Vol. 19, No. 1, Spring, 2023, 5-15
DOI: 10.22055/IVJ.2022.360692.2495
DOR: 20.1001.1.17356873.1402.19.1.1.6
Journal Homepage: http://www.ivj.ir/

Original Article

Evaluation of epidemiological and clinical findings of canine hyperadrenocorticism in Iran

Mohammad Asadi Iraee[1], Reza Avizeh[2*], Mohammad Razijalali[2] and Mahdi Pourmahdi Borujeni[3]

[1] DVSc Student of Small Animal Internal Medicine, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
[2] Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
[3] Professor, Department of Food Hygiene, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

Received: 05.09.2022 Accepted: 03.11.2022

Abstract

Hyperadrenocorticism (HAC), also known as Cushing's syndrome, is caused by chronic exposure to excessive glucocorticoids. The objective of this study was to determine the epidemiological and clinical (especially ophthalmic) findings of dogs with HAC to increase recognition of suspicious cases in clinical routines. This study was examined on thirty dogs from Tehran, Mazandaran, and Guilan provinces between April 2021 and May 2022. The dogs included in the current study, who all had confirmed Hyperadrenocorticism, were selected based on the clinical findings suggestive Cushing disease as well as positive low-dose dexamethasone-suppression test. Then, general information, clinical signs, and ophthalmic factors were examined and recorded. The data were analyzed using the Chi-square test, Fisher's exact test, McNemar test, independent samples t-test, one-way ANOVA and LSD post hoc test. The mean age for the dogs with HAC was 9.7 years. The risk of HAC was also higher in neutered than intact dogs and also in terrier breed than other ones. Furthermore, significant differences were statistically observed concerning ophthalmic evaluations, including eye lesions, palpebral reflex, ophthalmic structural disorders, conjunctival, sclera, lens, retina, iris, and optic nerve involvement. However, gender, breed, common clinical manifestations, behavioural status, PLR test, menace test, dazzle test, cotton test, and corneal involvement did not show significant differences statistically. It was concluded that indoor and gonadectomized dogs had higher frequency in the studied population. We conducted epidemiological and clinical study of Cushing's disease in dogs in Iran, and for the first time, we examined the eye factors associated with this syndrome. These results support a better understanding of the canine hyperadrenocorticism in Iran. According to this study, the studied population resembles the profile described in European and North American epidemiologic studies, and the clinical picture of the HAC dog appears to be similar worldwide.

Key words: Polyuria, Polydipsia, Hyperadrenocorticism, Dog, Eye

Introduction

Hyperadrenocorticism (HAC), is characterized by chronic exposure to high levels of glucocorticoids (Gilor and Graves, 2011; Martins et al, 2019). This disorder is commonly referred to as Cushing's syndrome, named after Harvey Cushing, a Boston neurosurgeon who first identified HAC in humans in 1932 (Galac, 2010). In

* **Corresponding Author**: Reza Avizeh, Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
E-mail: avizeh@scu.ac.ir

small animal practice, Cushing's syndrome is one of the more common endocrinopathies (Carotenuto et al, 2019). Excess glucocorticoids lead to physical and biochemical changes that significantly affect the animal's quality of life. Hypercortisolism generally results from pathological overproduction of adrenocorticotropic hormone (ACTH) by either a functional pituitary tumor (PDH, pituitary-dependent hypercortisolism) or a primary adrenal disorder (ADH, adrenal-dependent hypercortisolism) (Behrend, 2010; Carotenuto et al, 2019). Other causes such as ectopic ACTH secretion or food-dependent hypercortisolemia have been reported in dogs; however, these conditions seem rare (Carotenuto et al, 2019; Castillo et al, 2014). In older dogs and certain breeds such as Miniature Poodles, Boxers, and Dachshunds, there appears to be a significant predisposition to HAC (Burkhardt et al, 2013; Fracassi et al, 2015; Martins et al, 2019; Van Rijn et al, 2016). Researchers have reported a potential predisposition for female dogs in some studies (Carotenuto et al, 2019; Gallelli et al, 2010; Wood et al, 2007). Most clinical manifestations occur slowly and gradually. Among these manifestations, polyuria, polydipsia, polyphagia, and abdominal enlargement are notable. On the other hand, ocular complications are common in animals with endocrine disease. Regarding laboratory findings, stress leukograms, alkaline phosphatase activity increases, and hypertriglyceridemia is prominent (Behrend, 2015). The diagnosis is based on the patient's history, a clinical evaluation, imaging studies, and hormonal tests, including the Low-Dose Dexamethasone Suppression Test (LDDST) and the ACTH stimulation test (Behrend et al, 2013). A variety of therapeutic options, including surgical and pharmacological treatments are available. The HAC etiologic classification determines the therapeutic approach since most pituitary neoplasms are treated with medications, in contrast to adrenal neoplasms, which are treated with adrenalectomy as the first-line treatment. The prognosis of canine HAC varies depending on the severity of the condition and its comorbidities (Behrend, 2015). Several epidemiological studies were conducted on Cushing's disease, the factors affecting the development of this disease, as well as investigating the symptoms caused by this disease in different countries (Barker et al, 2005; Burkhardt et al, 2013; Carotenuto et al, 2019; Fracassi et al, 2015; Gallelli et al, 2010; O'Neill et al, 2016; Van Rijn et al, 2016).

The objective of this study was to determine the epidemiological, clinical, and ophthalmological findings in dogs with HAC to increase recognition of suspicious cases in clinical routines. This is the first epidemiological study conducted on Cushing's disease in dogs in Iran. Moreover, this study evaluated the eye factors caused from the syndrome for the first time.

Material and methods

In this study, forty one dogs, suspected to have Cushing's disease were studied between April 2021 and May 2022. Several clinical symptoms, including polydipsia, polyuria, polyphagia, abdominal enlargement and hair loss were associated with these dogs. These features are clinical signs of Cushing's syndrome (Nelson and Couto, 2020). The dogs were randomly selected from the three provinces of Tehran, Mazandaran, and Guilan and referred to one of the well-equipped clinics in Tehran province following prior coordination for a definitive diagnosis. First, we performed the disease confirmation test using the LDDST in suspicious dogs. To conduct this test, the blood was taken from the cephalic vein (at zero time), and dexamethasone (Darou Pakhsh Co.) was injected intravenously at a 0.01 mg/kg dose. Additionally, 4 hours (first time) and 8 hours (second time) after dexamethasone injection, some blood was collected again from the cephalic vein, and the amount of cortisol was measured (Nelson and Couto, 2020). Dogs with hypothyroidism, liver failure, diabetes mellitus, and chronic kidney disease and/or dogs being treated with glucocorticoids, phenobarbital and furosemide were excluded from the study. Based on the results of diagnostic tests and clinical symptoms, only 30 of the 41 dogs used to this study had Cushing's disease. Then, all of the information regarding the dogs, such as their age, sex, breed, neutered or intact status, place of life (indoor or outdoor), referring provinces, and clinical signs such as polydipsia, polyuria, polyphagia, abdominal enlargement, muscle weakness, skin disorders, alopecia, panting, behavioral status like anxiety, memory dysfunction, depression, disorientation and ophthalmic signs, was recorded in the prepared forms in advance. The ophthalmic factors were examined via a slit lamp examination, followed by intraocular pressure (IOP) measures, tear secretion, neurological eye tests, and tear break-up time (TBUT). Using a slit lamp device, eyelids, conjunctiva, cornea, iris, sclera, lens, retina and optic nerve were measured and classified into normal and abnormal. The eye pressure in both eyes was measured using a digital tonometer (iCare TONOVET), generally between 15 and 25 mmHg in normal dogs (Maggs, 2016). We also recorded the amount of tear secretion after sixty seconds in both eyes using a Schirmer tear test (STT) strip (ERC Schirmer tear test strip Co.) without using an anesthetic drug. In normal dogs, the standard amount of tear secretion is 15-25 mm in 60 seconds (Maggs, 2016). To maintain similar conditions, all STTs were conducted in the morning (from 9:00 am to 1:00 pm), and for all measurements, the same brand of Schirmer paper was used to eliminate probable errors. In order to measure eye nerves and the animal's vision, several neurological tests, including Pupillary Light Reflex (PLR), Palpebral Reflex (PR), menace reflex and cotton ball were conducted. Another test was the TBUT, which measured the tear film break-up time. In this test, the eye's corneal surface was first stained with a fluorescein strip (Elham Teb Co.); then, after blinking the eye two to three times with our own hands, a time was recorded until the first dry spot appeared on the cornea. For normal dogs, this time is greater than 20 seconds (Maggs, 2016).

The data were analyzed using the Chi-square test, Fisher's exact test, McNemar test, independent samples t-test, one-way ANOVA and LSD post hoc test. As a result, the differences were considered statistically significant ($P \leq 0.05$).

Results

The overall data consisted of 41 dogs attending three provinces in Iran between April 2021 and May 2022. Based on the history, clinical findings, and positive results of the LDDS test, 30 dogs (73.17%) were identified with HAC. The distribution of percentages of cases is shown by frequency and place of life in Figure 1 .

According to the number of cases referred, the prevalence of dogs with HAC in indoor living locations was almost four times greater than that in outdoor living spaces, indicating a statistically significant difference ($p<0.001$) (Figure 1).

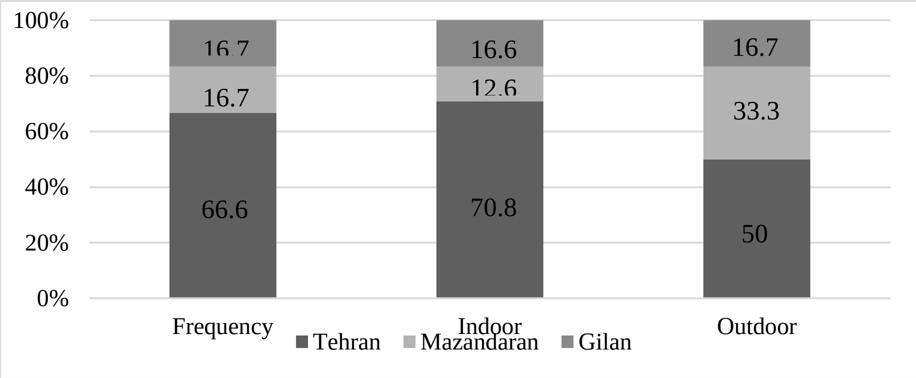

Figure 1. Dog percentage distribution with HAC according to the frequency and location of life

Only thirty out of forty one dogs with HAC had information regarding their age. The mean (± SD) age for dogs with HAC was 9.7 (± 1.9) years, and only 3 of 30 dogs (10%) were less than 8 years old. For all 30 dogs with HAC, gender data (Figure 2) were also available. Female dogs appeared to be at a higher risk for HAC than males but the difference was not significant ($p>0.05$). In addition, neutered dogs had a higher risk of HAC than intact dogs, which had a statistically significant difference ($p<0.05$) (Figure 2).

Among 30 dogs with HAC admitted to the three provinces during the study period, in spite of the existence of differences between breeds, no statistically significant differences were observed ($p>0.05$) (Table 1).

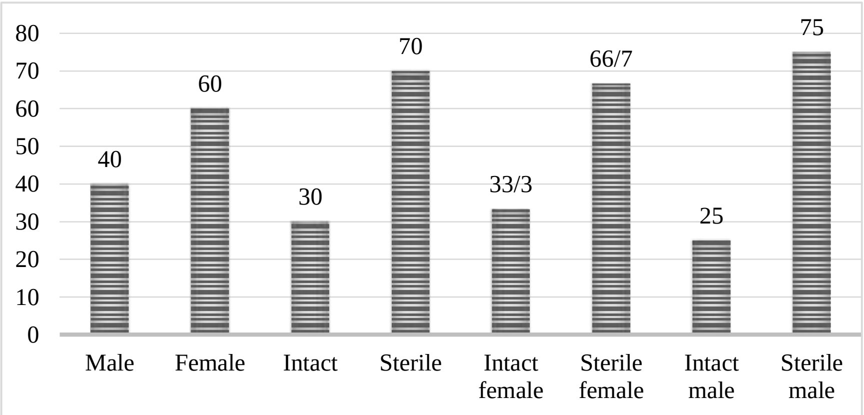

Figure 2. Distribution percentage of sex status's in dogs with HAC

Table 1. Breed distribution of dogs with HAC in three provinces of Tehran, Mazandaran, Guilan

Breed	Frequency	Percentage
Boxer	3	10
German shepherd	4	13.3
Crossbred	4	13.3
Pomeranian	6	20
Poodle	4	13.3
Shih Tzu	2	6.7
Terrier	7	23.3
Total	30	100

A summary of the most common clinical manifestations in this case series is shown in Figure 3. As is shown, polyuria, polydipsia, and polyphagia were observed in most cases. Additionally, other clinical symptoms with no significant difference were abdominal enlargement, alopecia, ophthalmic disorders, skin disorders, muscle weakness, and panting (p>0.05).

According to Figure 4, dogs with HAC showed memory dysfunction, anxiety, depressive behavior, and disorientation; however, no significant difference was found. (p>0.05).

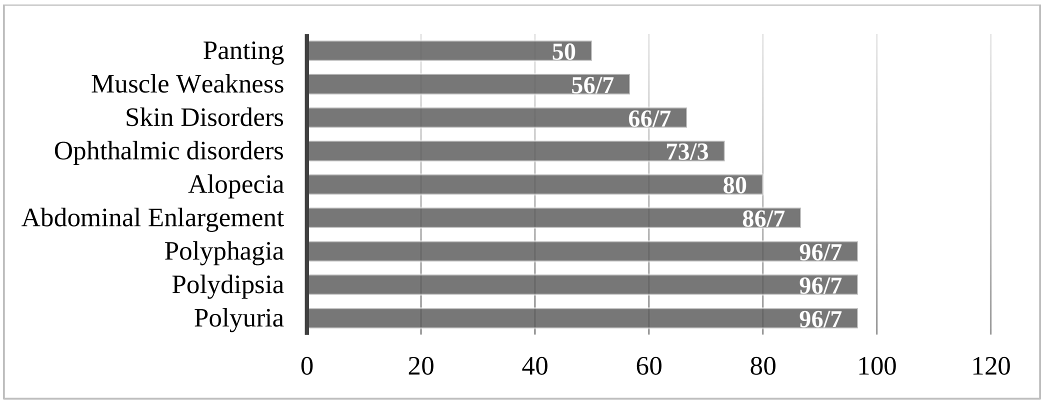

Figure 3. Distribution percentage of clinical manifestation's in dogs with HAC in three provinces of Tehran, Mazandaran, Guilan

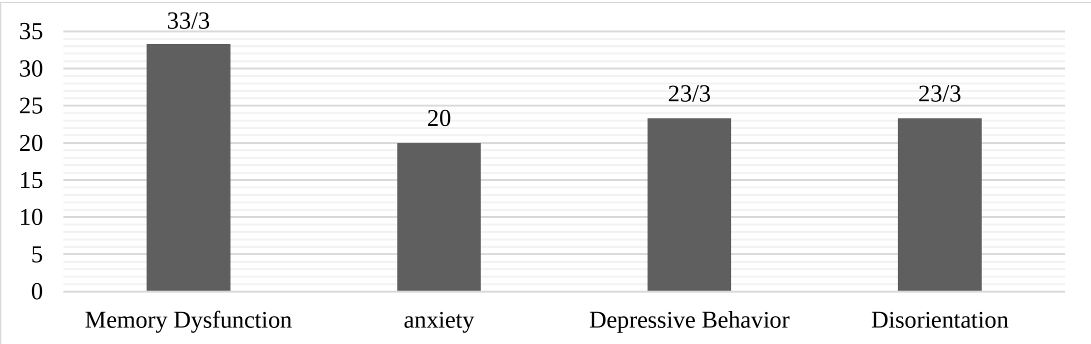

Figure 4. Distribution percentage of behavioural status's in dogs with HAC in three provinces of Tehran, Mazandaran, Guilan

According to this study, most cases had at least one ocular lesion, indicating a significant difference (p<0.05). A description of the neurological eye tests in this case series is illustrated in figure 5 in which a negative result of this test indicates an unhealthy eye and a positive result indicates a healthy eye. Regarding the PLR test, although positive PLR was higher than negative in both the oculus dextrus (OD) and oculus sinister (OS), these differences were not statistically significant (p>0.05). Additionally, in the palpebral test, positive results were approximately nine times greater than negative results in both OD and OS, indicating a statistically significant difference (p>0.05). Furthermore, according to the menace test, despite the discrepancies between the positive and negative results, the difference between OD and OS was not statistically significant (p>0.05). Moreover, the dazzle test showed a greater proportion of positivity than negativity in OS and OD; however, this was not statistically significant (p>0.05). Additionally, although the positive results were higher than the negative ones in OS and OD, no statistically significant differences were observed (p>0.05).

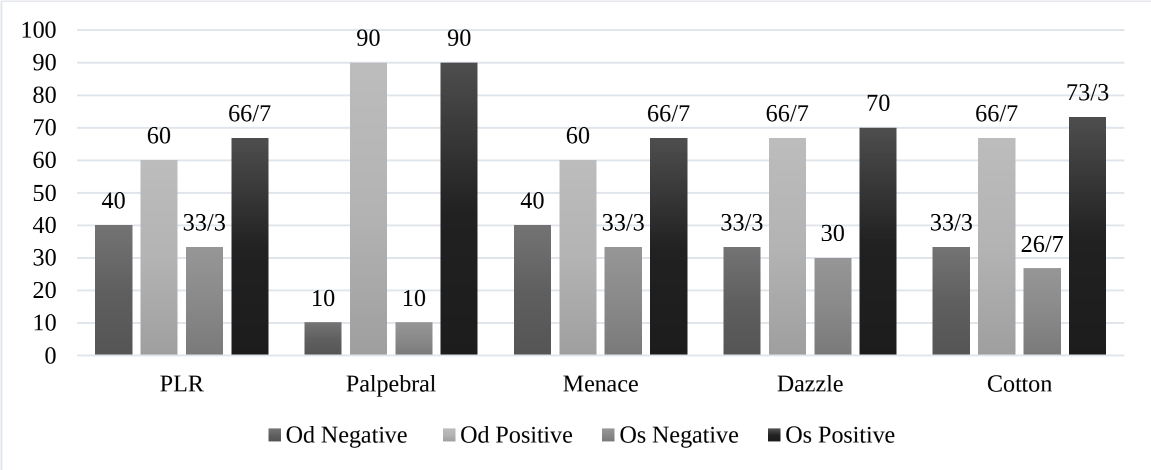

Figure 5. Distribution of ophthalmic neurological tests in dogs with HAC in three provinces of Tehran, Mazandaran, Guilan. PLR: Pupillary light reflex, Od: oculus dextrus, Os: oculus sinister

In the structural study of the eyes, negative indicates a healthy structure, while positive indicates an unhealthy one. Among dogs with HAC and ophthalmic structure disorders, eyelid involvement was significant both in OS and OD ($p<0.05$). Moreover, the number of healthy eyes among dogs with HAC was statistically significantly lower than the number of eyes that had conjunctival involvements ($p<0.05$). Additionally, regarding corneal involvement, no significant differences were observed ($p>0.05$). In contrast, the results of the positive tests were significantly greater than those of the negative tests based on the involvement of the iris ($p<0.05$). In addition, in terms of sclera involvement, the positive results were significantly more than negative ones in both eyes ($p<0.05$). The results of the lens lesions were such that 13.3% of the right eye and 10% of the sinister eye were negative, indicating a statistically significant difference ($p<0.05$). Additionally, more eyes with retinal involvement were observed in OD and OS, which was statistically significant ($p<0.05$). Finally, optic nerve involvement was highly prevalent in dogs with HAC, indicating a significant difference ($p<0.05$) (figure 6).

In terms of IOP, TBUT, and STT, the mean values for Od were lower than those for Os, which was statistically significant ($p<0.001$) (table 2).

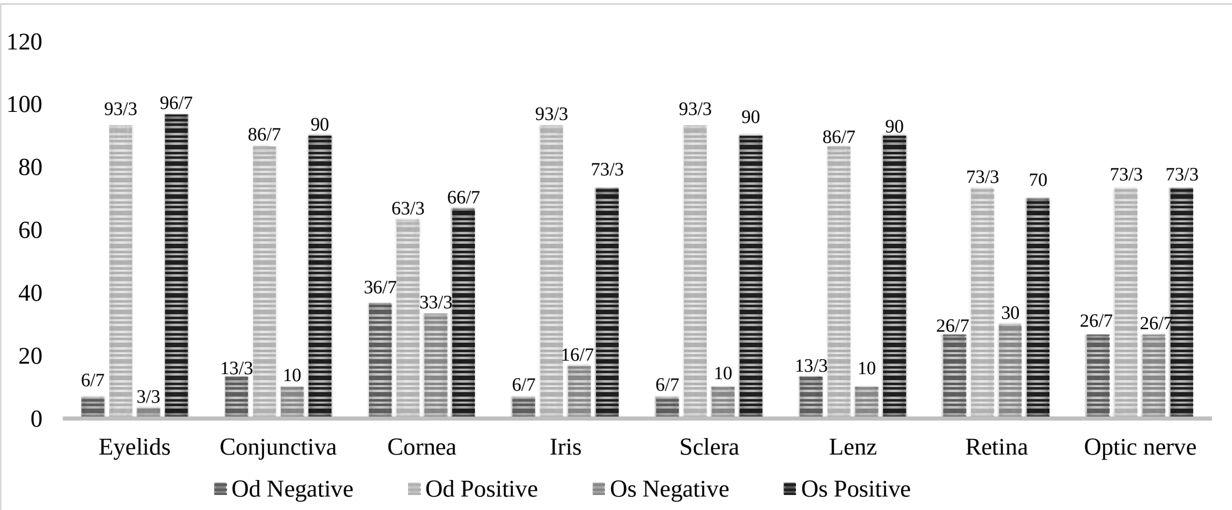

Figure 6. Ophthalmic structure disorders in dogs with HAC in three provinces of Tehran, Mazandaran, Guilan. Od: oculus dextrus, Os: oculus sinister

Table 2. Mean values, standard deviation, range, and reference interval for the IOP, TBUT, STT in dogs with HAC in three provinces of Tehran, Mazandaran, Guilan. Od: oculus dextrus, Os: oculus sinister

Parameters	Mean (standard deviation)		Range		Reference range
	Od	Os	Od	Os	
IOP	18.86 (±2.64)	19.06 (±3.15)	9.00	10.00	15-25
TBUT	22.76 (±6.59)	23.70 (±7.20)	22	24	20s<
STT	17.70 (±5.01)	17.73 (±5.39)	18	18	15-25

Discussion

An accurate clinical-epidemiological profile contributes to the development of a diagnosis. Thus, it is essential to determine the clinical and epidemiological aspects of diseases. During the present study, classic disease presentations were observed, with well-defined clinical findings; however, clinical manifestations were discreet in some patients. These cases did not present alterations considered to be frequent such as polyuria and polyphagia. Despite all the advances in technology and methodology regarding hormonal analysis, clinical aspects and complementary exams are essential to determining the diagnosis (Behrend, 2015; Benchekroun et al, 2010; Martins et al, 2019).

During the period between April 2021 and May 2022, this rate of involvement was determined by suspected cases with clinical symptoms, not from all cases referred to clinics, which differs from a study of 119 primary-care veterinary practices in the United Kingdom that estimated the prevalence of HAC involvement in all referred cases (not suspicious cases with clinical symptoms) (O'Neill et al, 2016). In addition, 80% of indoor dogs had HAC, which may have been caused by different factors than outdoor dogs. It is due to several factors, such as the referral of more indoor dogs to clinics and the lack of supervisors to monitor the health and treatment of outdoor dogs. There is, however, a possibility that the incidence of this disease may be the same in both forms of living. In contrast, increased exposure to endocrine disruptors, such as food contaminants (Koestel et al, 2017), toys, or plastic utensils, may also be contributing factors (Wooten and Smith, 2013). Such substances interfere with several physiological mechanisms, from the inhibition of hormone synthesis, that happens with lindane reducing StAR protein expression, and decreasing steroidogenesis, to steroid receptors binding, altering the process of transduction, signalling, and modulating enzymatic pathways in the metabolism of sexual hormones (for example, analogues of dichlorodiphenyltrichloroethane) (Koestel et al, 2017; Martins et al, 2019; Wooten and Smith, 2013).

In the present study, the age of diagnosis of this syndrome was 9.7 (±1.9) years, which was consistent with the age mentioned (approximately 9–11 years) in other studies (Barker et al, 2005; Burkhardt et al, 2013; Carotenuto et al, 2019; Fracassi et al, 2015; Gallelli et al, 2010; O'Neill et al, 2016; Van Rijn et al, 2015).

Research has consistently shown that HAC occurs more often in female dogs (Gallelli et al, 2010; Pöppl et al, 2016; Reusch and Feldman, 1991). However, there was no consensus regarding the existence of a gender predisposition over time. HAC was also more prevalent in female dogs in the present evaluation. On the other hand, in another study, ACTH-dependent HAC was more prevalent in female dogs. In contrast, ACTH-independent HAC was more prevalent in male dogs (Martins et al, 2019). Regarding reproductive health, studies have not shown a higher incidence of HAC diagnosis in gonadectomized dogs (O’Neill et al, 2016). Despite this, Belanger et al (2017) found that gonadectomy was significantly associated with a higher risk of developing HAC in both males and females. Based on the results of the current study, HAC seems to be associated with gender. Furthermore, neutered dogs had a higher risk than intact ones and neutered females had a higher risk than intact females, which is in agreement with Peterson (2007), who states that females are more predisposed to developing HAC because of the interaction between female sexual hormones and the hypothalamic-pituitary axis. The only environmental risk factor identified in studies on canine HAC was gonadectomy in female patients (Martins et al, 2019).

Dachshunds, Terriers, and Boxers have been identified to have a significantly higher risk of developing HC. Similar conclusions were also reached by many other studies (Bell et al., 2006; Burkhardt et al, 2013; Carotenuto et al, 2019; Fracassi et al, 2015; Hanson et al, 2007; Helm et al, 2011; O’Neill et al, 2016; Rodriguez Piñeiro et al, 2011; Van Rijn et al, 2015, 2016). This finding has been confirmed and reinforced in the present study. According to this study, the terrier had the highest percentage (23.3%), although this breed had been associated with much lower risks in other studies (Carotenuto et al, 2019; Fracassi et al, 2015; Hanson et al, 2007; Helm et al, 2011; O’Neill et al, 2016; Van Rijn et al, 2016). In contrast, breeds like Pomeranian, included in this study, have not been found to have a significant risk difference; for example, O'Neill et al. (2016) reported an elevated risk for Bichon Frisé, which was not included in this study. The reason for the differences between the results of our study and those of other previously published reports may be the result of either the different distribution/representation of canine breeds in different geographical areas or the defining features of other studies that did not take into account the prevalence of different breeds. Even though there are overlaps among the studies, none examines the same breeds. In our study, we found a high risk in the Pomeranian (20%), a breed that was not described as predisposed in other studies (Carotenuto et al, 2019; Fracassi et al, 2015; Hanson et al, 2007; Helm et al, 2011; O’Neill et al, 2016; Van Rijn et al, 2016).

According to O'Neill et al (2016), large breed dogs present a lower risk of developing ACTH-dependent HAC than small breed ones. In the formation and maintenance of modern breeds, selective pressure may have led to significant changes in size and muscle mass due to the diversity among dog breeds. Medium and small-sized dogs were more HAC affected, which could be explained by data from a study that compared gene expression among dog sizes, identifying variants regarding a lower expression of IRS-4, IGSF-1 and ACSL-4 in small and medium-sized dogs (Martins et al, 2019; Plassais et al, 2017). Similarly, most dogs suffering from HAC syndrome in this study were small. There is evidence that such substrates are essential in pituitary development (Martins et al, 2019; Wang et al, 2017) and steroidogenesis (Martins et al, 2019; Midzak and Papadopoulos, 2016), which may explain the correlation between the occurrence of HAC and size.

Based on the results of the present study, the main clinical manifestations of HAC are classified as frequent, less frequent, and infrequent. However, a greater understanding of this endocrinopathy has identified subtle clinical signs. Besides, more classic manifestations in this study, led to less frequent ones such as skin disorders, muscle weakness and panting. There are also infrequent ones, such as abdominal enlargement, alopecia, and ophthalmic disorders. Additionally, polyuria, polydipsia, and polyphagia were frequent symptoms. In other studies, less frequent signs such as lethargy/apathy, hyperpigmentation, comedones, pyoderma, poor hair regrowth and infrequent ones, such as thromboembolism, ligament ruptures, facial nerve paralysis, cutis calcinosis, testicular atrophy, myopathy and persistent anestrous were observed (Behrend, 2010; Martins et al, 2019).

Furthermore, Notari et al (2016) suggest that previous experience with glucocorticoids may be associated with behavior problems caused by fear, anxiety, and frustration. A study of the adverse effects of HAC on behavior and cognition in dogs is imperative since these changes constantly impair the dog-owner relationship; that is, owners can consider when making treatment decisions. In this study, memory dysfunction was associated with a higher risk (33.3%) than depressive behavior (23.3%), disorientation (23.3%), and anxiety (20%), correlating to da Silva et al (2007) stating that dogs with HAC exhibited a higher final score of cognitive dysfunction, specifically, higher memory dysfunction. Hypercortisolism appears to accelerate neurodegenerative processes, leading to more intense behavioral and cognitive changes than observed in age-matched dogs without HAC. There is, however, a lack of studies in veterinary medicine on the effects of chronic hypercortisolism on dog cognition and behavioral symptoms that might be associated with HAC.

Several ocular abnormalities were observed in the structural disorders and neurological tests of this study. Approximately 73% of all eyes were affected by one or more abnormalities, which is a significant number. However, some of these abnormalities, such as cataracts, are linked to ageing in dogs. On the other hand, the left eye is more involved in neurological tests than the right eye, for which no specific reason can be identified. In another study, ocular abnormalities were found in both hyperthyroid and euthyroid cats, with approximately 75% of all eyes affected (Van der Woerdt and Peterson, 2000). According to the results of the STT and TBUT tests, there is an increase in IOP and eye dryness associated with this disease.

Nevertheless, this is the first epidemiological, clinical, and ophthalmological study on canine HAC in Iran. This study concludes that the profile of the population studied resembles that described in European epidemiologic researches, and the clinical picture of the HAC dog across the globe is similar. This clinicopathological characterization of the north and central Iranian population contributes to a better understanding of this challenging and frequent disease in Iran. In the presence of vague clinical signs or minor laboratory or ultrasound abnormalities that are compatible with HAC, special attention should be paid. Because dogs have a longer life expectancy and are more likely to be diagnosed with HAC when they are young, it is beneficial to know how local cases of HAC behave in contrast to international literature to support accurate diagnosis in clinical routine. In addition, unusual HAC-associated signs are likely to appear in some dogs more prominently than the clinical signs of classic HAC. It is essential to recognize the vast range of clinicopathological abnormalities secondary to this endocrine disease in order to improve suspicion and investigation of HAC.

Ackwnowledgments

The authors express their gratitude to the Research Council of Shahid Chamran University of Ahvaz for its financial support.

Conflict of interest

The authors declare that they have no known conflict of interest.

Funding

This research was carried out in the form of a thesis with the financial support of Shahid Chamran University of Ahvaz.

References

Barker, E. N., Campbell, S., Tebb, A. J., Neiger, R., Herrtage, M. E., Reid, S. W., & Ramsey, I. K. (2005). A comparison of the survival times of dogs treated with mitotane or trilostane for pituitary-dependent hyperadrenocorticism. *Journal of Veterinary Internal Medicine, 19*(6): 810-815.

Behrend, E.N. (2015). *Canine and feline endocrinology* (4th ed., pp. 377-444). St Louis, SL: W.B. Saunders.

Behrend, E. N., Kooistra, H. S., Nelson, R., Reusch, C. E., & Scott-Moncrieff, J. C. (2013). Diagnosis of spontaneous canine hyperadrenocorticism: 2012 ACVIM consensus statement (small animal). *Journal of Veterinary Internal Medicine*, *27*(6): 1292-1304.

Belanger, J. M., Bellumori, T. P., Bannasch, D. L., Famula, T. R., & Oberbauer, A. M. (2017). Correlation of neuter status and expression of heritable disorders. *Canine Genetics and Epidemiol*ogy, *4*(1): 6.

Bell, R., Neiger, R., Mcgrotty, Y., & Ramsey, I. K. (2006). Study of the effects of once daily doses of trilostane on cortisol concentrations and responsiveness to adrenocorticotrophic hormone in hyperadrenocorticoid dogs. The *Veterinary Record*, *159*(9): 277-281.

Benchekroun, G., de Fornel-Thibaud, P., Rodríguez Piñeiro, M. I., Rault, D., Besso, J., Cohen, A., Hernandez, J., Stambouli, F., Gomes, E., Garnier, F., Begon, D., Maurey-Guenec C., & Rosenberg, D. (2010). Ultrasonography criteria for differentiating ACTH-dependency from ACTH independency in 47 dogs with hyperadrenocorticism and equivocal adrenal asymmetry. *Journal of Veterinary Internal Medicine, 24*(5): 1077-1085.

Burkhardt, W. A., Boretti, F. S., Reusch, C. E., & Sieber-Ruckstuhl, N. S. (2013). Evaluation of baseline cortisol, endogenous ACTH, and cortisol/ACTH ratio to monitor trilostane treatment in dogs with pituitary-dependent hypercortisolism. *Journal of Veterinary Internal Medicine, 27*(4): 919-923.

Carotenuto, G., Malerba, E., Dolfini, C., Brugnoli, F., Giannuzzi, P., Semprini, G., & Fracassi, F. (2019). Cushing’s syndrome an epidemiological study based on a canine population of 21,281 dogs. *Open Veterinary Journal, 9*(1): 27-32.

Castillo, V. A., Pessina, P. P., Garcia, J. D., Hall, P., Gallelli, M. F., Miceli, D. D. & Cabrera Blatter, M. F. (2014). Ectopic ACTH syndrome in a dog with a mesenteric neuroendocrine tumour: a case report. *Veterinary Medicina, 59*(7): 352-358.

Da Silva, C. C., Cavalcante, I., de Carvalho, G. L. C. & Pöppl, Á. G. (2021). Cognitive dysfunction severity evaluation in dogs with naturally-occurring Cushing´ s syndrome: A matched case-control study. *Journal of Veterinary Behavior, 46*: 74-78.

Fracassi, F., Corradini, S., Floriano, D., Boari, A., Aste, G., Pietra, M., Bergamini, P. F. & Dondi, F. (2015). Prognostic factors for survival in dogs with pituitary-dependent hypercortisolism treated with trilostane. *The Veterinary Record*, *176*(2): 49-55.

Galac, S. (2010). Recent developments in canine Cushing`s syndrome. Utrecht Universiteit Utrecht, Faculteit Diergeneeskunde Thesis Universiteit Utrecht. - With ref. - With summary in Dutch and Slovene. *1,* 978.

Gallelli, M. F., Cabrera M. F. B. & Castillo V. (2010). A comparative study by age and gender of the pituitary adenoma and ACTH and alpha-MSH secretion in dogs with pituitary-dependent hyperadrenocorticism. *Research in Veterinary Science, 88*(1): 33-40.

Gilor, C. & Graves T. K. (2011). Interpretation of laboratory test for canine Cushing’s syndrome. Topics in *Companion Animal Medicine, 26*(2): 98-108.

Hanson, J. M., Teske, E., Voorhout, G., Galac, S., Kooistra, H. S. & Meij, B. P. (2007). Prognostic factors for outcome after transsphenoidal hypophysectomy in dogs with pituitary-dependent hyperadrenocorticism. *Journal of Neurosurgery, 107*(4): 830-840.

Helm, J. R., Mclauchlan, G., Boden, L. A., Frowde, P. E., Collings, A. J., Tebb, A. J., Elwood, C. M., Herrtage, M. E., Parkin, T. D. & Ramsey, I. K. (2011). A comparison of factors that influence survival in dogs with adrenal-dependent hyperadrenocorticism treated with mitotane or trilostane. *Journal of Veterinary Internal Medicine, 25*(2): 251-260.

Koestel, Z. L., Backus R. C., Tsuruta, K., Spollen, W. G., Johnson S. A., Javurek, A. B., Ellersieck, M. R., Wiedmeyer, C. E., Kannan, K., Xue, J., Bivens, N. J., Givan, S. A. & Rosenfeld, C. S. (2017). Bisphenol A (BPA) in the serum of pet dogs following short-term consumption of canned dog food and potential healthconsequences of exposure to BPA. *The Science of the Total Environment*, *579*: 1804-1814.

Lane, IF., Roberts, S. T. & Lappin, M. R. (1993). Ocular manifestations of vascular disease: Hypertension, hyperviscosity, and hyperlipidemia. *Journal of American Animal Hospital Association*, *29*: 28-36.

Maggs, D. J., Miller, P., & Ofri, R. (2016). *Slatter's Fundamentals of Veterinary Ophthalmology* (6th ed., pp. 79-109). St Louis, SL: W.B. Saunders.

Martins, F. S., Carvalho, G. L. C., Jesus, L., Pöppl, Á. G., & González, F. H. (2019). Epidemiological, clinical, and laboratory aspects in a case series of canine hyperadrenocorticism: 115 cases (2010-2014). *Pesquisa Veterinária Brasileira, 39(11):* 900-908.

Midzak, A. & Papadopoulos, V. (2016). Adrenal mitochondria and steroidogenesis: from individual proteins to functional protein assemblies. *Frontiers in Endocrinology*, *7*: 106.

Nelson, R. W. and Couto, C. G. (2020). *Small Animal Internal Medicine* (6th ed., pp. 857-897). St Louis, SL: Elsevier.

Notari, L., Burman, O. &, Mills, D. S. (2016). Is there a link between treatments with exogenous corticosteroids and dog behavior problems?. *The Veterinary Record, 179*(18): 462-467.

O'Neill, D. G., Scudder, C., Faire, J. M., Church, D. B., Mcgreevy, P. D., Thomson, P. C. & Brodbelt, D. C. (2016). Epidemiology of hyperadrenocorticism among 210,824 dogs attending primary-care veterinary practices in the UK from 2009 to 2014. *The Journal of Small Animal Practice, 57*(7): 365-373.

Peterson, M. E. (2007). Diagnosis of hyperadrenocorticism in dogs. *Clinical Techniques in Small Animal Practice*, *22*(1): 2-11.

Plassais, J., Rimbault M., Williams F. J., Davis B.W., Schoenebeck J. J. & Ostrander E. A. (2017). Analysis of large versus small dogs reveals three genes on the canine X chromosome associated with body weight, muscling and back fat thickness. *PLoS Genet*ics, *13*(3), e1006661.

Pöppl, A. G., Coelho, I. C., Silveira, C. A., Moresco, M. B., & Carvalho, G. L. C. (2016). Frequency of endocrinopathies and characteristics of affected dogs and cats in southern Brazil (2004-2014). *Acta Scientiae Veterinariae*, *44*(1): 1379.

Reusch, C. E., & Feldman, E. C. (1991). Canine hyperadrenocorticism due to adrenocortical neoplasia: pretreatment evaluation of 41 dogs. *Journal of Veterinary Internal Medicine*, *5*(1): 3-10.

Rodriguez Piñeiro, M. I., De Fornel-Thibaud, P., Benchekroun, G., Garnier, F., Maurey-Guenec, C., Delisle, F., & Rosenberg, D. (2011). Use of computed tomography adrenal gland measurement for differentiating ACTH dependence from ACTH independence in 64 dogs with hyperadenocorticism. *Journal of Veterinary Internal Medicine*, *25*(5): 1066-1074.

Van der Woerdt, A. & Peterson, M. E. (2000). Prevalence of ocular abnormalities in cats with hyperthyroidism. *Journal of Veterinary Internal Medicine*, *14*(2): 202-203.

Van Rijn, S. J., Galac, S., Tryfonidou, M. A., Hesselink, J. W., Penning, L. C., Kooistra, H. S., & Meij, B. P. (2016). The influence of pituitary size on outcome after transsphenoidal hypophysectomy in a large cohort of dogs with pituitary-dependent hypercortisolism. *Journal of Veterinary Internal Medicine, 30*(4): 989-995.

Van Rijn, S. J., Hanson, J. M., Zierikzee, D., Kooistra, H. S., Penning, L. C., Tryfonidou, M.A., & Meij, B. P. (2015). The prognostic value of perioperative profiles of ACTH and cortisol for recurrence after transsphenoidal hypophysectomy in dogs with corticotroph adenomas. *Journal of Veterinary Internal Medicine*, *29*(3): 869-876.

Wang, Y., Brûlé, E., Silander, T., Bak, B., Joustra, S. D., & Bernard D. J. (2017). The short mRNA isoform of the immunoglobulin superfamily, member 1 gene encodes an intracellular glycoprotein. *PLoS One*, *12*(7): e0180731.

Wood, F. D., Pollard, R. E., Uerling, M. R. Feldman, E.C. (2007). Diagnostic imaging findings and endocrine test results in dogs with pituitary-dependent hyperadrenocorticism that did or did not have neurologic abnormalities: 157 cases (1989– 2005). *Journal of the American Veterinary Medical Association*, *231*(7): 1081-1085.

Wooten, K. J., & Smith, P. N. (2013). Canine toys and training devices as sources of exposure to phthalates and bisphenol A: quantitation of chemicals in leachate and in vitro screening for endocrine activity. *Chemosphere, 93*(10): 2245-2253.

Received: 05.09.2022
Accepted: 03.11.20

مقاله کامل

دوره نوزدهم ـ شماره ۱ ـ بهار ۱۴۰۲
DOI: 10.22055/IVJ.2022.360692.2495
DOR: 20.1001.1.17356873.1402.19.1.1.6

بررسی یافته‌های اپیدمیولوژیک و بالینی پرکاری قشر غده فوق کلیه سگ در ایران

محمد اسدی ایرایی[۱]، رضا آویزه[۲*]، محمد راضی جلالی[۲] و مهدی پورمهدی بروجنی[۳]

[۱] دانشجوی دکتری تخصصی بیماری‌های داخلی دام‌های کوچک، دانشکده دامپزشکی، دانشگاه شهید چمران اهواز، اهواز، ایران

[۲] استاد گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه شهید چمران اهواز، اهواز، ایران

[۳] استاد گروه بهداشت مواد غذایی، دانشکده دامپزشکی، دانشگاه شهید چمران اهواز، اهواز، ایران

تاریخ دریافت: ۱۴۰۱/۶/۱۴ تاریخ پذیرش: ۱۴۰۱/۸/۱۲

چکیده

هیپرآدرنوکورتیزیسم که به عنوان سندرم کوشینگ نیز شناخته می‌شود، در اثر مواجهه مزمن با گلوکوکورتیکوئیدها ایجاد می‌شود. هدف از این مطالعه، بررسی یافته‌های اپیدمیولوژیک و بالینی (به ویژه چشمی) سگ‌های مبتلا به هیپرآدرنوکورتیزیسم، به منظور بهبود روند تشخیص موارد مشکوک به این بیماری، در موارد بالینی است. در این مطالعه ۳۰ قلاده سگ از استان‌های تهران، مازندران و گیلان در فاصله زمانی فروردین ۱۴۰۰ تا اردیبهشت ۱۴۰۱ مورد بررسی قرار گرفتند. سگ‌های مطالعه حاضر همگی مبتلا به پرکاری قشر غده فوق کلیه بودند و بر اساس یافته‌های بالینی حاکی از بیماری کوشینگ و همچنین مثبت بودن تست سرکوب دگزامتازون با دوز پایین انتخاب شدند. سپس اطلاعات کلی، علائم بالینی و فاکتورهای چشمی بررسی و ثبت گردید. داده‌ها با استفاده از آزمون‌های مربع کای، آزمون دقیق فیشر، آزمون مک نمار، آزمون تی مستقل، آنالیز واریانس یک طرفه و آزمون تعقیبی LSD مورد تجزیه و تحلیل قرار گرفت. میانگین سنی سگ‌های دارای هیپرآدرنوکورتیزیسم، ۹/۷ سال بود. فراوانی هیپرآدرنوکورتیزیسم نیز در سگ‌های عقیم شده بیشتر از سگ‌های سالم و همچنین در نژاد تریر بیش‌تر از سایر نژادها بود. علاوه بر این، تفاوت‌های آماری معنی‌داری در ارزیابی‌های چشم از جمله ضایعات چشمی، رفلکس پلکی، اختلالات ساختاری چشم، ملتحمه، صلبیه، عدسی، شبکیه، عنبیه و درگیری عصب بینایی مشاهده شد. با این حال، جنسیت، نژاد، تظاهرات بالینی، وضعیت رفتاری، تست پاسخ مردمک به نور، تست تهدید، تست خیره شدن، تست پنبه و درگیری قرنیه، تفاوت‌های آماری معنی‌داری را نشان ندادند و سگ‌های داخل خانه و عقیم شده، فراوانی بیشتری در جمعیت مورد مطالعه داشتند. این مطالعه اولین بررسی اپیدمیولوژیک و بالینی سندرم کوشینگ در کنار سنجش نشانگان چشمی مرتبط با این سندرم در ایران است که نتایج این مطالعه منجربه درک بهتر بیماری پرکاری قشر غده فوق کلیه سگ در ایران می‌شود. طبق این مطالعه، مشخصات بالینی جمعیت مورد مطالعه مانند مشخصات توصیف شده در مطالعات اپیدمیولوژیک اروپا و آمریکای شمالی است.

کلمات کلیدی: پلی‌اوری، پلی‌دیپسی، هیپرآدرنوکورتیزیسم، سگ، چشم

* نویسنده مسئول: رضا آویزه، استاد گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه شهید چمران اهواز، اهواز، ایران

E-mail: avizeh@scu.ac.ir