus (FeLV), a member of the gammaretrovirus group, is an important pathogen in domestic cats, recognized for its tumorigenic potential and its association with the development of neoplasms. This study systematically investigated the relationship between FeLV infections and the occurrence of tumors in felines, with emphasis on etiology and observed clinical signs. A comprehensive literature review was conducted using the PubMed, SciELO, Wiley, SpringerLink, and Google Scholar databases, employing the descriptors "FeLV AND Neoplasia AND Case Report." A total of 35 neoplastic cases associated with the virus were evaluated. The collected data were analyzed using statistical methods, particularly Pearson's chi-square test and the Kruskal-Wallis test, to identify possible associations among tumor morphology, sex, and age group. The results demonstrated that lymphoma was the most common neoplasm (71.43%), including mediastinal, periocular, multicentric, alimentary, and encephalic forms. Other neoplastic processes included carcinomas (11.43%), osteochondromas (5.71%), and melanocytomas (2.9%). No statistically significant association was found between tumor occurrence and sex ($p = 0.237$), and age was not associated with tumor type ($p = 0.31$). Geographically, Brazil accounted for the highest number of reported cases (57.14%), possibly reflecting lower vaccination rates against FeLV in the country. Statistical analysis confirmed a strong association between FeLV infection and lymphoma development ($p < 0.001$), supporting the role of the virus in carcinogenesis through insertional mutagenesis, particularly involving proto-oncogenes such as c-myc. Therefore, FeLV is considered a causal factor in the development of feline lymphomas, with mechanisms of tumor induction that are well documented in the scientific literature. The absence of significant influences of sex or lifespan suggests a

generalized susceptibility among cats infected with the retrovirus. These findings reinforce the importance of FeLV vaccination and early diagnosis as essential strategies for reducing oncological risks, providing valuable information for clinicians responsible for the management of FeLV-positive feline populations.

Keywords: Felines; Gammaretrovirus; Oncology.

RESUMO

O agente da leucemia felina (FeLV), pertencente aos gammaretrovirus, constitui um importante microrganismo em felinos domésticos, destacado por sua capacidade tumoral e vínculo com a gênese de neoplasias. Esta investigação examinou sistematicamente o vínculo entre infecções por FeLV e o aparecimento de tumores em felinos, priorizando a causa e os sinais clínicos observados. Procedeu-se levantamento bibliográfico minucioso nas plataformas PubMed, SciELO, Wiley, *Springerlink* e Google Acadêmico, utilizando os descritores "*FeLV AND Neoplasia AND Case Report*". Avaliaram-se 35 ocorrências neoplásicas relacionadas ao vírus, cujos indicadores foram coletados e tratados por provas estatísticas, notadamente qui-quadrado de Pearson e Kruskal-Wallis, buscando conexões entre morfologia tumoral, gênero e faixa etária. Os dados demonstraram que o linfoma representou a neoplasia mais comum (71,43%), com as variantes mediastinal, periocular, multicêntrica, digestiva e encefálica devidamente registradas. Diferentes processos oncológicos abrangeram carcinomas (11,43%), osteocondromas (5,71%) e também melanocitomas (2,9%). Não se detectou inclinação estatística relevante quanto ao gênero ($p = 0,237$), e a maturidade não apresentou nexos com a natureza do tumor ($p = 0,31$). Geograficamente, o território brasileiro apresentou a maior casuística (57,14%), possivelmente relacionada a índices vacinais

reduzidos no país. O processamento estatístico ratificou a sólida conexão entre FeLV e linfomas ($p < 0,001$), corroborando a ação viral na carcinogênese via mutagênese de inserção, atingindo especialmente proto-oncogenes como o c-myc. Assim, o FeLV configura-se como elemento causal para o desenvolvimento de linfomas felinos, possuindo vias de indução tumoral amplamente descritas na literatura. A inexistência de influência por gênero ou tempo de vida indica uma vulnerabilidade generalizada em animais portadores do retrovírus. Tais evidências reforçam a relevância da imunização anti-FeLV e da detecção antecipada para reduzir perigos oncológicos, oferecendo subsídios fundamentais aos clínicos que assistem colônias de gatos reagentes ao vírus.

Palavras-chave: Felinos; Gammaretrovirus; Oncologia.

1. INTRODUCTION

Feline leukemia virus (FeLV) is an oncogenic retrovirus belonging to the family *Retroviridae* and the genus *Gammaretrovirus*. This retrovirus is considered one of the most clinically significant viral pathogens affecting domestic and wild felids (DALECK; NARDI, 2016; ERBECK *et al.*, 2021; LITTLE *et al.*, 2009; VILLALBA-BRIONES *et al.*, 2022).

FeLV is an enveloped RNA virus comprising several biologically relevant subgroups. FeLV-A is the transmissible subgroup and can spread horizontally through close contact with infected animals and exposure to virus-containing biological secretions. FeLV-B arises through recombination between exogenous FeLV-A and endogenous FeLV-related sequences (enFeLV), particularly involving the envelope (*env*) gene, and represents the most frequently

identified recombinant FeLV subgroup (RAMOS *et al.*, 2019; MINOVICH *et al.*, 2020).

The progression of FeLV infection is generally more rapid and pathogenic than that associated with feline immunodeficiency virus (FIV), accounting for a substantial number of deaths resulting from infection-related complications. Nevertheless, unlike FIV infection, a significant proportion of FeLV-infected cats can control viral replication during the early stages of infection and subsequently develop a persistent latent state known as regressive infection. The structural organization of FeLV resembles that of FIV, although its capsid exhibits an icosahedral rather than conical morphology (SYKES; HARTMANN, 2014).

FeLV is an important feline pathogen associated with several neoplastic and degenerative disorders. Among the major clinical manifestations associated with infection are lymphoma, sarcoma, and immunosuppressive disorders (PAULA *et al.*, 2014). Lymphoma, in particular, is one of the most frequently diagnosed neoplasms in cats and accounts for more than 50% of all feline hematolymphoid tumors (OLIVEIRA *et al.*, 2020). The detection of FeLV RNA within neoplastic lymphoma cells, as demonstrated in cases of primary neural B-cell lymphoma, suggests that the virus may play a direct role in feline oncogenesis (SZILASI *et al.*, 2020).

FeLV infection represents a considerable challenge in veterinary medicine because of its ability to induce immunosuppression, thereby predisposing affected cats to secondary infections and potentially worsening their prognosis. The objective of the present study was to systematically review the association between FeLV infection and the development of neoplasms in cats, addressing

epidemiological characteristics, clinical manifestations, diagnostic methods, and therapeutic strategies. Through the analysis of case reports available in the scientific literature, this study also sought to improve the understanding of the relationship between FeLV infection and the occurrence of different neoplastic disorders, thereby contributing to the scientific knowledge available to veterinary professionals and to the optimization of clinical management and care of infected cats.

2. METODOLOGY

This systematic review was conducted using a comprehensive search strategy across the PubMed, Google Scholar, SciELO, Wiley, and SpringerLink databases to identify case reports describing an association between FeLV infection and the development of neoplasms in cats. The following search terms were used: (FeLV) AND (neoplasm), (FeLV) AND (case report), and FeLV. The publication period was restricted to studies published between 2009 and 2025. This time frame was selected to include relatively recent scientific evidence and to account for potential changes in the relationship between FeLV infection and oncogenesis resulting from diagnostic and epidemiological advances over recent decades.

The study selection process was conducted in two distinct stages to ensure methodological rigor. During the initial screening stage, only studies whose abstracts explicitly described case reports involving neoplasms in FeLV-positive cats were considered eligible. The identified articles were catalogued and organized using the Zotero reference management software, thereby facilitating subsequent retrieval, organization, and review.

During the second stage of the selection process, the full texts of the preselected articles were thoroughly evaluated, with particular attention to the clinical and epidemiological characteristics reported for each case. To ensure data consistency and comparability, only case reports providing complete information regarding breed, age, sex, FeLV and FIV status, diagnostic methods, treatment, clinical outcome, country of origin, and histopathological classification of the neoplasm were included. Cases involving FeLV-negative cats or those lacking essential information were excluded, thereby ensuring that the subsequent analyses were based on sufficiently complete and comparable evidence.

Following completion of the selection process, data were systematically organized into structured spreadsheets using Microsoft Excel and Google Sheets. The variables collected included the digital object identifier (DOI), unique case identification, general and specific neoplasm classification, breed, sex, age, clinical manifestations, diagnostic methods, treatment, clinical outcome, and geographical location of the report. This standardized data organization enabled a detailed assessment of the included cases and facilitated the identification of epidemiological and clinical patterns and potential associations among the investigated variables.

Statistical analyses were performed using the R statistical computing environment to investigate potential associations between FeLV infection and the different types of neoplasms identified in the selected case reports. The chi-square test was applied to determine whether the distribution of the major neoplastic categories occurred randomly or whether statistically significant differences existed among the observed frequencies. In

addition, contingency tables were constructed to compare case frequencies according to sex, neoplastic subtype, country of origin, and age group, thereby providing a comprehensive overview of the distribution of the collected data.

Finally, the Kruskal–Wallis test was performed to assess differences in age distribution among the investigated groups and to determine whether specific neoplastic disorders were associated with particular age groups. This analytical approach aimed not only to investigate associations previously described in the scientific literature but also to identify potential epidemiological trends that have not yet been fully elucidated, thereby contributing to a more comprehensive understanding of the relationship between FeLV infection and oncogenesis in cats.

3. RESULTS AND DISCUSSION

The present systematic review identified 35 cases of neoplasms associated with feline leukemia virus infection, as described in case reports published in different countries. The collected data enabled a comprehensive analysis of the epidemiological, clinical, and therapeutic characteristics of the included cases, highlighting the diversity of neoplastic manifestations and their respective clinical outcomes. Overall, data extraction identified a total of 35 documented clinical cases of neoplasia in FeLV-positive cats.

The findings were categorized according to general and specific neoplastic classification, sex distribution, age group, and geographical occurrence, thereby providing a detailed epidemiological overview of the investigated sample.

3.1. Prevalence Of Neoplasms

Regarding the general classification of the identified neoplasms, lymphoma was the most prevalent neoplastic disorder, accounting for 71.43% of the total sample (25 cases). Carcinomas were the second most frequently reported neoplasms (11.43%, n = 4), followed by adenocarcinomas (8.57%, n = 3), osteochondromas (5.71%, n = 2), and melanocytoma (2.86%, n = 1). Analysis of specific neoplastic manifestations demonstrated that mediastinal lymphoma was the most frequently reported subtype, accounting for 14.29% (n = 5) of all cases. Other relevant presentations included periocular lymphoma (11.43%, n = 4) and intraocular lymphoma (8.57%, n = 3). Alimentary, cerebral, and multicentric lymphomas each accounted for 5.71% (n = 2) of the investigated sample. Osteochondromatosis was also identified in 5.71% of the evaluated cats.

Tipo de Neoplasia (Geral)	Ocorrência (n)	Frequency (%)
Linfoma	25	71,43%
Carcinoma	4	11,43%
Adenocarcinoma	3	8,57%
Osteochondroma	2	5,71%
Melanocytoma	1	2,86%

3.2. Demographic Profile: Sex And Age

The assessment of sex distribution revealed a higher prevalence among males, which accounted for 60.00% (n = 21) of the study population, whereas females represented 40.00% (n = 14) of the cases.

Regarding age distribution, the sample exhibited considerable heterogeneity. The highest frequencies were observed among very young animals (classified as “a few months old”) and 6-year-old cats, each accounting for 14.29% ($n = 5$) of the cases. Four-year-old animals represented 11.43% ($n = 4$) of the records. The remaining ages ranged from 1 to 17 years, with lower frequencies distributed throughout the age range.

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3.4. Geographical Distribution

Analysis of the geographical origin of the case reports demonstrated a marked concentration of cases in Brazil, which accounted for 57.14% ($n = 20$) of the documented occurrences. Other countries, including the United States, Hungary, Italy, and Japan, each accounted for 5.71% ($n = 2$) of the cases. The remaining reports (2.86% each) originated from South Africa, Chile, South Korea, Ecuador, England, Iran, and New Zealand.

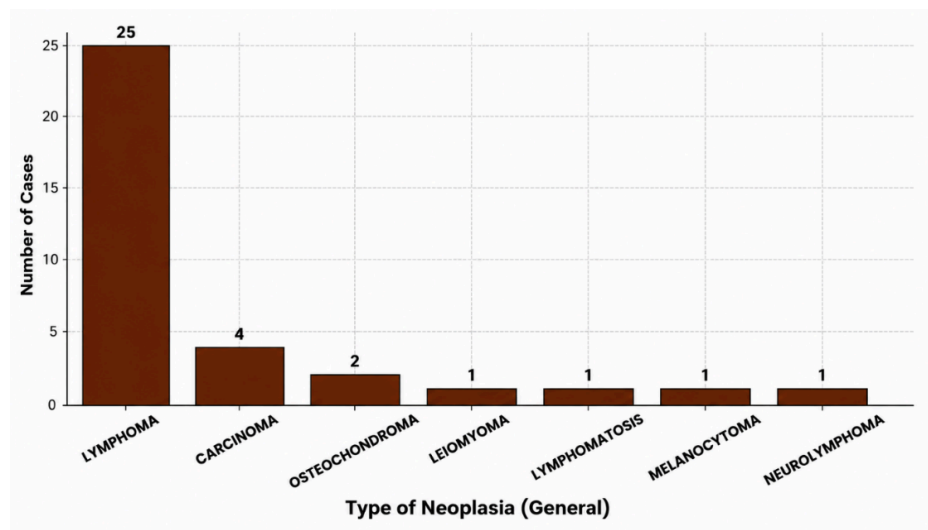
Thus, the findings corroborate the high prevalence of lymphoma in feline clinical medicine, which is frequently associated with viral etiologies such as feline leukemia virus (FeLV) infection. The predominance of cases reported in Brazil raises the hypothesis that local epidemiological factors, including vaccination coverage and population control strategies, may influence the observed distribution and warrant further investigation in future studies. The higher occurrence among males and the bimodal age distribution, involving very young and middle-aged adult cats, represent relevant findings that may contribute to the development and implementation of targeted diagnostic protocols.

3.5. Quantitative And Statistical Analyses

Lymphoma was the most frequently identified neoplasm (71.43%), as shown in Figure 1, and exhibited several anatomical presentations, including mediastinal (14.29%), periocular (11.43%), multicentric (5.71%), alimentary (5.71%), and cerebral (5.71%) forms. Less frequently reported neoplasms included carcinomas (11.43%), melanocytomas (2.9%), osteochondromas (5.71%), and leiomyomas (2.9%).

Most cases occurred in mixed-breed cats (91.4%), reinforcing the widespread susceptibility to FeLV infection regardless of genetic background. Regarding sex distribution, 60% of the cases occurred in males and 40% in females. Age varied considerably, ranging from kittens only a few months old to geriatric cats aged 17 years, with a mean age of 5.3 years. Geographically, Brazil accounted for the largest proportion of reported cases (57.14%), followed by the United States, New Zealand, and other countries.

Figure 1. Occurrence of Secondary Neoplasms in Cats Infected with FeLV.



Authors: Hartmann (2012); Little (2020).

Among the lymphoma cases, mediastinal lymphoma was the most frequently reported presentation, with the predominant clinical signs including dyspnea, tachypnea, and weight loss, and it occurred primarily in young cats, with a mean age of 1.6 years. Multicentric lymphoma, in turn, was characterized by generalized lymphadenomegaly and systemic clinical manifestations such as apathy and hyporexia. Among the clinical findings associated with alimentary lymphoma, vomiting, diarrhea, and intestinal wall thickening were observed, with affected cats having a mean age of 6.5 years. In cases of cerebral lymphoma, neurological signs such as ataxia and paralysis were reported, frequently associated with a guarded prognosis.

The analyzed cases demonstrated considerable diversity in diagnostic and therapeutic approaches, with a predominance of methods such as histopathological examination (47.2%), cytological examination (30.6%), and diagnostic imaging techniques (25.0%), including radiography, ultrasonography, and computed tomography. Regarding treatment, 42.9% of the animals received no specific

therapeutic intervention, whereas 28.6% underwent chemotherapy protocols and 14.3% received adjunctive pharmacological treatment. Post-treatment outcomes revealed high mortality (51.4%) and euthanasia rates (25.7%), frequently associated with the severity of the neoplastic disease or the absence of a satisfactory therapeutic response. Cases treated with surgical interventions, such as tumor excision, exhibited more favorable outcomes in cases of adenocarcinoma, with 11.4% of the 35 cases achieving a “healthy” clinical status. Notably, FIV positivity (reactive test results) was identified in 17.1% of the cases.

Statistical analysis using the chi-square test (χ^2) demonstrated a significant difference in the distribution of neoplasm types ($\chi^2 = 94.8$; $df = 6$; $p < 0.001$), reinforcing the strong association between FeLV infection and lymphoma, as previously described in the scientific literature (HARTMANN, 2012; LITTLE et al., 2020). Regarding sex distribution, no statistically significant difference was identified ($\chi^2 = 1.4$; $df = 1$; $p = 0.237$), indicating that the development of FeLV-associated neoplasms did not exhibit an evident sex-related bias, although some studies have suggested greater susceptibility among male cats (GOMES-KELLER et al., 2006). The ages of the affected animals varied considerably and exhibited a non-normal distribution (Shapiro–Wilk test, $W = 0.922$; $p = 0.017$). The Kruskal–Wallis test revealed no statistically significant differences among the neoplasm groups ($H = 7.119$; $df = 6$; $p = 0.31$), suggesting that age was not a determining factor for the type of neoplasm developed, although the median ages exhibited a relatively homogeneous distribution among groups.

The findings of the present study confirm a strong association between FeLV infection and the development of neoplasms in cats,

particularly lymphomas, which accounted for 71.43% of the cases, with statistical significance ($p < 0.001$). Nevertheless, certain limitations should be considered when interpreting these findings. The analysis was predominantly based on case reports, which may introduce publication bias because severe, unusual, or atypical cases are more likely to be reported in the scientific literature.

3.6. FeLV And Lymphoma

Feline lymphoma is a multifactorial disease; however, several viral etiologies have been recognized, particularly feline leukemia virus and feline immunodeficiency virus infections (OLIVEIRA *et al.*, 2020; ALMEIDA *et al.*, 2019; KRONIT *et al.*, 2022). Lymphoma is one of the most frequently diagnosed neoplasms in cats and accounts for more than 50% of all feline hematolymphoid tumors (OLIVEIRA *et al.*, 2020).

FeLV infection increases the risk of domestic cats developing lymphoma or leukemia (MAGALHÃES *et al.*, 2019). The association between FeLV and feline lymphoma is probably related to the virus's ability to induce insertional mutagenesis. During this process, the viral genome integrates into the host cell DNA and may activate proto-oncogenes, such as *c-myc* and *fli-1*, thereby initiating the neoplastic transformation of infected cells (ALMEIDA *et al.*, 2019; SYKES; HARTMANN, 2011).

This etiological association is particularly evident in progressive infections, in which FeLV actively replicates, resulting in persistent viremia and subsequent viral dissemination to the bone marrow, lymph nodes, and other lymphoid tissues (SYKES; HARTMANN, 2011; SZILASI *et al.*, 2020). The high statistical significance observed in the

present study ($p < 0.001$) further supports the hypothesis that this association is not random and reinforces the potential direct influence of FeLV on feline oncogenesis.

Clinical cases further support the association between FeLV infection and aggressive extranodal lymphomas. One example involved an angiocentric/angioinvasive T-cell lymphoma affecting the tympanic bulla of an FeLV-positive female cat, in which viral antigens (gp70 and p27) were detected within neoplastic cells by immunohistochemistry, supporting a direct oncogenic role of FeLV in this particular case (SANTAGOSTINO *et al.*, 2015). In another case described by Szilasi *et al.* (2020), large amounts of FeLV RNA were detected within neoplastic cells from a primary neural B-cell lymphoma.

Bone marrow involvement represents a critical factor in disease pathogenesis because it allows the virus to infect hematopoietic precursor cells, providing a favorable environment for the induction of hematological malignancies, including lymphoma and leukemia (SYKES; HARTMANN, 2011). Although the widespread implementation of diagnostic testing and vaccination programs has reduced the incidence of FeLV-associated disease, approximately 80% of thymic lymphoma cases in cats have been reported to be positive for FeLV antigen. Furthermore, FeLV has been implicated in multicentric, renal, and ocular forms of lymphoma, with most of these neoplasms being of T-lymphocyte origin (SYKES; HARTMANN, 2011).

3.7. Higher Proportion Of Infections In Brazil

The high proportion of FeLV-associated neoplasms observed in Brazil, accounting for approximately 57% of the cases included in the present review, warrants an analysis of contextual factors that may influence viral prevalence. One relevant hypothesis for this regional disparity concerns accessibility to and implementation of FeLV vaccination programs. Internationally, vaccination has been demonstrated to be an effective strategy for reducing the incidence of FeLV infections and, consequently, associated diseases, including lymphoma (COSTA PEREIRA DOS SANTOS *et al.*, 2025). In contrast, the absence of widespread vaccination policies or limited adherence to preventive immunization programs in certain regions of Brazil may contribute to the persistence of high FeLV infection rates among feline populations (BIEZUS *et al.*, 2019).

The prevalence of FeLV infection among unvaccinated feline populations tends to be significantly higher than that observed in populations covered by immunization programs (HARTMANN, 2011). This difference may be attributed to the ability of vaccination to contribute to the interruption of viral transmission by reducing individual susceptibility to infection and limiting viral circulation within feline populations (HARTMANN, 2011). In Brazil, regional variations in FeLV prevalence may be partially attributed to heterogeneity in animal management practices and disparities in access to preventive veterinary care, including vaccination (FARIA *et al.*, 2024; BIEZUS *et al.*, 2019).

4. CONCLUSION

The present study aimed to conduct a systematic review of the association between FeLV infection and the development of neoplasms, based on published case reports of FeLV-infected cats

that subsequently developed neoplastic diseases. Furthermore, statistical analyses were performed using data extracted from the studies included in the systematic review to assess the association between FeLV infection and neoplasm development. Additional statistical tests were conducted to investigate potential associations between the occurrence of these neoplasms and demographic variables, particularly sex and age group.

Therefore, the evidence gathered in this systematic review demonstrates that FeLV acts as a direct etiological factor in the development of several subtypes of feline lymphoma, with statistical analysis confirming a significant association ($p < 0.001$). FeLV exerts its oncogenic effects primarily through mechanisms involving proviral integration into the host genome, which may result in oncogene activation and uncontrolled lymphocyte proliferation, with substantial clinical implications for feline medicine. Conversely, the analyses of the associations between neoplasm development and sex or age group revealed no statistically significant differences, suggesting that neither age nor sex significantly influenced the occurrence or pathogenesis of the neoplasms evaluated in the present study.

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