

ASSESSMENT OF HEAVY METALS AND TRACE ELEMENTS IN HAIR SAMPLES FROM CATS WITH GASTROINTESTINAL LYMPHOMA

Emanuela BADEA¹, Gheorghe Valentin GORAN¹, Cristina ȚOCA², Miruna Cârlan¹

¹University of Agronomic Sciences and Veterinary Medicine of Bucharest, Faculty of Veterinary Medicine, 105 Splaiul Independenței, 050097, District 5, Bucharest, Romania

²IDAHA of Bucharest, 63 Doctor Staicovici, 050557, District 5, Bucharest, Romania

Corresponding author email: emanuela.badea@gmail.com

Abstract

The link between heavy metals and gastrointestinal lymphoma in cats is an area of growing concern among researchers and veterinarians. The present study assessed the concentrations of some heavy metals and trace elements in cats with gastrointestinal lymphoma, by hair sample analysis, and compared them with the elements' concentrations in clinically healthy cats. Hair samples were collected from clinically healthy cats (n = 10) and cats suffering from gastrointestinal lymphoma (n = 10). The samples underwent wet mineralization (with HNO₃ and HCl), with heavy metals and trace elements being evaluated by ICP-MS analysis. Statistical analysis was done using SPSS software. Heavy metals and trace elements were generally higher in cats with GI lymphoma. The median concentrations of Cr, As, and Se in cats with GI lymphoma were significantly higher (p < 0.05) compared to clinically healthy cats. Although this research found significantly higher concentrations of Cr in cats with gastrointestinal lymphoma, available studies present either no or weak evidence indicating that Cr can lead to GI lymphoma. Further research is needed to better understand the causes of this type of neoplasm in cats.

Key words: cats; hair; heavy metals; trace elements; ICP-MS.

INTRODUCTION

Lymphoma is reported to be the most commonly diagnosed neoplasm in felines and also represents the most common gastrointestinal cancer in both dogs and cats (Darie et al., 2023; Holland, 2020; Richter, 2003). The association between lymphoma and Feline Immunodeficiency Virus (FIV) and Feline Leukaemia Virus (FeLV) infections in cats is well established. Studies showed that cats infected with FIV have a risk of almost 6 times higher than FIV-negative cats to develop lymphoma, or that lymphoma was diagnosed in 21% of cats infected with FIV, the most common location being the gastrointestinal tract (Grover, 2005; Richter, 2003). Another study detected FeLV viral nucleic acids in over 60% of cats with gastrointestinal lymphoma using PCR (Feder & Hurvitz, 1990). However, due to development and implementation of FeLV vaccination over the years, the incidence has decreased, with alimentary lymphoma being now considered the most common type, arguing that mucosa-associated bacteria or changes in the diet or the environment may be

involved in the etiopathogenesis (Hoehne et al., 2016).

Environmental pollution is undeniable, with the 20th century's increase in industrial activity, pollution occurring especially with heavy metals. The bioaccumulation of these toxic elements can cause harmful consequences in various tissues and organs, including carcinogenic effects, potentially triggering cellular changes that promote cancerous growth. Heavy metal exposure is associated, among other types of cancers, like the ones targeting the liver, kidneys, lungs, or urinary bladder, with gastrointestinal malignancies (Aalami et al., 2022; Badea et al., 2023; Morris & Dobson, 2001; Tabrez et al., 2014).

There are numerous studies that have explored the hypothesis of using animal hair as a bioindicator of environmental pollution (Badea et al., 2017; Goran et al., 2021; Kozak et al., 2002; Skibniewska et al., 2011; Skibniewski et al., 2013).

The present research assessed the levels of some heavy metals and trace elements in cats with gastrointestinal lymphoma, by hair sample analysis, and compared them with the

elements' concentrations in clinically healthy cats. Understanding and mitigating heavy metal exposure is crucial for feline health and cancer prevention.

MATERIALS AND METHODS

Hair was sampled from cats suffering from intestinal lymphoma (study group; $n = 10$) and clinically healthy cats (control group; $n = 10$). The diagnosis of intestinal lymphoma was confirmed in all patients using histopathological examination. Hair samples were collected from the flank area, packaged in envelopes and labelled. Polypropylene tubes were used to weigh 0.5 g of each hair sample with the help of an analytical scale. Organic matter disintegration was carried out by wet mineralization at room temperature, with the addition of 5 ml HNO_3 and 1 ml HCl in each tube. Mineralization was complete after two weeks, after which ultrapure water was added up to a total volume of 10 ml in each sample. The concentrations of Pb, Ni, Cr, As, Se, Cd, Hg were dosed using inductively coupled plasma mass spectrometry (ICP-MS). Statistical analysis implied the use of the Mann-Whitney test to evaluate potential differences in elements' concentrations between groups.

RESULTS AND DISCUSSIONS

The median concentrations of Pb, Ni, Cr, As, Se, Cd, Hg (ppb) of the study group and control group, together with the results of the statistical analysis, are presented in Table 1. Median concentrations (ppb) of Pb and Ni are presented in Figure 1, median concentrations of Cr, As, and Se in Figure 2, and median concentrations of Cd and Hg are shown in Figure 3.

Table 1. Pb, Ni, Cr, As, Se, Cd, Hg median concentrations (ppb) in the study and control groups

	Study group	Control group
Pb	98.12 ^a	57.46 ^a
Ni	91.67 ^a	82.10 ^a
Cr	1134.35 ^a	940.65 ^b
As	248.90 ^a	137.63 ^b
Se	474.11 ^a	378.13 ^b
Cd	12.78 ^a	16.33 ^b
Hg	5.11 ^a	8.19 ^b

Values with different superscripts between columns in a row vary significantly at $p < 0.05$.

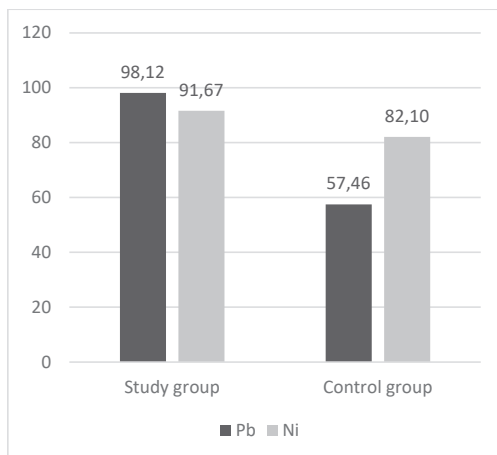


Figure 1. Median Pb and Ni concentrations in the study group and the control group (ppb)

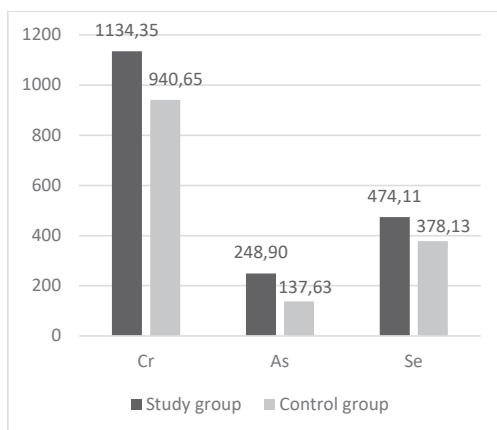


Figure 2. Median Cr, As and Se concentrations in the study group and the control group (ppb)

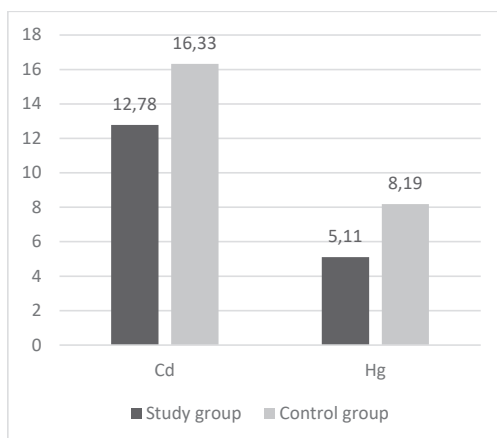


Figure 3. Median Cd and Hg concentrations in the study group and the control group (ppb)

The present study found median concentrations of Pb of 98.12 ppb in the study group, compared to 57.46 ppb in the control group, the difference having no statistical significance ($p > 0.05$). Benderli Cihan et al. (2011) evaluated some elements' concentrations in hair samples of breast cancer patients and clinically healthy humans, and found 136 ppb in breast cancer patients compared to 6196 ppb in healthy humans' hair. Higher Pb levels in the control group were also found in a study assessing heavy metal levels in dogs with mammary neoplasms, with 740 ppb in hair samples from dogs with mammary cancer and 1250 ppb in clinically healthy dogs (Badea et al., 2018).

The median concentrations of Ni were 91.67 ppb in the study group, and 82.10 ppb in the control group, but the difference was not statistically significant ($p > 0.05$).

The median concentrations of Cr were highly significantly different between the groups ($p < 0.01$), with a higher concentration in the study group (1134.35 ppb) compared to the control group (940.65 ppb). Reddy et al. (2004) analyzed trace elements in human cancerous intestinal tissue samples by PIXE technique, finding that the concentrations of Cr and Ni are higher in the neoplastic tissue of the intestine than those observed in the normal tissue.

The study group had statistically significant ($p < 0.05$) higher median concentrations of As (248.90 ppb) compared to the control group (137.63 ppb). Aalami et al. (2022) mentions arsenic exposure being associated with human lymphomas. Badea et al. (2018) found 840 ppb As in the hair of dogs with mammary adenocarcinomas; the level of As in clinically healthy dog's hair was below the method's detection limit.

The median concentrations of Se were 474.11 ppb in the study group, and 378.13 ppb in the control group, the difference being statistically significant ($p < 0.05$). Several researches showed that improper Se status is associated with long term health effects in dogs, such as mammary and prostate cancers (Fico et al., 1986; Waters et al., 2005).

The control group registered higher levels of Hg (8.19 ppb) than the study group (5.11 ppb), the difference being statistically significant ($p < 0.05$).

The control group also registered higher levels of Cd (16.33 ppb) compared to the study group (12.78 ppb), the difference being statistically significant ($p < 0.05$). Byrne et al. (2013) showed that Cd forms a high-affinity complex with estrogen receptors in the mammary gland in patients with breast cancer, suggesting an accumulation of Cd in the tissue rather than in the hair, potentially providing an explanation for the findings of the present research, since Cd's carcinogenic effects are also very well known. Cd is a potent carcinogen for humans, preferentially causing gastro-intestinal, lung, and prostate cancers (Tabrez et al., 2014).

CONCLUSIONS

Pb median concentration was higher in cats with intestinal lymphomas than in clinically healthy cats. Even if the difference is not statistically significant, it is consistent with current knowledge regarding Pb carcinogenicity.

Hg and Cd are also known carcinogens, their concentrations being however lower in the hair of cats with intestinal lymphoma compared to the controls; other studies focusing on other types of cancers showed the affinity of some heavy metals for malignant tissues, opening possibilities of further research in the present study's context as well.

As is known for inducing lymphomas in humans, which is consistent with the findings of the present research, cats with intestinal lymphomas having higher As levels compared to controls.

The scarce information regarding heavy metal and trace elements levels in cats, or animals in general, with lymphomas leaves room for continuing the research in this field, for a better understanding of the implications of potentially toxic elements in this pathology, with hope of using the findings of future studies in much needed cancer prevention.

REFERENCES

- Aalami, A. H., Hoseinzadeh, M., Manesh, P. H., Sharahi, A. J., & Aliabadi, E. K. (2022). Carcinogenic effects of heavy metals by inducing dysregulation of microRNAs: A review. *Mol Biol Rep*, 49(12), 12227-12238.

- Badea, E., Goran, G. V., Țoca, C., & Crivineanu, V. (2017). Heavy metals in cat hair depending on keeping conditions. *Lucrari Stiintifice Medicina Veterinara*, 60(19-P1), 160-166.
- Badea, E., Goran, G. V., Țoca, C., & Crivineanu, V. (2018). Assessment of heavy metal and mineral levels in hair samples from dogs with mammary neoplasms. *Bulletin UASVM Food Science and Technology*, 75(1).
- Badea, E., Goran, G. V., Țoca, C., & Mușetescu, C. (2023). Comparative levels of lead and cadmium in sheep wool and cow hair. *Scientific Works. Series C. Veterinary Medicine*, LXIX(2), 13-16.
- Benderli Cihan, Y., Sözen, S., & Öztürk Yıldırım, S. (2011). Trace elements and heavy metals in hair of stage III breast cancer patients. *Biol Trace Elem Res*, 144(1-3), 360-379.
- Byrne, C., Divekar, S. D., Storchan, G. B., Parodi, D. A., & Martin, M. B. (2013). Metals and Breast Cancer. *J Mammary Gland Biol Neoplasia*, 18(1), 63-73.
- Darie, L., Gagniuc, E., Rădulescu, A., Mihai, A. S., Gontoiu, A. D., & Ciobotaru-Pîrvu, E. (2023). Secondary cardiac involvement of mediastinal T-cell lymphoma in a young scottish fold cat - case report. *Scientific Works. Series C. Veterinary Medicine*, LXIX(1), 13-18.
- Feder, B. M., & Hurvitz, A. I. (1990). Feline immunodeficiency virus infection in 100 cats and association with lymphoma. *J Vet Intern Med*, 4(2), 110.
- Fico, M. E., Poirier, K. A., Watrach, A. M., Watrach, M. A., & Milner, J. A. (1986). Differential effects of selenium on normal and neoplastic canine mammary cells. *Cancer Res*, 46(7), 3384-3388.
- Goran, G. V., Badea, E., Țoca, C., & Crivineanu, V. (2021). Assessment of lead, cadmium, and mercury total concentrations in cats based on their lifestyle and feeding conditions. *Scientific Works. Series C. Veterinary Medicine*, LXVII(1), 73-78.
- Grover, S. (2005). Gastrointestinal Lymphoma in Cats. *Compendium*, 741-751.
- Hoehne, S. N., McDonough, S. P., Rishniw, M., & Simpson, K. W. (2016). Identification of Mucosa-Invasive and Intravascular Bacteria in Feline Small Intestinal Lymphoma. *Vet Pathol*, 54(2), 234-241.
- Holland, M. (2020). *Gastrointestinal Disease*: Wiley & Sons, Inc.
- Kozak, M., Kralova, E., Sviatko, P., Bilek, J., & Bugarsky, A. (2002). Study of the content of heavy metals related to environmental load in urban areas in Slovakia. *Bratisl Lek Listy*, 103(7-8), 231-237.
- Morris, J., & Dobson, J. (2001). *Small Animal Oncology*. UK: Blackwell Science Ltd.
- Reddy, S. B., Charles, M. J., Raju, G. J. N., Reddy, B. S., Reddy, T. S., Lakshmi, P. V. B. R., & Vijayan, V. (2004). Trace elemental analysis of cancer-afflicted intestine by PIXE technique. *Biol Trace Elem Res*, 102(1-3), 265-282.
- Richter, K. P. (2003). Feline gastrointestinal lymphoma. *Vet Clin North Am Small Anim Pract*, 33(5), 1083-1098.
- Skibniewska, E. M., Skibniewski, M., Kosla, T., & Urbanska-Slomka, G. (2011). Hair zinc levels in pet and feral cats (*Felis catus*). *Journal of Elementology*, 16(3), 481-488.
- Skibniewski, M., Kośla, T., & Skibniewska, E. M. (2013). Domestic cat (*Felis catus*) as a bioindicator of environmental lead contamination. *Environmental Protection And Natural Resources*, 24(4(58)), 47-50.
- Tabrez, S., Priyadarshini, M., Priyamvada, S., Khan, M. S., Na, A., & Zaidi, S. K. (2014). Gene-environment interactions in heavy metal and pesticide carcinogenesis. *Mutat Res Genet Toxicol Environ Mutagen*, 760, 1-9.
- Waters, D. J., Shen, S., Glickman, L. T., Cooley, D. M., Bostwick, D. G., Qian, J., Combs Jr, G. F., & Morris, J. S. (2005). Prostate cancer risk and DNA damage: translational significance of selenium supplementation in a canine model. *Carcinogenesis*, 26(7), 1256-1262.