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Feline asthma: A cross-sectional study on determinant and conditioning factors

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Table of contents

List of figures.....	iii
List of tables	iii
List of abbreviations.....	iii
Title page	1
Abstract	2
Keywords.....	2
<i>Resumo</i>	3
<i>Palavras-chave</i>	3
1. Background.....	4
2. Materials and methods.....	5
2.1 Data collection.....	5
2.2 Data analysis	6
3. Results	6
3.2. Feline asthma	8
3.3. Stress	11
3.4. Body condition	13
3.5. Environment	13
4. Discussion	14
Acknowledgements	16
References	17
Annexes	I
Annex 1: Questionnaire applied	II

List of figures

Figure 1- Geographical distribution of inquired cats	8
Figure 2- Symptoms associated with asthma crisis among diagnosed cats (n=16).	10
Figure 3- Circumstances associated with increased symptoms or triggering crisis.	10
Figure 4- Relative frequency (%) of symptoms associated with cat stress, as reported by owners.....	12
Figure 5- Stress related behaviors in the presence of co-inhabitating cats.	12

List of tables

Table 1- Characterization of studied cat population by signalment, lifestyle and acquisition. ..	7
Table 2- Characterization of cats with respiratory disease studied by signalment, lifestyle and acquisition.	9
Table 3- Features of the disease in asthmatic cats.	11
Table 4- Characterization of body condition regarding all the studied population and cats with asthma/respiratory disease.	13
Table 5- Characterization of environment regarding all the studied population and cats with asthma/respiratory disease	14

List of abbreviations

EU – European Union

WASA - World Small Animal Veterinary Association

SAS – Statistical analysis system

Feline asthma: A cross-sectional study on determinant and conditioning factors

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Abstract

Feline asthma is a chronic inflammatory disease of the lower respiratory airways that has shown an increased incidence in the past decades. It is important to acknowledge that feline and human asthma are very similar in their pathophysiology and symptomatology, which can be justified by common predisposing and conditioning factors.

Given the above, the present study aimed to investigate some of the possible determining and conditioning factors associated with the occurrence of feline asthma, previously reported in literature. With such purpose, a cross-sectional (self-completed) questionnaire-based study targeting Portuguese speaking owners of cats was carried out. The questionnaire comprised five main sections, regarding animal identification and characterization, respiratory disease, animal stress, animal physical condition, and animal housing conditions. After constructed, the questionnaire was validated and applied in both paper and digital form, between September 2018 and March 2019.

One hundred and eighty nine questionnaires were analyzed, of which 16 corresponded to cats diagnosed with asthma and two other with feline cough. Eighty two percent of studied cats, as well as cats with asthma or respiratory disease, were of mixed breed and 76% were neutered, living 62% indoor exclusively and with other cats as co-inhabitants (68%), mainly in and urban area (56%) from the north (47%) and central (37%) mainland regions. Equal male/female ratio was also observed in both groups. According to the owners' perception, the cats were mostly active and with the ideal weight. The symptoms that owners more often associated with asthma crisis were respiratory wheezes and cough, whereas the worsening of such symptoms occurred in spring and autumn, and in case of changes in the environment. Frequently reported symptoms of stress were excessive hygiene and not sleeping with belly up. The correlation between stress-related diseases and asthma was close to significance ($p=0.065$), being urinary tract infection the disease more frequently associated with stress. Statistical analysis showed that cats with access to both indoor and outdoor showed less symptoms of stress ($p=0.032$). Although close to significance ($p=0.07$), the presence of pollutant industries was not correlated to asthma in enrolled cats. Finally, in most of the houses in which an asthmatic cat lived in, no owner or other co-inhabitant relatives with asthma existed (78.8%).

The identification of further conditioning and determining factors of feline asthma was hindered by the relatively small number of asthmatic cats enrolled and the fact that feline asthma is frequently underdiagnosed. Nevertheless, the prevalence was slightly superior (8.5%) to the ones previously reported (3-5%). The paucity of similar epidemiological studies in cats demonstrates the importance of the current work and the need to conduct further studies on risk factors associated with the disease, both in humans and cats, and eventually to assess if cats could be used as sentinels for the disease.

Keywords

Allergens, environment, feline asthma, obesity, pollutants, risk factors, stress

Resumo

A asma felina é uma doença inflamatória crônica das vias respiratórias inferiores com um aumento na incidência nas últimas décadas. É importante reconhecer que asma felina e humana são muito semelhantes, na fisiopatologia e sintomatologia, o que pode ser justificado por fatores predisponentes e condicionantes comuns.

Nesta sequência, o presente estudo teve como objetivo investigar alguns dos possíveis fatores determinantes e condicionantes associados à ocorrência de asma felina, anteriormente descritos na literatura. Com este propósito, foi realizado um estudo transversal baseado em questionário (auto-preenchido) dirigido a tutores lusófonos de gatos. O questionário incluiu cinco seções principais, referentes à identificação e caracterização, doenças respiratórias, stress, condição corporal e condições de alojamento dos animais. Após construído, o questionário foi validado e aplicado, em suporte físico e digital, entre setembro de 2018 e março de 2019.

Cento e oitenta e nove questionários foram analisados, dos quais 16 correspondiam a gatos diagnosticados com asma e dois com tosse felina. Oitenta e dois por cento dos animais em estudo, assim como os gatos com asma ou doença respiratória, eram de raça indeterminada e 78% estavam castrados, vivendo 62% exclusivamente dentro de casa e com outros gatos como coabitantes (68%), principalmente em áreas urbanas (56%) das regiões norte (47%) e central do continente (37%). Igual rácio macho/fêmea foi observado em ambos os grupos. De acordo com a percepção dos tutores, os gatos eram maioritariamente ativos e com o peso ideal. Os sintomas que os tutores mais frequentemente associaram a crises de asma foram “assobios” respiratórios e tosse, enquanto o agravamento de tais sintomas ocorre na primavera e outono, e em caso de mudanças no ambiente. Os sintomas de stress mais frequentemente relatados foram higiene excessiva e não dormir com a barriga para cima. A correlação entre as doenças relacionadas com o stress e a asma esteve próxima da significância ($p=0,065$), sendo a infecção do trato urinário a doença mais frequentemente associada ao stress. A análise estatística mostrou que os gatos com acesso ao interior e ao exterior apresentaram menos sintomas de stress ($p=0,032$). Embora próximo da significância ($p = 0,07$), a presença de indústrias de poluentes não foi correlacionada com a asma em gatos em estudo. Finalmente, na maioria das casas em que um gato asmático vivia, não havia tutor ou outros parentes co-residentes com asma (78,8%).

A identificação de outros fatores condicionantes e determinantes da asma felina foi dificultada pelo número relativamente pequeno de gatos asmáticos registados e pelo fato de que a asma felina é frequentemente subdiagnosticada. No entanto, a prevalência foi ligeiramente superior (8,5%) à reportada anteriormente (3-5%). A escassez de estudos epidemiológicos semelhantes em gatos demonstra a importância do trabalho atual e a necessidade de realizar mais estudos sobre os fatores de risco associados à doença, tanto em humanos quanto em gatos, e eventualmente avaliar se os gatos poderiam ser usados como sentinelas para a doença. .

Palavras-chave

Alergenos, ambiente, asma felina, obesidade, poluentes, factores de risco, stress

1. Background

Feline asthma is a chronic and recurrent inflammatory disease of the lower respiratory airways and it is becoming one of the most frequent pathologies affecting the respiratory tract of cats, causing significant morbidity and even mortality (Reinero, 2011; Rosenberg & Druey, 2018; Taylor, 2017).

Asthma is characterized by a reversible airflow limitation caused by an airway hyperactivity, increased mucus production and smooth muscle hypertrophy due to lower airway inflammation (type I hypersensitivity reaction) (Rosenberg & Druey, 2018; Venema & Patterson, 2010).

According to recent literature, asthma affects approximately 1-5% of cats across all ages, breeds and genders, although some studies show an increased incidence in Siamese breed and age of occurrence between four and five years, although it can occur at any age (Dunbar Gram, J. Milner, & Lobetti, 2018; Rosenberg & Druey, 2018; Vapalahti *et al.*, 2016; Venema & Patterson, 2010).

Despite feline asthma being the most frequently diagnosed lower airway disease, there are other non-infectious, inflammatory diseases affecting cats, such as feline cough, that are often not properly diagnosed or misdiagnosed as asthma (Taylor, 2017), for this reason they were included in this study.

In the same way as feline asthma, an increase in human asthma during the latter part of the 20th century in developed countries was also noticed. In fact, the disease itself is very similar. The coexistence of cats and humans in the same environment raises the hypothesis that it can be triggered by common risk factors and that cats can be considered as sentinels for human asthma (Heller, Lee-Fowler, Liu, Cohn, & Reinero, 2014; Mueller, Janda, Rhyner, & Marti, 2016; Neo & Tan, 2017; Reinero, 2011; Toskala & Kennedy, 2015).

To better understand this disease and its etiology several experimental models were developed to replicate clinical and pathophysiologic features of the naturally developing conditions and to test clinically relevant allergens in both humans and cats. Bermuda grass, house dust mites and other grasses and weeds, cat litter, strong chemical smells, building dust, perfumes, hairspray, tobacco smoke, and other environmental pollutants, were associated with the development of the disease in cats, being most of them also common to human asthma (Fehrenbach, Wagner, & Wegmann, 2017; Reinero, 2009, 2011; Taylor, 2017).

On the other hand, although environmental pollutants, exercise, stress, obesity, infections and allergens are the most common risk factors associated to human asthma, most haven't been studied in cats (Reinero, 2011; Toskala & Kennedy, 2015). Besides outdoor pollution, a known major risk factor for the development of asthma, nowadays indoor pollution has also been recognized and became an important risk factor in human asthma and probably also in feline asthma, as reported in recent studies (Lin, Lo, Wu, Chang, & Wang, 2018).

Risk factors as stress and obesity were positively correlated to an increase in childhood asthma in humans, and even though their prevalence is increasing in both species, such correlation lacks confirming studies in cats (Toskala & Kennedy, 2015).

Furthermore, in human asthma the hygiene hypothesis was also analyzed, and correlates an exposure to infection and allergens in infancy with a decrease in developing allergic diseases in adulthood (Toskala & Kennedy, 2015). Indeed previous studies showed a negative correlation between neonatal

exposure to allergens and the development of feline asthma (Heller *et al.*, 2014; Toskala & Kennedy, 2015)

Even though the avoidance of certain allergens has been reported as beneficial in decreasing clinical signs, most of the time is not possible to identify the cause, as there is still very little information about its etiology, reinforcing the importance of further research in this field for better understand treatment and prevention (Reinero, 2011).

Given the above, the present study aimed to investigate some of the possible determining and conditioning factors associated with the occurrence of feline asthma.

2. Materials and methods

2.1 Data collection

This was a cross-sectional (self-completed) questionnaire-based study targeting Portuguese owners of cats with or without asthma diagnosed. The inclusion criteria included being a cat owner with at least 18 years old, living in Portugal or of Portuguese language, and living with and taking care of the cat. Exclusion criteria were based on the extent of reply of the questionnaire, being excluded if one or more sections were not completely answered.

The study design complied with the recent General Data Protection Regulation (Regulation (EU) 2016/679 in force since May 2018 as well as other relevant legislation. The Scientific Council of University School Vasco da Gama, Coimbra, approved the study.

The initial drafting version of the questionnaire was constructed after a literature review regarding feline and human asthma. To enable internal validation, a panel composed by one veterinary epidemiologist, one statistical professional and five small animal veterinarian clinicians was asked to answer the questionnaire and give their direct feedback to the authors, regarding the extension and structure of the questionnaire, and if responses were clear and correctly evaluated the issue, allowing data analysis. In addition, in the validation phase, 10 cat owners were also asked to answer the questionnaire to assess the extension of the questionnaire and if responses were unambiguous and of simple understanding. The questionnaire was adjusted accordingly and the final version (Annex 1) included 55 questions structured in five main groups, regarding information on [A] animal identification and characterization, with 9 questions, [B] respiratory disease, with 10 questions, [C] animal stress, with 18 questions, [D] animal physical condition, with 4 questions and [E] animal housing conditions, with 14 questions.

The first group [A], included questions regarding the breed, age, sex and reproductive stage, weight, district of residence, lifestyle and acquisition site.

In the second group [B], the questions addressed the presence or absence of respiratory disease. If present, the frequency and characteristics of the episodes and in which type of scenarios it worsened. In this same group, questions were included relating to the exposure and development of diseases in the pediatric period.

In the third group [C], to perceive the animal's stress level, a grading scheme with several circumstances related to stress was presented, the existence of other animals and their behavior with the cat was also questioned as well as the occurrence of urinary tract infections (Atkinson, 2018; Mariti *et al.*, 2017).

The fourth group [D] considered the cat's physical condition through the adaptation of a body condition score scheme system based in a five-point scale adapted from the WSAVA (World Small Animal Veterinary Association) scale (Laflamme & Bjornvad, 2013), it was also assessed the cat's activity and the amount of treats given.

The fifth and last group [E], was directed at the environment in which the animal lives. Absence or existence (with corresponding distance) of outdoor main pollution producers, as industries and highways, was questioned. As for indoor pollutants, questions regarded the use of chemicals, gas ovens, fireplaces and smoke. Lastly, it was asked if the owner or other co-inhabitant relatives were diagnosed with asthma.

Both paper form (hard copies) and digital form questionnaires were distributed. Paper questionnaires were distributed via personal contacts and via veterinary clinics (Fozcanis - Hospital Veterinário da Figueira da Foz and Hospital Veterinário de Santa Marinha). The digital questionnaire was developed in Google platform Google forms™ following the same structure as the paper questionnaire. Digital questionnaires were disseminated through email to different veterinary care centers, as well as in social media platforms, namely Facebook™ and Instagram™. Questionnaires were received between September 2018 and March 2019.

2.2 Data analysis

Before analysis, coding was applied to all the questions. A descriptive analysis of the responses to each question was performed. After this, a series of independence tests with Chi-Square, through SAS (Statistical Analysis System) program PROC FREQ (SAS Institute Inc., 2019), was performed to evaluate associations between the different variables included in the questionnaire.

The probability of an animal having respiratory disease was analyzed by logistic regression with the same SAS program, with a model that included the several risk factors individually. Subsequently, probability ratios were estimated between the different risk factors levels that significantly influenced the probability of respiratory disease development in inquired animals.

Other variables, as weight, were submitted to several variance analyses developed with SAS program PROC GLM, to understand which significantly influenced it individually.

3. Results

A total of 210 questionnaires were received, but only 189 met the defined inclusion and exclusion criteria, and thus only 90.0% were included in this study. Of the 189 included, 27 were responded in paper form, with only three cats diagnosed with respiratory disease (two with asthma and one with feline cough), whereas the remaining ones (n=162) were replied in digital form, of which 16 cats were diagnosed with asthma and one with feline cough.

3.1. Individual identification and characterization

Among the study population, with the characterization summarized in table 1, the breed with the higher prevalence was the European or mixed breed (82.0%). The male/female ratio was practically equal (95:93), being most of the cats sterilized (78.3%). The mean age was 5 ± 3 years old, ranging from one to 15 years old and the mean weight was 4 ± 1 kg, ranging from 0.5 to 8kg.

Table 1- Characterization of studied cat population by signalment, lifestyle and acquisition.

Variable	Categories	Absolute frequency (Relative, %)
Breed	European or mixed breed	n = 155 (82.0%)
	Siamese	n = 16 (8.5%)
	Other	n = 18 (9.5%)
Gender	Male	n = 95 (50.2%)
	Female	n = 93 (49.2%)
	No response	n = 1 (0.5%)
Reproductive status	Neutered	n = 148 (78.3%)
	Non-neutered	n = 40 (21.2%)
	No response	n = 1 (0.5%)
Age	< 3 years	n = 91 (48.2%)
	4 - 7 years	n = 48 (25.4%)
	8 - 11 years	n = 31 (16.4%)
	12 - 15 years	n = 14 (7.4%)
	> 15 years	n = 2 (1.0%)
	No response	n = 3 (1.6%)
Weight	< 2kg	n = 18 (9.5%)
	3 - 5kg	n = 126 (66.7%)
	6 - 8kg	n = 30 (15.9%)
	No response	n = 15 (7.9%)
Residence area	North mainland region	n = 89 (47.1%)
	Centre mainland region	n = 70 (37.0%)
	South mainland region	n = 18 (9.5%)
	Extra-continental	n = 6 (3.2%)
	No response	n = 6 (3.2%)
Lifestyle	Outdoor only	n = 10 (5.3%)
	Outdoor & indoor	n = 62 (32.8%)
	Indoor only	n = 117 (61.9%)
Acquisition	Street	n = 108 (57.1%)
	Pet shop	n = 10 (5.3%)
	Breeder	n = 8 (4.2%)
	Acquaintance	n = 61 (32.3%)
	No response	n = 2 (1.1%)

Geographical origin of participating owners was broad, with questionnaires been completed also by Portuguese emigrants living in foreign countries. Considering only the Portuguese mainland residents (96.6%), the higher number of respondents lived in the north region (48.6%) as shown in figure 1.

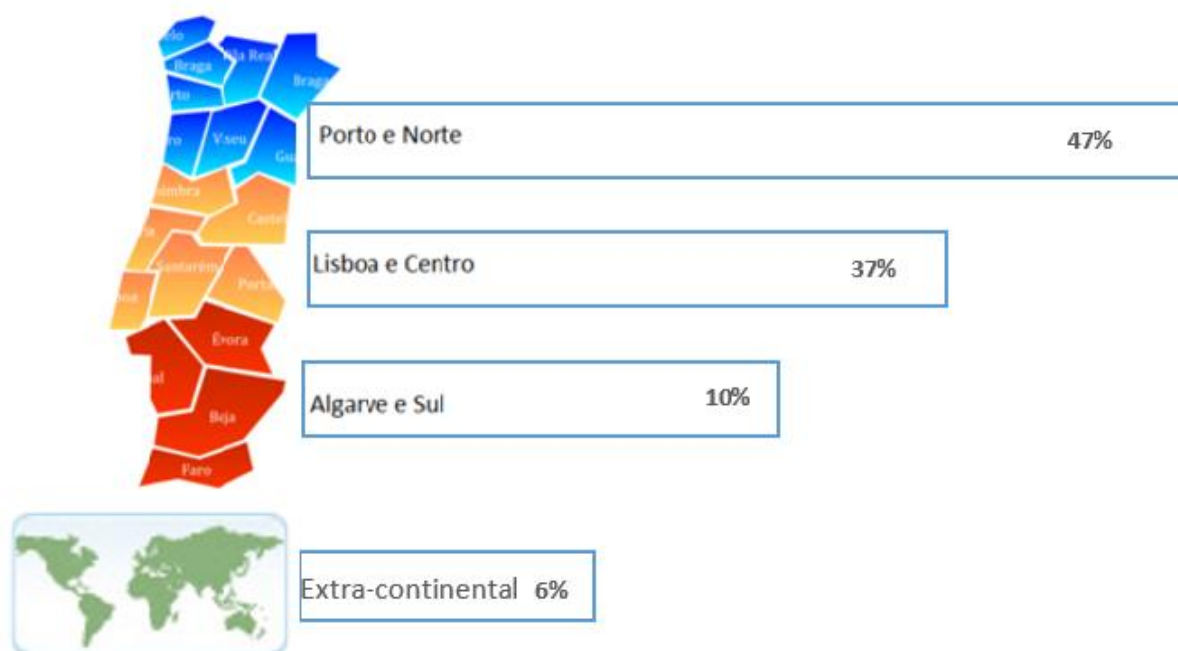


Figure 1- Geographical distribution of inquired cats

Regarding lifestyle, the vast majority of respondents identified their cats as “indoor only” (61.9%). In most cases (57.8%) cats were taken off the streets, and only 5.3% were commercially acquired in pet shops. None of the variables addressed in this group of questions was found to be statistically associated with asthma.

3.2. Feline asthma

Respiratory disease was only present in 18 (9.5%) of cats, of which 16 were diagnosed with feline asthma and two with feline cough. The mean age of the cats with respiratory disease (Table 2) was 6 ± 3 years old, ranging from one to 15 years. Their mean weight was 4 ± 1 kg, varying from three up to six kilogram.

Table 2-Characterization of cats with respiratory disease studied by signalment, lifestyle and acquisition.

Variable	Categories	Absolute frequency (Relative, %)
Breed	European	n=13 (72.2%)
	Siamese	n=3 (16.7%)
	Other	n=2 (11.1%)
Gender	Male	n = 9 (50.0%)
	Female	n = 9 (50.0%)
Reproductive status	Neutered	n = 17 (94.4%)
	Non-neutered	n = 0 (0%)
	No response	n = 1 (5.6%)
Age	< 3 years	n = 6 (33.3%)
	4 - 7 years	n = 6 (33.3%)
	8 - 11 years	n = 4 (22.2%)
	12 - 15 years	n = 2 (11.1%)
	> 15 years	n = 0 (0%)
Weight	< 2kg	n = 0 (0%)
	3 - 5kg	n = 15 (83.3%)
	6 - 8kg	n = 1 (5.6%)
	No response	n = 2 (11.1%)
Residence area	North mainland region	n = 10 (55.6%)
	Centre mainland region	n = 7 (38.9%)
	South mainland region	n = 1 (5.5%)
	Extra-continental	n = 0 (0%)
Lifestyle	Outdoor only	n = 0 (0%)
	Outdoor & indoor	n = 5 (27.8%)
	Indoor only	n = 13 (72.2%)
Acquisition	Street	n = 8 (44.4%)
	Pet shop	n = 3 (20%)
	Breeder	n = 1 (5.5%)
	Acquaintance	n = 6 (33.3%)

Of those diagnosed with feline asthma, 43.8% (n=7) were diagnosed before the first year of age and 37.5% (n=6) between the second and the fifth year.

The symptoms that owners more often associated with asthma crisis were (by decreasing order) respiratory wheezes and cough (Figure 2).

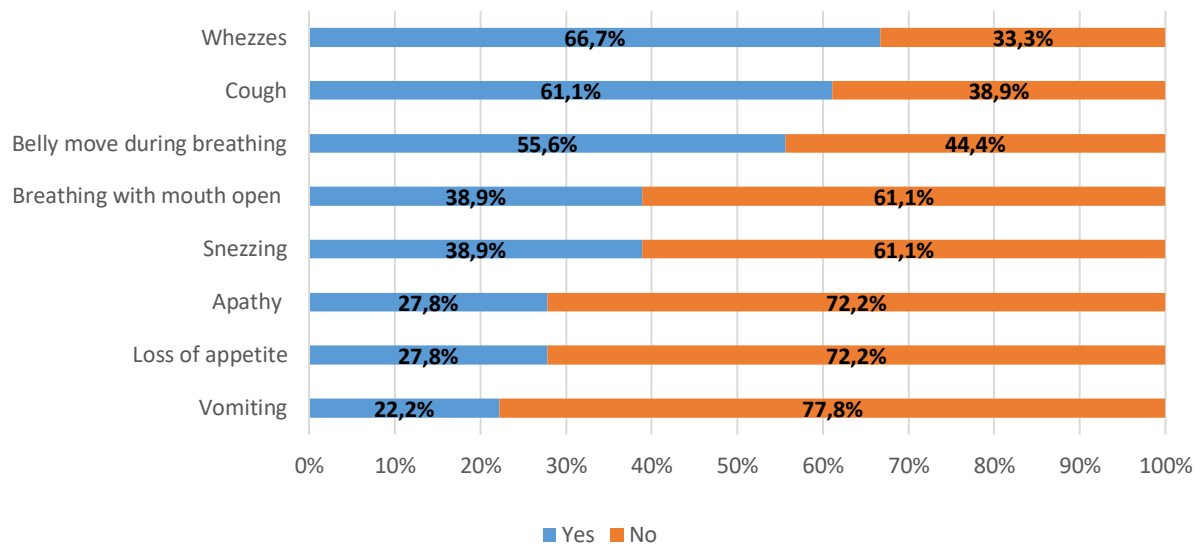


Figure 2- Symptoms associated with asthma crisis among diagnosed cats (n=16).

There are also situations in which the owners observed a worsening of symptoms or that were associated with triggering asthma crisis. As detailed in Figure 3, owners reported worsening of symptoms mostly associated with season (specifically spring and autumn) and change of environment (namely stress, humidity, smoke or wind).

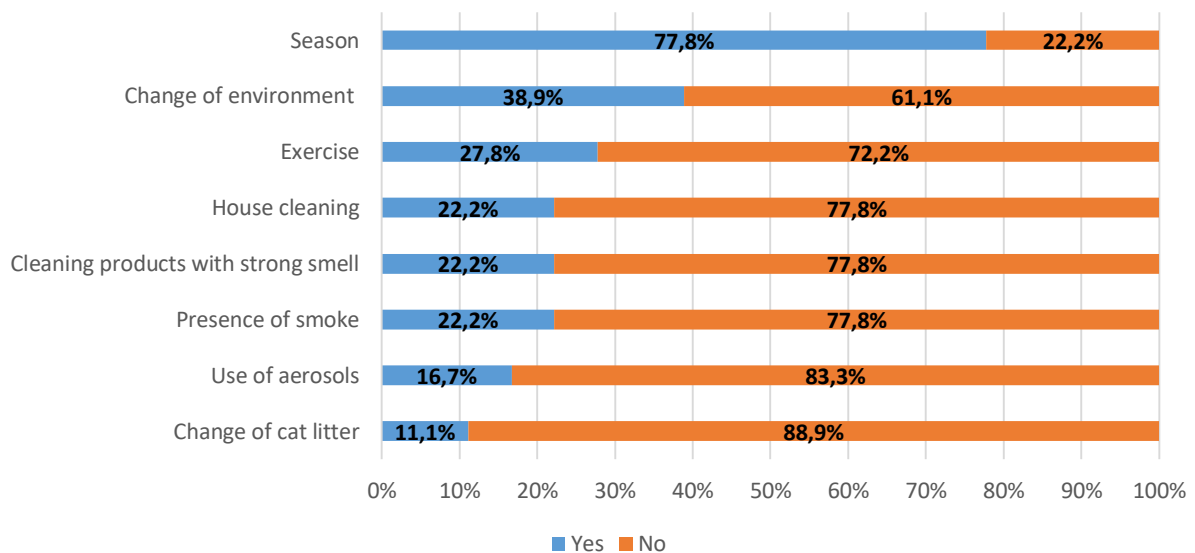


Figure 3- Circumstances associated with increased symptoms or triggering crisis.

With the results gathered it was possible to identify some features of the disease in asthmatic cats, as displayed in table 3. Crisis and medication intake were not frequent, with nearly half of the animals not being subjected to any medication.

Most cats had access to the outdoors in the pediatric age, and most did not develop any disease in this period. However, when they developed disease during the pediatric age, it was mainly asthma.

Table 3- Features of the disease in asthmatic cats.

Variable	Categories	Absolute frequency (Relative, %)
Crisis frequency	1-2 times a year	n =7 (43.8%)
	Monthly	n =4 (25.0%)
	Weekly	n =1 (6.3%)
	Daily	n = 1 (6.3%)
	No response	n = 3 (18.6%)
Asthma medication	Yes	n = 9 (56.2%)
	No	n = 7 (43.8%)
Last medication	Daily	n = 2 (12.5%)
	Weekly	n = 1 (6.3%)
	Monthly	n = 1 (6.3%)
	In the last 6 months	n = 2 (12.5%)
	In the last year	n = 4 (25.0%)
	No response	n = 6 (37.4%)
Exterior access during pediatric age	Yes	n = 9 (56.2%)
	No	n = 3 (18.8%)
	No knowledge	n = 4 (25.5%)
Respiratory disease in pediatric age	Yes	n = 4 (25.0%)
	No	n = 6 (37.5%)
	No knowledge	n = 6 (37.5%)
Disease developed in pediatric age	Feline asthma	n = 4 (25.0%)
	No response	n = 12 (75.0%)

3.3. Stress

The frequency of the major situations that are commonly the cat's manifestations of stress as reported by respondent owners are displayed in figure 4. To those that usually vocalize during traveling it was asked the frequency of the travelling, and most of them did it only about one to two times a year (83.3%). Regarding other co-inhabitant animal as a potential source of stress, most of the enrolled cats lived with another cat(s) (68.3%), but co-inhabitants were also from other species, namely dogs, birds or small mammals. None of co-inhabitant cats was diagnosed with feline asthma, and the majority slept, ate and played together (Figure 5).

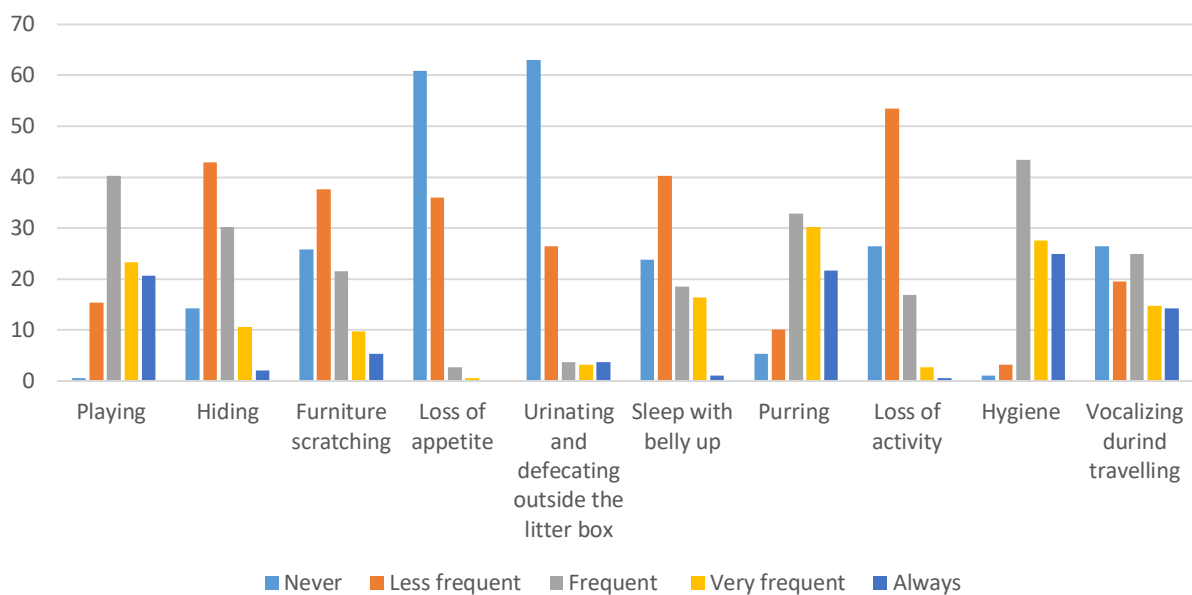


Figure 4- Relative frequency (%) of symptoms associated with cat stress, as reported by owners.

Diseases correlated to stress had low prevalence (10.6%), being urinary tract infection the most frequently reported one (65%). Among the different correlations tested, it was observed a significant association between lifestyle and stress ($p=0.032$). The smaller percentage of animals with disease were the ones who had access to both indoor and outdoor. Additionally, although not statistically significant, the correlation between stress-related diseases and asthma was close to significance ($p=0.065$).

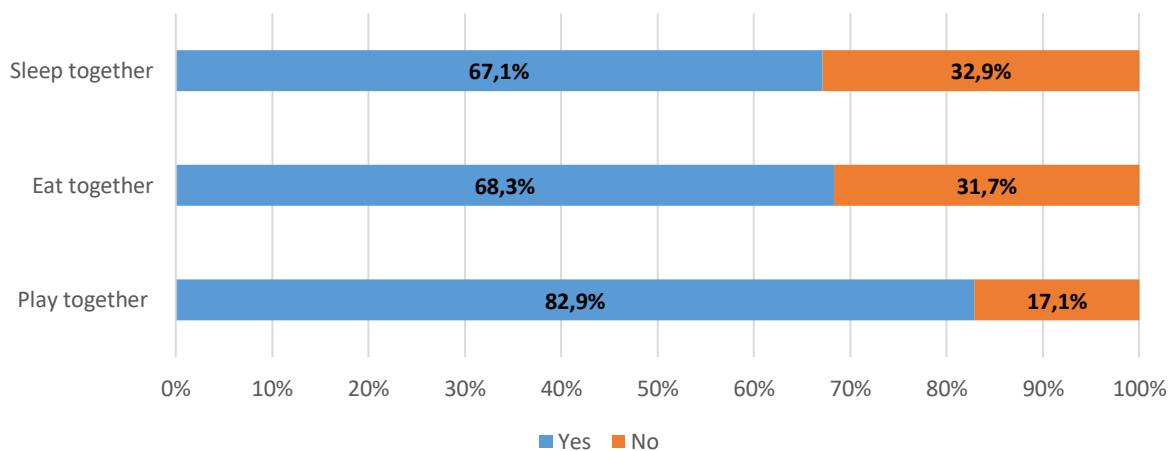


Figure 5- Stress related behaviors in the presence of co-inhabiting cats.

3.4. Body condition

Most owners identified their cat as being in the ideal weight (54.4%) and active (84.4%). The majority did not give treats frequently to their cats (64. 2%) (Table 4).

Table 4- Characterization of body condition regarding all the studied population and cats with asthma/respiratory disease.

Variable	Categories	Absolute frequency (Relative, %)		P value
		Total cat population (n=189)	Cats with asthma/ respiratory disease (n=18)	
Body condition	Lean	n = 42 (22.2%)	n = 2 (11.1%)	p=0.38
	Ideal	n = 102 (54.0%)	n = 10 (55.5%)	
	Overweight	n = 44 (23.3%)	n = 6 (33.3%)	
	No response	n = 1 (0.5%)	n = 0 (0%)	
Activity	Active	n = 157 (83.1%)	n =13 (72.2%)	p=0.35
	Sedentary	n = 29 (15.3%)	n = 4 (22.2%)	
	No response	n = 3 (1.6%)	n = 1 (5.6%)	
Treat given	Frequent	n = 67 (35.4%)	n =4 (22.2%)	p=0.21
	Not frequent	n = 120 (63.5%)	n =14 (77.8%)	
	No response	n = 2 (1.1%)	n = 0 (0%)	

It was possible to prove a significant relation between weight and age, being weight only significantly influenced by age ($p < 0.01$). There was no specific correlation found with asthma.

3.5. Environment

The majority of the respondents lived in an urban environment (55.6%). Among those living in urban areas, a public park or garden existed in 71.8% of cases, frequently (87.7%) less than a kilometer away. Regarding smoking habits, most respondents had no smokers in the house (66.1%), but of those who actually smoked, most did so in the areas to which the cat had access (48.4%).

Other indoor pollution sources included gas ovens or heaters (42.0%), fireplaces (36.5%) and aerosols sources (28.0%).

Proximity with highways or freeways was observed in 32.3% of all enrolled cats, being in most cases at two to five kilometers away (61.4%) (Table 5).

Presence of nearby pollutant industries only occurred for 10.1% of the participants and most of them were two to 10 kilometer away (62.5%). Although close to significance ($p=0.07$), the presence of these industries was not correlated to asthma in enrolled cats.

None of the remaining environmental factors showed to be significantly correlated with asthma.

Finally, in the last question that inquired if anyone living in the household had asthma, most answered negatively (78.8%).

Table 5- Characterization of environment regarding all the studied population and cats with asthma/respiratory disease

Variable	Categories	Absolute frequency (Relative, %)		P value
		Total cat population (n=189)	Cats with asthma/ respiratory disease (n=18)	
Urban vs. Rural	Urban	n = 105 (55.6%)	n =8 (44.4%)	p=0.30
	Rural	n = 84 (44.4%)	n =10 (55.5%)	
Smoking	Yes	n = 52 (27.5%)	n = 5 (27.8%)	p=0.50
	No	n = 125 (66.1%)	n = 13 (72.2%)	
	No response	n = 12 (6.4%)	n = 0 (0%)	
Pollutant industries	Yes	n = 19 (10%)	n = 4 (22.2%)	p=0.07
	No	n = 170 (90%)	n = 14 (77.8%)	
Highways/ freeways	Yes	n = 61 (32.3%)	n = 6 (6.4%)	p=0.92
	No	n = 128 (67.7%)	n = 12 (66.7%)	

4. Discussion

This study enrolled a considerable number of animals (n=189), nevertheless most of the correlations tested did not had a statistically significant association. This was probably because of the small number of asthmatic cats (n=16) and the fact that feline asthma is frequently underdiagnosed. In fact, asthma was present in approximately 8.5% of the animals analyzed, which is slightly superior to the results found in literature (1-5%) (Dunbar Gram et al., 2018; Rosenberg & Druey, 2018; Venema & Patterson, 2010). A possible justification for this was the fact that this work was disseminated, namely online, as being a study regarding respiratory disease in cats. It is also important to mention that besides feline asthma, feline cough, another respiratory disease was considered. Feline cough has a similar pathophysiology and can be related to the same risk factors, although it corresponded to only two of the 18 cats with respiratory disease, which hindered further analysis (Reinero, 2011).

The increasing incidence of this disease, in both humans and cats, as well as the paucity of similar studies in cats demonstrates the importance of the current study. In addition, considering the studies conducted in humans, most are focused in treatment and not so much in prevention. It would be important to conduct further studies and try to understand if exposure to the same risk factors can lead to the development of the disease both in humans and cats and even if cats could be used as sentinels for the disease (Neo & Tan, 2017).

Although most of the correlations proposed were not statistically proven, this study enabled us to better characterize cats with respiratory disease, namely asthma. Several studies related that there were no correlation found between parameters like breed, age or sex and asthma (Dunbar Gram *et al.*, 2018; Rosenberg & Druey, 2018; Venema & Patterson, 2010), but others have found a higher prevalence in the Korat (19%) and Siamese breed (7%) (Vapalahti *et al.*, 2016). Such finding was not observed in the present study.

Disease prevalence in the different Portuguese areas, which was not up studied until now, was higher in the north mainland region (55.5%), although no significant correlation was found between asthma and any Portuguese region in particular.

It was observed that respiratory wheezes and coughing were the most frequently reported symptoms associated with crisis. Season was the main reported leading cause of worsening of symptoms, probably related to aeroallergens like pollens and fungal spores, usually associated with spring, capable of inducing bronchial obstruction and increasing asthma symptoms in humans (D'Amato, Liccardi, D'Amato, & Holgate, 2005), and probably also in cats.

Other aspects of the cat's life have also been hypothesized as being associated with asthma, namely pediatric exposure to pathogens. Benefits were found in both human and feline immunity with exposure and development of diseases in the pediatric period (Heller *et al.*, 2014; Toskala & Kennedy, 2015), although recurrent respiratory infections in infancy has been correlated to the development of asthma in humans later on (Arshad, Kurukulaaratchy, & Fenn, 2005; Subbarao, Mandhane, & Sears, 2009). A study developed in cats determined that exposure to allergens in early neonatal period, until the fourth to sixtieth month of age, failed to develop airway eosinophilia when exposed to the same allergens later on (Heller *et al.*, 2014). In the cited study, no statistical correlation between early exposure to allergens and asthma was found, although most of the animals in the study evidenced pediatric exposure and did not develop any respiratory disease in early life nor in adult life.

Stress was also a studied variable because, even though there are no studies analyzing possible correlation between asthma and stress in cats, in humans evidence exist that suggests a casual association between both (Reinero, 2011; Toskala & Kennedy, 2015). For example, in children living in the north hemisphere there is a predictable annual exacerbation of symptoms every September, correlated to seasonal allergens and possibly the stress of returning to school (Subbarao *et al.*, 2009). Thus, it could be reasonable to assume that in cats other stress related circumstances can lead to symptom exacerbation (Atkinson, 2018; Mariti *et al.*, 2017). Nevertheless such correlations were not found regarding the studied variables in the present study. It is worth mentioning that, although failed to reach significance, the association of stress related diseases with asthma was close to significance ($p=0.065$).

An association was also described with asthma and obesity in humans (Toskala & Kennedy, 2015; Venema & Patterson, 2010). However, Subbarao *et al.* (2009) suggested that such relation might be casual given their mutual increase. Associated with obesity, a sedentary lifestyle was also positively associated with asthma symptoms in humans (Beasley, Semprini, & Mitchell, 2015). Nevertheless such significant association was not found in the present study, as most of the animals enrolled had an ideal body condition and an active lifestyle, according to the owners' perception.

Although there are studies relating a rural environment to a reduced risk of development of asthma in children such relation was not found in this study. In the other hand it was observed an increased prevalence of asthma in humans in urban areas for diverse factors like vehicle emissions and industrialization (Beasley *et al.*, 2015; D'Amato *et al.*, 2005). Although no positive correlation between asthma and urban area residence was determined, the correlation between proximity with pollutant

industries and occurrence of feline asthma was close to significance ($p= 0.07$). Along with industries, tobacco smoke, chemicals, and highways are recognized as producers of different pollutants that can lead to the development of the disease and that are associated with increasing respiratory symptoms in children (D'Amato *et al.*, 2005; Lin *et al.*, 2018; Taylor, 2017), although this correlations were not found to be significant in the current study.

Lastly, it was asked if someone in the house was diagnosed with asthma, to assess if cats could be sentinels for the disease (Neo & Tan, 2017), however such correlation was also not found.

Although this study aimed to address feline asthma and its corresponding determining and conditioning factors, it has provided important information regarding overall housing and health conditions in Portuguese cats. Most of the cats are of European or mixed breed and sterilization is a common practice, among the cats enrolled in the study. In addition, most of the cats (61.9%) live exclusively indoor which is in line with what is described by the study GFKTrack.2Pets (64%; 2015). As for stress-correlated parameters most of them were very low or even nonexistent, leading us to believe that studied cats have a low level of stress, or at least they were not detected by the criteria used to evaluate this parameter. Obesity was also mostly not present, with the majority of responses in the ideal body condition section. It would be important to do further research in this area, with increasing number of enrolled animals, to try to understand if such results are transversal to different study populations and eventually identify further predisposing and conditioning factors that may be involved in the disease both in cats and in humans.

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Annexes



Annex 1: Questionnaire applied

Questionário para tutores de felinos participantes no estudo intitulado “Asma Felina - Questionário sobre factores determinantes e condicionantes”

As respostas a este questionário são anónimas e confidenciais e destinam-se exclusivamente a fins académicos. As respostas apresentadas não têm associadas respostas correctas ou incorrectas.

A. IDENTIFICAÇÃO E CARACTERÍSTICAS INDIVIDUAIS

A1. Raça: _____

A2. Sexo:

A2.1. ☐ Masculino ☐ Feminino

A2.2. ☐ Castrado ☐ Não castrado

A3. Idade: _____ anos/meses (riscar o que não interessa)

A4. Peso: _____ (kg)

A5. Área de residência: (Freguesia; Concelho)

A6. Vive dentro ou fora de casa?

☐ Exclusivamente dentro de casa

☐ Dentro e fora de casa

☐ Exclusivamente fora de casa

A7. Onde foi adquirido?

☐ Rua ☐ Loja de animais ☐ Outro: _____

A8. Quando foi adquirido? (Mês/Ano) _____

B. ASMA FELINA

B1. Diagnosticado com Doença respiratória? ☐ Sim ☐ Não

B1.1 Se sim, qual?

Asma Felina ☐

Outra ☐ Qual? _____

B1.2 Se sim, Com que idade foi diagnosticado? _____

Se respondeu “Sim”, por favor, responda às questões seguintes desta secção.

Se respondeu “Não” pode passar para a SECÇÃO C (página 3)

B2. Assinale os sintomas que estão associados a uma crise de asma no seu gato:

- ☐ Tosse
- ☐ Espirros
- ☐ “Assobios” respiratórios
- ☐ Respiração com boca aberta
- ☐ Movimenta a barriga quando respira
- ☐ Perda de apetite
- ☐ Mais parado (apático)
- ☐ Vômito
- ☐ Outros:

Qual (quais)? _____

B4. Assinale o(s) momento(s) em que note aumento/pioria dos sintomas:

- ☐ Exercício
- ☐ Fumo no ambiente
- ☐ Mudança de areia
- ☐ Uso de produtos de limpeza com cheiro forte (p.e. lixívia, Sonasol®)
- ☐ Uso de aerossóis como laca ou ambientadores
- ☐ Estação do ano

Qual? _____

- ☐ Mudança de ambiente

Para qual: _____

- ☐ Limpeza de casa (após aspirar/ varrer, limpar o pó)
- ☐ Outros:

Qual(Quais): _____

B5. Qual a frequência das crises de asma, no último ano?

B6. Faz medicação para a doença respiratória?

- ☐ Sim
- ☐ Não

B7. Quando foi a última vez que fez medicação para asma? (Mês/Ano)

B8. O animal teve acesso ao exterior durante a idade pediátrica (3 dias até aos 6 meses de idade)?

☐ Sim ☐ Não ☐ Não sei

B9. Desenvolveu alguma doença respiratória durante a idade pediátrica (até aos 6 meses de vida)?

☐ Sim ☐ Não ☐ Não sei

B9.1 Se sim, qual? _____

C. Stress

C1. Classifique (assinalando com um X) cada uma das seguintes situações:

O seu gato:	Nunca	Pouco frequente	Frequente	Muito frequente	Sempre
C1.1. gosta de brincar?					
C1.2. esconde-se?					
C1.3. arranha os móveis?					
C1.4. perde o apetite?					
C1.5. urina/defeca fora da caixa?					
C1.6. dorme de barriga para cima?					
C1.7. ronrona no seu colo?					
C1.8. costuma ficar pouco ativo?					
C1.9. costuma lambe-se?					
C1.10. mia durante as viagens?					

Se costuma miar durante as viagens, com que frequência faz viagens? _____

C2. Existem outros animais em casa?

☐ Gato ☐ Cão ☐ Ave ☐ Outro: _____

Se existirem outros gatos em casa:

C2.1. diagnosticados com asma felina? ☐ Sim ☐ Não

C2.2. brincam uns com os outros? ☐ Sim ☐ Não

C2.3. costumam dormir juntos? ☐ Sim ☐ Não

C2.4. costumam comer juntos? ☐ Sim ☐ Não

C4. O seu gato foi alguma vez diagnosticado com inflamação da bexiga/infeção urinária ou outra doença relacionada com *stress*?

☐ Sim ☐ Não ☐ Não sei

C4.1. Se sim, qual? _____

D. Obesidade

D1. Como classificaria o seu gato?

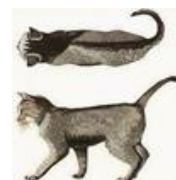
1. Costelas facilmente palpáveis e sem gordura visível. ☐



2. Costelas facilmente palpáveis e com pouca gordura visível. ☐



3. Costelas palpáveis com uma camada moderada de gordura. ☐



4. Costelas dificilmente palpáveis e ausência de contorno da cintura. ☐



5. Ausência de cintura e abdómen pendular. ☐



D6. O seu gato é ativo?

☐ Sim ☐ Não

D7. Fornece regularmente guloseimas ao seu gato (tudo o que não seja ração)?

☐ Sim ☐ Não

D7.1 Se sim, com que regularidade?

☐ Uma vez por semana ☐ Uma vez por dia ☐ Sempre que ele pede
☐ Outra. Qual? _____

E. Ambiente

E1. Reside em área urbana ou rural?

☐ Urbana ☐ Rural

E1.1. Se urbano, existe algum parque/jardim?

☐ Sim ☐ Não

E1.2. Se sim, a que distância? _____ Km

E2. Existem fumadores em casa?

☐ Sim ☐ Não ☐ Pouco frequente

E2.1. Se sim, fumam em divisões a que o gato tenha acesso?

☐ Sim ☐ Não

E3. Usa fornos ou aquecimento a gás?

☐ Sim ☐ Não ☐ Pouco frequente

E4. Usa lareira?

☐ Sim ☐ Não ☐ Pouco frequente

E5. Uso de químicos com cheiros fortes (tintas, vernizes, etc.)?

☐ Sim ☐ Não ☐ Pouco frequente

E6. Uso frequente de aerossóis na habitação (p.e. ambientadores/ difusores de cheiro, laca de cabelo, etc.)?

☐ Sim ☐ Não ☐ Pouco frequente

E7. Existem indústrias poluentes nos arredores?

☐ Sim ☐ Não

E7.1 Se sim, a que distância? _____ Km

E8. Existem autoestradas ou vias rápidas nos arredores?

☐ Sim ☐ Não

E8.1 Se sim, a que distância? _____ Km

E9. Alguém no agregado familiar está diagnosticado com asma?

☐ Sim ☐ Não

Por favor, certifique-se que respondeu a todas as questões. Para esclarecimentos adicionais ou quaisquer dúvidas referentes ao estudo pode enviar um e-mail para jcrg10@gmail.com.
Muito obrigada pela sua colaboração!