Prevalence of and risk factors for feline hyperthyroidism in Hong Kong

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Abstract

A study was conducted to determine the prevalence of and potential risk factors for feline hyperthyroidism in Hong Kong. Serum total thyroxine (T_4) was measured in 305 cats aged 10 years and older that presented at various veterinary clinics in Hong Kong. The prevalence of hyperthyroidism ($T_4 > 50$ nmol/l) within this population was 3.93% and there was no significant difference in prevalence between healthy (3.16%) and sick (4.37%) cats. Older cats (>15 years) were more likely to be affected and domestic shorthair cats were less likely to be diagnosed with hyperthyroidism than the other breeds combined. No specific association between the development of feline hyperthyroidism and food type was observed. The prevalence of feline hyperthyroidism in Hong Kong was less than that reported for most other parts of the world, despite the presence of previously identified risk factors.

Introduction

Feline hyperthyroidism is a multi-systemic disorder resulting from excessive circulating concentrations of l-tri-iodothyronine (T_3) and, or, l-thyroxine (T_4).[1, 2, 3 and 4] The illness occurs in middle to old age cats, with a reported range of 4–22 years (median age approximately 13 years).[4] Only 5% of hyperthyroid cats are younger than 10 years of age at the time of diagnosis.[4] The disease was first reported in cats in 1979 and has since been recognised with increasing frequency.[5, 6, 7, 8, 9, 10 and 11] It is now accepted as the most common endocrine

disorder in cats and the most important cause of morbidity in middle-aged cats in the United States[9, 10 and 12] and the United Kingdom.[3] The disease is also commonly seen in Australia, Canada, Europe, Japan and New Zealand.[12, 13, 14, 15, 16, 17 and 18]

Not much is known about the worldwide distribution of feline hyperthyroidism and there are very few published incidence rates or prevalence estimates.[9] A report on the hospital prevalence in veterinary hospitals in North America suggested that there was a marked increase between 1979 and 1985.[8] The average prevalence in 1979 was 0.3% and in 1985 that number had increased to 4.5%. Edinboro et al[19] reported that age-adjusted hospital prevalence in North America increased from 0.1% in 1978–1982 to 2% in the period of 1993–1997. An increase in the hospital prevalence was also reported in Germany where the number of affected cats increased from 0.2% in 1987–1994 to 2.6% in 1998.[20] Miyamoto et al[16] reported a prevalence of 8.9% in cats 9 years and older that were brought to hospitals in two areas in Japan whilst Sassnau[18] reported a prevalence of 11.4% among cats 8 years and older in an urban population in Germany. Wakeling et al[21] reported a yearly incidence of 11.92% for cats older than 9 years of age in a first opinion hospital in the United Kingdom. So far the cause of the worldwide occurrence as well as the increased incidence has eluded scientists and it has been postulated that immunological, infectious, nutritional (eg, iodine), environmental (eg, toxins or goitrogens), or genetic factors may play a role in the development of the condition.[9, 12, 13, 22 and 23]

The first published case–control study of cats with hyperthyroidism found associations between hyperthyroidism and consumption of canned food in the 5 years prior to diagnosis, partial or complete indoor housing, non-Siamese breed, and regular exposure to fertilizers, herbicides and pesticides used on the lawn and flea control products.[8] A subsequent study found that consumption of canned commercial cat food and use of cat litter were significantly associated with greater risk of hyperthyroidism.[24] Use of topical ectoparasite preparations was less strongly associated with increased risk of developing hyperthyroidism. Both Siamese and Himalayan cats had significantly lower risk compared to other cat breeds. A further study found that increasing age and preference for fish or liver and giblets flavours of commercial canned food in the present diet were associated with greater risk of hyperthyroidism.[25] A more recent study concluded that the increase of feline hyperthyroidism was not solely the result of ageing of the cat population and a significant association was found between hyperthyroidism and consumption of canned food, particularly pop-top cans.[19] In that study the risk for hyperthyroidism was found to be greater for female than for male cats. Olczak et al[17] also found that female cats, cats eating canned food and cats sleeping on

the floor, were at greater risk of developing hyperthyroidism. In addition, they found that purebred cats were at much lower risk of being diagnosed with hyperthyroidism than domestic short- and longhaired cats. In a small survey in 2006, Sassnau found that the prevalence of feline hyperthyroidism increased with age. Significantly more male than female cats were affected in that study.

All these studies suggest that diet may play a role in the pathogenesis of feline hyperthyroidism and the iodine content of different cat foods has been investigated.[26 and 27] The concentration of iodine varies widely in commercial cat foods in the United States and New Zealand, with some foods containing very small amounts and others have amounts dramatically exceeding current recommendations for cats. This variation has fuelled speculation that cats eating diets varying in iodine content over time may be more likely to develop hyperthyroidism.

Further research into the worldwide prevalence as well as presence of possible causative factors would help to shed light on the cause and pathogenesis of this disease and lead to preventative measures.[9] As far as the authors are aware, no prevalence studies have been completed in Hong Kong, a geographic area in which hyperthyroidism in cats is thought to be rare. The main aims of this study were to determine the prevalence of feline hyperthyroidism in Hong Kong and to determine the presence of potential risk factors associated with the disease in this specific geographic location.

Materials and methods

The study was conducted on cats that were presented at various veterinary practices in Hong Kong between June 2006 and August 2007. Cats were included in the study if they were 10 years of age or older and had spent their whole life in Hong Kong. Cats were excluded from the study if they were imported to Hong Kong from other countries, if they presented in shock or were moribund, if their physical state precluded the collection of a blood sample, if they were undergoing chemotherapy or if they had been treated with drugs that potentially affect T_4 concentrations such as carbimazole, glucocorticoids and trimethoprim-potentiated sulphonamides. The veterinarians taking the samples completed a questionnaire regarding the health of each cat. Each owner completed a questionnaire regarding vaccination history, internal and external parasite control, diet and the environment of their cat.

Blood samples were collected by jugular venepuncture, transferred into plain tubes and centrifuged prior to separating the serum. The sera were stored at −70°C and shipped on dry ice to the Veterinary Faculty at the University of Pretoria, South Africa where they were

stored at −80°C. Serum total T_4 concentration was determined by use of a commercially available radioimmunoassay (RIA) kit (Coat-A-Count canine total T_4, DPC, Los Angeles CA). For total T_4 the feline reference interval was 12.8–50.0 nmol/l (1.0–3.9 μg/dl).[28] All cats with a serum total T_4 concentration greater than 50 nmol/l were classified as hyperthyroid. Serum alanine aminotransferase (ALT) and alkaline phosphatase (ALP) activities were measured in all the samples by use of a modified colorimetric method (ALT) and a modified kinetic measurement (ALP), both from Alfa Wasserman clinical Chemistry systems (ACE & NExCT).

Prevalence of hyperthyroidism, with exact binomial 95% confidence intervals (CIs), was calculated for all cats combined, for cats classified as healthy (no clinically significant disease identified) and for those classified as sick. Prevalence was compared between healthy and sick cats using a two-tailed Fisher's exact test.

Univariable associations between potential risk factors and hyperthyroidism were assessed using a two-tailed Fisher's exact test. Thereafter, all predictors were entered into a multiple logistic regression model to estimate their effect on the risk of hyperthyroidism. To determine whether age should be included as a continuous or categorical variable, it was categorised into quintiles and the log odds of hyperthyroidism for each quintile was estimated using logistic regression.[29] Because a monotonic change in estimated log odds was not seen with each successive quintile, age was modelled as a categorical variable with three categories (10–14 years, 15–19 years and ≥20 years). The model was developed by backward elimination by successively dropping the least significant predictor until all remaining independent variables were significant in the model with $P_{Wald} \leq 0.1$.

Associations between clinical signs and hyperthyroidism were assessed on a univariable level using a two-tailed Fisher's exact test. Associations between raised ALT activities and hyperthyroidism, and between raised ALP activities and hyperthyroidism, were assessed using a two-tailed Fisher's exact test.

The fit of the final logistic regression model for risk factors was assessed using the Hosmer–Lemeshow goodness-of-fit test. All analyses were done using STATA version 10.0 (Stata Corporation, College Station, TX, USA).

Results

The study population consisted of 305 cats. Most of the cats were sampled at the Society for the Prevention of Cruelty to Animals (SPCA), Hong Kong clinics in Wanchai (250 cats), Kowloon (26 cats) and Hang Hau (seven cats). The remaining cats were sampled at private

veterinary practices in Mid-Levels (17), Wanchai (three) and Happy Valley (two). Breeds included domestic shorthair (DSH) (181), domestic longhair (DLH) (61), Persian and Persian crosses (38), Angora (10), Himalayan (seven), Chinchilla (four), Siamese and Siamese crosses (three) and one British Shorthair. There were 166 females (153 ovariohysterectomised) and 139 males (120 castrated). The median age of the cats was 13 (range 10–26 years).

Of the 305 cats, 62 were presented for annual vaccinations, 57 were presented for routine visits and 184 were presented for various illnesses. Two cats were presented for unknown reasons. On the basis of the veterinary assessment the cats that were presented for routine visits were classified as 'healthy' or 'sick' and this brought the total of healthy cats to 95 and the total of the sick cats to 206. The health status was not recorded for four cats.

Twelve cats were diagnosed as hyperthyroid (total T_4 > 50 nmol/l). Their signalment and laboratory values are depicted in Table 1. The prevalence of hyperthyroidism in the entire study population was 3.93% (95% CI: 2.05–6.77) and there was no significant difference in prevalence of hyperthyroidism between healthy (3.16%) and sick (4.37%) cats (P = 0.76) (Table 2).

Table 1.

Signalment and laboratory values of 12 hyperthyroid cats

Cat number	Sex	Breed	Age	TT$_4$ (nmol/l) (µg/dl)[1]	ALT (U/l)[2]	ALP (U/l)[3]
3	NF	DLH	14	172.33 (13.36)	421	75
21*	NF	DLH	17	53.36 (4.14)	195	45
452	NM	Chinchilla	16	66.62 (5.16)	72	55
620	NF	DLH	14	57.43 (4.45)	70	63
628	NM	Persian	17	83.39 (6.46)	83	45
745	NF	DSH	17	166.31 (12.89)	204	241
752*	NM	Persian	19	104.21 (8.08)	69	56
763*	NF	DSH	18	62.05 (4.81)	88	80
774	NF	DSH	10	72.09 (5.59)	42	47
784	NF	DLH	10	52.29 (4.05)	37	55
812	NF	DLH	14	111.41 (8.64)	154	66

Cat number	Sex	Breed	Age	TT$_4$ (nmol/l) (µg/dl)[1]	ALT (U/l)[2]	ALP (U/l)[3]
835	NF	DSH	22	109.21 (8.47)	470	163

N = neutered, F = female, M = male, TT$_4$ = total T$_4$.

Reference ranges: [1]total T$_4$ 12.8–50.0 nmol/l (1.0–3.9 µmol/dl); [2]ALT 3.6–42 IU/l; [3]ALP 35–123 IU/l.

[*] These cats were considered healthy at the time of sampling.

Table 2.

Prevalence of hyperthyroidism (total T$_4$ > 50 nmol/l) in 305 cats 10 years and older presented to veterinary clinics in Hong Kong

	Number of cats	Prevalence (%)	95% CI
Sick cats	9/206	4.37	2.02–8.13
Healthy cats	3/95	3.16	0.66–8.95
Disease status unknown	0/4	0.00	0.00–52.71
Total	12/305	3.93	2.05–6.77

Although there were more female cats (5.42%) with hyperthyroidism than male cats (2.16%), the difference was not statistically significant (Table 3). There was no statistically significant relationship between vaccinations, parasite control or indoor environment and the development of hyperthyroidism. There was also no statistically significant relationship between the consumption of a canned food diet by the cats and hyperthyroidism.

Table 3.

Univariable analysis of risk factors for hyperthyroidism (total T$_4$ > 50 nmol/l) in cats 10 years and older presented to veterinary clinics in Hong Kong

Variable	Category	N	Hyperthyroid cats		
			n	*%*	*P**
Age	10–14 years	208	5	2.4	0.06
	15–19 years	91	6	6.59	

Variable	Category	N	Hyperthyroid cats		
			n	%	P*
	20–26 years	6	1	16.67	
Sex	Female	166	9	5.42	0.2
	Male	139	3	2.16	
Breed	DSH	181	4	2.21	0.2
	DLH	61	5	8.2	
	Persian type	49	3	6.12	
	Angora	10	0	0	
	Other breed	4	0	0	
Number cats in house†	1	161	5	3.11	0.9
	2	60	2	3.33	
	>2	62	3	4.84	
Vaccination†	Yes	199	7	3.52	>0.999
	No	76	3	3.95	
De-wormed†	Yes	137	6	4.38	0.8
	No	129	4	3.1	
Flea control†	Yes	138	7	5.07	0.3
	No	124	3	2.42	
Exclusively indoors†	Yes	258	9	3.49	>0.999
	No	20	0	0	
Canned food diet†	Yes	159	7	4.4	>0.999
	No	101	4	3.96	
Water†	Tap unboiled	119	5	4.2	0.6
	Tap boiled	120	4	3.33	

Variable	Category	N	Hyperthyroid cats		
			n	**%**	**P***
	Other	17	1	5.88	

N = number of cats from study population, n = number of hyperthyroid cats.

* P-value for two-tailed Fisher's exact test.

† Data were not available for all of the cats in the study population.

Only breed and age were retained in the final logistic regression model of risk factors (Table 4). DSH cats tended to be less likely than all other breeds combined, to be diagnosed with hyperthyroidism (odds ratio (OR) = 0.30, 95% CI = 0.08–1.06), while there was a tendency for cats in the two older age categories to be more likely to be diagnosed with hyperthyroidism than 10–14 year old cats.

Table 4.

Final logistic regression model of risk factors for hyperthyroidism (total T_4 > 50 nmol/l) in cats 10 years and older presented to veterinary clinics in Hong Kong

Variable	Category	OR	95% CI	P
Breed	DSH	0.30	0.08–1.06	0.06
	Other*	1.00	–	–
Age	10–14 years*	1.00	–	–
	15–19 years	2.77	0.82–9.40	0.10
	20–26 years	11.88	1.06–133.7	0.05

Hosmer–Lemeshow goodness-of-fit test χ^2 = 0.38 (3 df), P = 0.95.

* Reference category.

Of the three hyperthyroid cats that were considered healthy, one presented for routine vaccination and two presented for routine health checks with no systemic signs. Of the nine hyperthyroid cats that were sick, three had gastrointestinal signs (vomiting and/or diarrhoea), two were seen because of weight loss, one was seen for an urocystolith and one was

producing dilute urine and came in for a routine blood test. In two cats the illnesses were not specified. The mean ± SD T_4 concentration in the three hyperthyroid cats classified as healthy was 73.2 ± 27.2 nmol/l, and that of the nine hyperthyroid cats classified as sick was 99.0 ± 44.8 nmol/l. This difference was not statistically significant ($P = 0.38$).

Table 5 lists the frequency of the main clinical features in the hyperthyroid cats. Weight loss and raised ALT activity were the most common findings, followed by vomiting, diarrhoea and polyphagia. Only one of the affected cats had a palpable thyroid lobe. Univariable analysis (Table 6) for these clinical signs as predictors of hyperthyroidism demonstrated that the presence of the following factors was significant ($P \leq 0.05$): polyphagia, diarrhoea and raised ALT and ALP activities.

Table 5.

Main clinical features in 12 hyperthyroid cats

Finding	Number of cats	%
Weight loss	7	63.6
Alanine aminotransferase > 126 (U/l)	5	41.7
Vomiting	4	36.4
Diarrhoea	3	27.3
Polyphagia	3	27.3
Tachycardia	3	27.3
Alkaline phosphatase > 123 (U/l)	2	16.7
Tachypnoea	2	16.7
Cardiac murmur	1	8.3
Palpable thyroid lobe	1	8.3

Table 6.

Univariable analysis of the clinical signs associated with hyperthyroidism (total $T_4 > 50$ nmol/l) in cats 10 years and older presented to veterinary clinics in Hong Kong*

Variable	Category	N	Hyperthyroid cats		
			n	%	*P†*
Weight loss	Yes	140	7	5.00	0.4

Variable	Category	N	Hyperthyroid cats		
			n	%	P†
	No	155	4	2.58	
Polyphagia	Yes	19	3	15.79	0.03
	No	278	8	2.88	
Heart rate	<200	183	7	3.83	0.6
	200–240	93	4	4.30	
	>240	12	1	8.33	
Cardiac murmur	Yes	39	1	2.56	>0.999
	No	260	11	4.23	
Respiration	Normal	269	10	3.72	0.5
	Increased	24	2	8.33	
	Dyspnoeic	8	0	0.00	
Vomiting	Yes	80	4	5.00	0.5
	No	217	7	3.23	
Diarrhoea	Yes	11	3	27.27	0.005
	No	283	8	2.83	
Palpable thyroid	Yes	2	1	50	0.08
	No	296	11	3.72	
Alanine aminotransferase > 126	Yes	41	5	12.20	0.01
	No	264	7	2.65	
Alkaline phosphatase > 123	Yes	6	2	33.33	0.02
	No	298	10	3.36	

[*] Data were not available for all of the cats in the study population.

† P-value for two-tailed Fisher's exact test.

Discussion

The prevalence of hyperthyroidism in the study population of geriatric cats in Hong Kong was 3.93%. This demonstrates that although this disease is present in Hong Kong the prevalence is lower than the reported prevalence in geriatric populations in Japan, the United Kingdom and Germany.[16, 18 and 21] The reason for the lower prevalence in Hong Kong could be due to differences in genetic factors, diet or environment and comparative epidemiological studies will be necessary to compare these factors between feline populations in Hong Kong and elsewhere.

There was no difference in the prevalence of hyperthyroidism between cats that were considered healthy and those that were considered sick. This highlights the fact that the disease is currently under-diagnosed in Hong Kong and that it is a challenging and insidious disease which, in its early stages, is often confused with other diseases or normal ageing changes.

Scarlett et al[8] and Kass et al[24] showed that Siamese cats have a significantly lower risk of developing hyperthyroidism compared with other breeds. In our study there were only three Siamese type cats and none of them had hyperthyroidism. However, when the DSH cats were compared with the rest of the cats, the shorthair group had a significantly lower likelihood of developing hyperthyroidism. It is, therefore, possible that there is a genetic protective factor involved in the DSH cats in Hong Kong. We suspect that a large percentage of the DSH cats in Hong Kong is of oriental (or Siamese) descent and this could explain the possible contribution of a genetic protective factor. None of the Angora cats in our study had hyperthyroidism, but the low number of Angora cats (10 cats) prevented any important conclusions.

In this study there was an increased risk of hyperthyroidism with increasing age, although the magnitude of this increase could not be estimated precisely due to the low number of cases. This is consistent with the findings of previous studies[25] and also concurs that feline hyperthyroidism is a disease of middle-aged to old cats. There were more female than male cats that had hyperthyroidism but the difference was not statistically significant. Most of the previously published studies reported no sex predilection for feline hyperthyroidism.[3, 7, 8, 10 and 24] There were, however, two studies that showed a significant association between female cats and hyperthyroidism[17 and 19] whereas in one study[18] there were significantly more male than female cats affected.

In the present study an association between feeding canned food and the development of hyperthyroidism was not found. This finding is in sharp contrast to previous studies where a strong association was found between feeding canned food and developing the disease.[8, 17, 19, 24 and 25] Seven of the hyperthyroid cats in our study ate a mixed canned/dry food diet and four cats ate an exclusive dry food diet. (Dietary information was not provided for the remaining cat.) The lack of evidence for canned food being associated with feline hyperthyroidism can be due to the low numbers of hyperthyroid cats in our study, different packaging materials or even different iodine content of the canned food in Hong Kong. The presence of hyperthyroidism in cats that are fed exclusively dry food can be due to the presence of a different causative factor in either the food or the environment of these cats. However, hyperthyroidism may have a multi-factorial aetiology and there could potentially be an interaction with a genetic predilection.

There were no characteristic clinical features amongst the cats that were hyperthyroid and only one cat exhibited the typical clinical syndrome of voracious appetite with severe weight loss that has been described elsewhere.[1, 3, 5, 7, 10 and 30] The lack of characteristic clinical signs could be due to the presence of a mild or early form of the disease, but could also be due to an atypical form of the disease. Despite the absence of recognisable clinical signs, this study showed that the disease needs to be considered if any of the following factors are present in an older cat: polyphagia, diarrhoea and raised ALT and ALP activities.

The present study had several limitations that need to be considered. The low prevalence of hyperthyroidism made it difficult to compare the group of hyperthyroid cases with the other cats. It is also possible that there could be some bias, because the study only included cats that were brought in to veterinary practices by their owners. However, the type of owner that brings their pet in for veterinary care is most likely the type of owner that could expose their cat unintentionally to the possible risk factors such as canned food, indoor environment and topical ectoparasite applications that have been described in previous studies. Another major limitation is the size of the study population – a bigger study population would have yielded more positive cats and might have produced more statistically significant results.

Another shortfall of this study was that hyperthyroid cats with early or subclinical disease or hyperthyroid cats with severe concurrent non-thyroidal illness would have been missed due to normal serum T_4 concentrations.[3, 22, 23 and 32] Peterson et al[31] found that 80 of 917 (8.7%) cats with hyperthyroidism had serum total T_4 concentrations within reference range. If this figure is extrapolated to the current study the total prevalence could have been as high as 4.3%.

This study concluded that the prevalence of hyperthyroidism in cats in Hong Kong is less than in most other parts of the world, despite the presence of previously identified risk factors. It is possible that the prevalence of the disease will increase in future unless we can identify and eliminate known risk factors. The disease should be considered in any aged cat that presents with polyphagia, diarrhoea or raised ALT and ALP activities.

Acknowledgements

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