

# Prevalence, clinical and epidemiological features of feline hyperthyroidism at a veterinary teaching hospital in Brazil: a retrospective study

## *Prevalência, características clínicas e epidemiológicas do hipertireoidismo felino em um hospital veterinário universitário no Brasil: um estudo retrospectivo*

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**ABSTRACT:** The hyperthyroidism is the most frequently endocrinopathy in cats. The increasing number of diagnoses over time is due to the greater familiarity with the disease and the development of increasingly sensitive diagnostic tools available. This study aimed to retrospectively evaluate the prevalence, clinical characteristics and risk factors of hyperthyroidism in cats admitted at one of the largest veterinary teaching hospital in Brazil. Between 2002 and 2007, 234 cats were admitted to the veterinary teaching hospital of the University of São Paulo, Brazil. Total thyroxine (T4t) serum concentration was measured from all cats. Also analyzed the medical charts of cats. Of the 234 cats, 26 (11.1%) were considered hyperthyroid (T4t  $\geq 3.8$   $\mu\text{g/dL}$ ). Of these 26 cats, only two (7.7%) were initially diagnosed as hyperthyroid. The age of cats ranged from 6 to 27 years old ( $13.1 \pm 4.5$  years). Twelve patients (46.2%) were female and 14 (53.8%) were male. Eight (30.8%) cats were Siamese, while the others were mixed breed (69.2%). Dry food was the most common food type consumed by cats. There was a high prevalence of hyperthyroid cats with concomitant chronic kidney disease (CKD). This study sheds light on the importance of routinely monitoring feline hyperthyroidism and brings epidemiological and clinical data of this endocrinopathy in cats from one of the largest veterinary teaching hospitals in the country.

**KEYWORDS:** Thyroid hormones; cats; endocrine disease.

**RESUMO:** O hipertireoidismo é a endocrinopatia mais frequente em gatos. O aumento do número de diagnósticos ao longo do tempo deve-se à maior familiaridade com a doença e ao desenvolvimento de ferramentas diagnósticas cada vez mais sensíveis. Este estudo teve como objetivo avaliar retrospectivamente a prevalência, características clínicas e fatores de risco do hipertireoidismo em gatos atendidos em um dos maiores hospitais veterinários universitários do Brasil. Entre 2002 e 2007, 234 gatos foram admitidos no hospital veterinário universitário da Universidade de São Paulo, Brasil. A concentração sérica total de tiroxina (T4t) foi mensurada em todos os gatos. Também foram analisados os prontuários médicos dos gatos. Dos 234 gatos, 26 (11,1%) foram considerados hipertireoideos (T4t  $\geq 3,8$   $\mu\text{g/dL}$ ). Desses 26 gatos, apenas dois (7,7%) foram diagnosticados inicialmente com hipertireoidismo. A idade dos gatos variou de 6 a 27 anos ( $13,1 \pm 4,5$  anos). Doze pacientes (46,2%) eram do sexo feminino e 14 (53,8%) do sexo masculino. Oito (30,8%) eram siameses, enquanto os demais eram mestiços (69,2%). A ração seca foi o tipo de alimento mais consumido. Houve alta prevalência de gatos hipertireoideos com doença renal crônica (DRC) concomitante. Este estudo esclarece a importância do monitoramento rotineiro do hipertireoidismo felino e traz dados epidemiológicos e clínicos desta endocrinopatia em gatos de um dos maiores hospitais veterinários do País.

**PALAVRAS-CHAVE:** Hormônios tireoidianos; gatos; endocrinopatia.

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## INTRODUCTION

Hyperthyroidism is a systemic disease due to abnormal thyroid gland activity, leading to excessive production of thyroid hormones (triiodothyronine and thyroxine) (PETERSON; BROOME; RISHNIW, 2016). Feline hyperthyroidism became evident about 35 years ago, since 1979 and 1980 when the first cases of clinical feline hyperthyroidism were reported. Since then, the understanding of the disease has evolved tremendously (CARNEY et al., 2016).

Currently, hyperthyroidism is the most frequently diagnosed endocrinopathy in middle-aged and older cats (PETERSON, 2012). The increasing number of diagnoses of feline hyperthyroidism over time is due to the greater familiarity with the disease and the development of increasingly sensitive diagnostic tools available in the small animal practice (BRUYETTE, 2001). In this study, we performed a retrospective analysis of hyperthyroidism cases in cats admitted to the largest veterinary teaching hospital in Brazil.

## METHODS AND MATERIALS

### Institutional approval

This study was approved by the Animal Care and Ethics Committee of the University of São Paulo and the owners signed written informed consents before enrolment in the study.

### Study population

Between 2002 and 2007, 234 cats presenting various clinical manifestations (suggestive or not of hyperthyroidism) were admitted to the veterinary teaching hospital of the University of São Paulo, Brazil.

### Sampling procedure

Blood samples were collected from all cats (with clinical manifestations suggestive or not of hyperthyroidism) for complementary exams (*i.e.*, complete blood cell counts or biochemical serum profile). Moreover, we blindly selected samples from all animals (n=234) for thyroid function testing. The samples were stored at -70°C.

Serum concentrations of total thyroxine (T4t) were determined using the radioimmunoassay method (Coat-Count T4t total). We considered animals as clinically affected by hyperthyroidism when serum levels of T4t were  $\geq 3.8 \mu\text{g/dL}$  (KIRK; BONAGURA, 1995). We also retrospectively evaluated the medical records of hyperthyroid patients.

As for statistical analysis, we used chi-square test. We analyzed the following simplified variables: diagnosis (urinary tract diseases, cardiovascular diseases, and others), age categories (6-10, 11-15, 16-20, and >25 years), sex (male/female), breed (Siamese/mixed), and nutrition (wet and non-wet food

combinations). We performed descriptive statistics (mean, median, standard deviation, minimum, and maximum) for each physical (heart rate, temperature, and weight) and physiological (T4t, urea, and creatinine) parameter.

The distribution of T4t was tested for normality with the Shapiro-Wilk test. We used the Kruskal-Wallis rank-sum test to relate T4t as a function of age, sex, breed, nutrition, and primary diagnosis. All statistical analysis was performed using R statistical software (version 2.14.0; R Foundation for Statistical Computing) at a  $p < 0.05$  significance level.

## RESULTS

Table 1 summarizes the main data from medical charts. Of the 234 cats, 26 (11.1%) were considered hyperthyroid (T4t  $\geq 3.8 \mu\text{g/dL}$ ) and, therefore, included in this study. Only one of these had its thyroid gland palpated during physical examination. Age ranged from 6 to 27 years old ( $13.1 \pm 4.5$  years). The proportion of each age category was statistically different (DF: 3;  $p < 0.05$ ), but the sample size differed among categories. As for sex ratio, 12 patients (46.2%) were females and 14 (53.8%) males, but such a difference was not significant (DF: 1;  $p > 0.05$ ). As for breed, eight (30.8%) were Siamese and the others mixed-breed (69.2%), with a significant difference (DF: 1;  $p < 0.05$ ). Dry food was the most common food type consumed by the cats in our study population (dry food exclusively in 41% of the cats). Twenty-four per cent of the cats consumed canned wet food combined with other diets, and this proportion was significantly different (DF: 1;  $p < 0.05$ ).

The most common clinical manifestations were anorexia and dysorexia, and some animals had more than one symptom. The primary diagnosis was chronic kidney disease (CKD) (n=12; 46.2%), two presented other urinary tract diseases (n=2; 7.7%), two (n=2; 7.7%) had no diagnosis at the time of consultation, and only two cats (n=2; 7.7%) were initially diagnosed as hyperthyroid. All other patients (n=8; 30.8%) presented other different disorders. There was a higher prevalence of cats with urinary tract diseases when compared to cardiovascular and other diseases (DF: 2;  $p < 0.05$ ).

Table 2 displays the data on vital parameters, and thyroid and renal serum biochemistry. Heart rate (HR) ranged between 64 to 250 bpm ( $170.7 \pm 53.2$  bpm). Tachycardia (HR > 220 bpm) was detected in five cats (25%). Body temperature ranged from 35.6 to 39.1°C ( $37.8 \pm 1.1^\circ\text{C}$ ), except for three cats that presented hyperthermia/pyrexia during the examination. Animal weight varied between 1.9 to 7.5 kg ( $4.0 \pm 1.4$  kg). Azotemia (urea > 56 mg/dL) was observed in 19 cats (76%). The mean value of T4t concentrations was 5.23  $\mu\text{g/dL}$  (67.31 nmol/L).

## DISCUSSION

In this study, we evaluated the prevalence of hyperthyroidism in cats admitted to the largest veterinary teaching hospital in Brazil. In this regard, we identified a high prevalence

**Table 1.** Information of the 26 cats obtained from the medical charts, referring to sex, breed, age, nutrition and primary diagnosis

Cat	Sex	Breed	Age	Nutrition	Primary Diagnosis
1	F	Mixed	14	D,C, HM	Hyperthyroidism
2	F	Siamese	19	D	CKD
3	F	Mixed	17	D, HM	CKD
4	M	Siamese	11	D	Nasal lymphoma
5	F	Mixed	13	D, C	CKD
6	M	Mixed	13	D, HM	Hyperthyroidism
7	F	Siamese	11	D	Feline lower urinary tract disease
8	F	Mixed	11	D	CKD
9	M	Mixed	16	D, HM	CKD
10	F	Siamese	27	C	Feline lower urinary tract disease; CKD
11	M	Mixed	10	D	Feline lower urinary tract disease
12	M	Mixed	15	D, C	Unclassified cardiomyopathy
13	M	Mixed	11	D	CKD
14	F	Mixed	9	D	Lipidosis
15	M	Mixed	15	D	Hypertrophic cardiomyopathy
16	M	Mixed	18	D,C, HM	CKD
17	F	Mixed	10	D, HM	CKD
18	M	Siamese	13	HM	Inconclusive
19	M	Siamese	13	HM	CKD
20	F	Siamese	16	D, HM	CKD
21	F	Mixed	9	D,C, HM	Inconclusive
22	M	Mixed	7	D	Sarcoma
23	M	Mixed	6	D	Feline Respiratory Disease Complex
24	F	Mixed	9	HM	CKD
25	M	Mixed	11	D	Constipation
26	M	Siamese	8	D	Restrictive cardiomyopathy

Nutrition: D - dry (extruded); C - canned (wet); HM - homemade; CKD: Chronic Kidney Disease.

**Table 2.** Descriptive statistics of each parameter for the 26 cats combined, referring to the values of urea, creatine, T4t, heart rate and temperature.

Variable	Mean	Median	DP	Min	Max
Urea (mg/dL)	87.3	66.6	54.4	22	236
Creatinine (mg/dL)	2.0	1.7	0.8	1.1	4.5
T4t *(µg/dL)	5.23	4.41	1.74	3.87	11.97
Heart Rate (bpm)	171	190	53	64	250
Temperature (°C)	37.8	38	1.1	35.6	39.1

\*Total thyroxine.

of hyperthyroid cats. Most likely, improvements in nutrition and veterinary care have increased the longevity of domestic cats. As a result, age-related chronic diseases, such as hyperthyroidism, have been increasingly reported. In general, the prevalence of feline hyperthyroidism has increased worldwide and has been currently diagnosed in 1.5-13.9% of older cats

(CARNEY et al., 2016; PETERSON; BROOME; RISHNIW, 2016; SORDO et al., 2020). In the United States of America, hyperthyroidism prevalence is about 10% in cats older than 10 years (PETERSON, 2012), but similar rates have been documented in many other countries such as European nations, Japan, and New Zealand (FELDMAN; NELSON, 2015). Other studies have reported even higher numbers, reaching a prevalence of 78% (BREE et al., 2018; BARBIERI; PÖPPL, 2019). These variations can be explained by differences in feline populations tested, inclusion and exclusion criteria used, and cutoff points for the thyroid hormone concentration used to diagnose hyperthyroidism (BREE et al., 2018). Specifically in Brazil, there is scarce information about hyperthyroidism, and to our knowledge, the first cases were reported in the late 2000s (BRUYETTE, 2001). This can be a result of its rarity or even underdiagnosed by Brazilian clinicians.

We observed lower T4t values in our cat population when compared to other studies. (PETERSON; MELIAN; RHETT,

2001; PETERSON, 2012; PETERSON, 2013; CARNEY et al., 2016). Serum measurement of T<sub>4t</sub> is used to confirm the diagnosis of feline hyperthyroidism. When its value is increased, the result is extra diagnostic-specific. Serum T<sub>4t</sub> concentrations are elevated in the majority (90-95%) of cats with hyperthyroidism. Only 5-10% of cats with hyperthyroidism have T<sub>4t</sub> within reference values in a first assessment (PETERSON, 2006; PETERSON et al., 2015). Thus, in the present study, the option to use the T<sub>4t</sub> as the only test for the confirmation of hyperthyroidism was in accordance with the international recommendations.

Lower T<sub>4t</sub> levels can be related to the co-manifestation of non-thyroid illnesses (PETERSON, 2013; PETERSON; NICHOLS; RISHNIW, 2017), as already observed in cats with CKD (FREEMAN et al., 2016; GORDON, 2019). When analyzing biochemical parameters, nineteen (76%) cats had azotemia, which has been frequently reported in middle-aged and elderly cats (FELDMAN; NELSON, 2015) and is also related to CKD (FREEMAN et al., 2016).

Regarding risk factors, we detected a high prevalence of hyperthyroidism in specific age, breed, diagnosis, and diet categories. Concerning age, cats had 13.1 years on average, which is considered the most common age cohort for feline hyperthyroidism (FELDMAN; NELSON, 2015; PAULELLI et al., 2018). When comparing breeds, we found that mixed-breed cats were more likely to present hyperthyroidism. A higher incidence in crossbreeds has also been detected in other studies (CROSSLEY et al., 2017).

Diet was another important risk factor in our population. Six cats affected by hyperthyroidism consumed wet food either exclusively or in combination with other food types. Canned wet food is rich in substances that can act as endocrine disruptors and may present inadequate iodine concentrations (CROSSLEY et al., 2017). Hence, several studies have demonstrated that cats fed canned commercial diets are more prone to develop hyperthyroidism (IKEDA et al., 2000; CROSSLEY et al., 2017; PAULELLI et al., 2018). In Brazil, wet food is not the most common type of food consumed (CROSSLEY et al., 2017). However, most commercial brands (either dry or wet) have a high content of plant-derived proteins, particularly soybeans, and another important endocrine disruptor (PAULELLI et al., 2018).

As for sex-effect, we found no sexual predisposition, which corroborates most findings in the feline literature (JONES; ENGDAHL; WEISS, 2019). Other parameters, however, disagree with previous findings. For instance, in our study, only three cats (15.7%) were hyperthermic, while other authors found that 70% of patients presented high body temperature (PETERSON; MELIAN; RHETT, 2001). Body temperature increase in hyperthyroid cats may be due to a direct action of thyroid hormones in the hypothalamic thermoregulatory center or secondary to the concomitant inflammatory disease (PETERSON; MELIAN; RHETT, 2001).

In our study, many cats with hyperthyroidism had concomitant CKD. Importantly, CKD is one of the most common comorbidities associated with feline hyperthyroidism (CARNEY et al., 2016). In this regard, CKD has been described to be unnoticeable in cats with hyperthyroidism due to an increased glomerular filtration rate imposed by endocrinopathy hypermetabolism; however, feline hyperthyroidism treatment may unmask the pre-existing CKD (CARNEY et al., 2016).

Another important issue is the thyroid gland palpation for diagnosing feline hyperthyroidism in an early stage so that further complications could be prevented. Indeed, thyroid gland palpation is a non-invasive and inexpensive procedure for screening cats with suspected hyperthyroidism (PAEPE et al., 2008). However, a recent study reported a high prevalence of cats with hyperthyroidism without a palpable gland (> 60%), reflecting the failure to detect hyperthyroidism by physical examination and, therefore, erroneously suggesting a low prevalence for this endocrinopathy (BREE et al., 2018).

With the increasing numbers of studies, training courses, and skilled professionals in the areas of veterinary endocrinology and feline medicine, hyperthyroidism can be more accurately diagnosed. However, additional research is needed to clarify the real prevalence of hyperthyroidism in feline species. An increased prevalence of this endocrinopathy, mostly in older cats, would be expected if thyroid palpation and thyroid hormones measurements were routinely performed.

## CONCLUSIONS

We identified that hyperthyroidism was more prevalent in old cats belonging to older-senior or geriatric age groups and occurred mostly in crossbred animals. Chronic kidney disease was the most prevalent comorbidity and canned wet food was the most consumed by the hyperthyroid cats.

By retrospectively assessing this hyperthyroid cat population, there are three major considerations about our results: i) hormonal assessment greatly improved the hyperthyroidism diagnosis; ii) most cats presented classic clinical manifestations of hyperthyroidism, but some of the symptoms were distinct from those reported in the feline literature; iii) hyperthyroidism was not among the main suspicions to diagnosis by practitioners since the thyroid palpation was not routinely performed in elderly feline patients.

Still, further studies addressing hyperthyroidism in domestic cats are welcome to determine the prevalence of this disease in Brazil.

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