# Atopic dermatitis: a restropective study of associated factors in a dermopathic canine population*

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**ABSTRACT.** Amarante C.F., Ramadinha R.R. & Pereira M.J.S. **Atopic dermatitis: a restropective study of associated factors in a dermopathic canine population.** [Dermatite atópica: um estudo retrospectivo dos fatores associados em uma população canina dermopata.] *Revista Brasileira de Medicina Veterinária, 37(Supl.1):13-17, 2015.* Curso de Pós-Graduação em Ciências Veterinárias, Instituto de Veterinária, Universidade Federal Rural do Rio de Janeiro, BR 465, Km 7, Seropédica, RJ 23897-970, Brasil. E-mail: cristinaf.amarante@gmail.com

Canine atopic dermatitis (AD) is a pruriginous inflammatory disease related to the production of IgE antibodies and frequently, diagnosed in the clinical veterinary practice. However, there are many controversies about the predisposing factors. The objective of this study was to analyze the contribution of the sex, age, breed, castration, time of year, the use of perfume and cleaning products as predisposing factors for the occurrence of AD using binomial generalized linear regression model estimating the prevalence ratio as a measure of effect. The clinical records of 2,280 dogs attended by the Section of Dermatology Small Animal Hospital of the Rural Federal University of Rio de Janeiro, between 2005 and 2010, were reviewed and 1,462 dogs were included in the study. Bivariate and multivariate analyses were performed using a generalized binomial linear regression model. Significance was set at a p-value of ≤ 0.05. Atopic dermatitis was diagnosed in 36.1% (528/1462) of the canine population studied and was associated with females [PR= 1.204 (1.048 to 1.384)], adults [PR= 2.045 (1.542 to 2.711)], the dry season [PR= 0.840 (0.734 to 0.962)], the use of perfumes [PR= 1.271 (1.089 to 1.483)]. Thus, atopic dermatitis prevalence in the study population was higher in females, adults, in which applied perfumes and in the rainy season. . This study constitutes a new approach to the epidemiological aspects of canine atopic dermatitis in Brazil, but requires a better understanding of the relationships between the explanatory variables and outcome through longitudinal studies.

KEY WORDS. Epidemiology, dermatology, dogs, associated factors.

**RESUMO.** Dermatite atópica canina (DA) é uma doença inflamatória pruriginosa relacionada com a produção de anticorpos IgE e frequentemente, diagnosticada na clínica veterinária. No entanto, existem muitas controvérsias sobre os fatores predisponentes. O objetivo deste estudo foi analisar a contribuição do sexo, idade, raça, castração, época do ano, o uso de perfume e produtos de limpeza como fatores predisponentes para a ocorrência de AD, utilizando o modelo de regressão linear generalizado binomial e estimando a razão de prevalência como medida de efeito. Os registros clínicos de 2.280 cães atendidos pelo Setor de Dermatologia do Hospital de Pequenos Animais da Universida-

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de Federal Rural do Rio de Janeiro, entre 2005 e 2010, foram revisados e 1.462 cães foram incluídos no estudo. Análises bivariadas e multivariadas foram realizadas por meio de modelos de Regressão linear generalizado binomial. A significância foi estabelecida em um p-valor de ≤ 0,05. A dermatite atópica foi diagnosticada em 36,1% (528/1462) da população canina estudada e foi associada com fêmeas [RP = 1,204 (1,048-1,384)], adultos [RP= 2,045 (1,542-2,711)], estação seca [RP = 0,840 (0,734-0,962)] e utilização de perfumes [RP = 1,271 (1,089-1,483)]. Assim, a prevalência dermatite atópica na população estudada foi maior em fêmeas, adultas, nas quais se aplicava perfumes e na estação chuvosa. Este estudo constitui uma nova abordagem para os aspectos epidemiológicos da dermatite atópica canina no Brasil, mas requer uma melhor compreensão das relações entre as variáveis explicativas e desfecho por meio de estudos longitudinais.

PALAVRAS-CHAVE. Atopia, cães, dermatologia, epidemiologia.

## INTRODUCTION

Canine atopic dermatitis (AD) is a cutaneous disease that presents clinical features of pruritic and inflammatory aspects and has been linked to a genetic predisposition that is usually associated with the production of IgE antibodies against environmental allergens (Halliwell 2006). AD is considered to be the most common allergic disease in canines (Scott & Paradis 1990), although in some regions, it is less frequent than fleabite allergic dermatitis (Carlotti & Costargent 1994, Scott et al. 2001, Tarpataki et al. 2006).

Apart from the genetic factors, other factors have also been linked to the probability of developing AD, including age (Pocta & Svoboda 2007, Picco et al. 2008), gender (Halliwell & Schwartzman 1971, Scott 1981), breed (Scott & Paradis 1990, Pocta & Svoboda 2007, Picco et al. 2008, Whilhem et al. 2011), and the time of year (Zur et al. 2002, Picco et al. 2008) However, no predisposition for this disease was found due to gender, birth season, environment, vaccination history, or deworming in a case-control study in which a multivariate regression analysis was used (Nødtvedt et al. 2007). The authors highlighted that these results were obtained from only 3 breeds in Sweden and may not be relevant to other populations (Nødtvedt et al. 2007). Although the literature discusses the predisposing factors for AD in canines, there remains a great deal of controversy regarding the roles of these factors. In most of these studies, no control techniques for confounding factors, such as multivariate regression analysis for the analysis of multifactorial events, was used (Katz 2006). Furthermore, the few studies that did utilize these techniques performed logistic regression analyses, which overestimate the effect measure when the prevalence of the event is high because these analyses estimate the odds ratio instead of the prevalence ratio (Medronho et al. 2009). Therefore, the objective of the present study was to evaluate the contributions of gender, age, breed, sterilization (spay/neuter), time of year, and the use of perfume and other cleaning products as predisposing factors for the occurrence of AD by using a generalized binomial linear regression model and estimating the prevalence ratio as a measure of effect.

## MATERIALS AND METHODS

The veterinary records of 2,280 dogs that were treated between 2005 and 2010 in the dermatology wing of the Veterinary Hospital of the Rural Federal University of Rio de Janeiro (Universidade Federal Rural do Rio de Janeiro) were reviewed, and the data regarding the presence or absence of all dermatopathies and the variables inherent to the animal, environment, and management were entered into a database using EPI INFO™ version 3.5.1 (Center for Diseases Control 2008).

After the exclusion of animals with incomplete records, the study population consisted of 1,462 animals. To assess whether these losses were systematic, the study population was compared to the total population with respect to age, gender, breed, and the time of the year in which a diagnosis was made.

The independent variables, gender (male/female), age (in months), sterilization (yes/no), breed, the time of year in which a diagnosis was made (date of service), the use of perfume (yes/no), and the use of cleaning products (yes/no), and the dependent variable, AD (presence/absence), underwent exploratory analysis.

Subsequently, the following groups were defined: the animals were divided according to age into puppies (up to 12 months), adults (13 to 96 months), and seniors (>96 months); the time of year was defined as either the rainy season (October to March) or the dry season (April to September); and the animals were divided according to breed into defined breed (DB) and without a defined breed (WDB). All independent variables were then analyzed for the presence of collinearity by using the Spearman ($\rho \geq 0.70$) correlation test.

Bivariate and multivariate analyses were performed to study the association between AD and the possible determinant factors of prevalence using a generalized binomial linear regression model. The log link function was used to estimate the prevalence ratio (PR) (Skov et al. 1998). In all analyses, the significance level of 5% was adopted.

Initially, all variables were included in the model, and at each step, variables were selected by the ba-

ckward method based on the Wald test. Model adjustment was evaluated using the Akaike Information Criterion (AIC). All analyses were performed using the R software for Windows, version 2.15.2 (R Development Core Team 2011).

## RESULTS AND DISCUSSION

The total population and the studied population had a similar distribution with regards to age, gender, breed, and the time of year at which a diagnosis was made (Table 1). AD occurred in 36.1% (528/1462) of the dogs in the studied population.

No explanatory variables showed collinearity, so all of the variables were introduced into the model. Table 3 shows the variables with statistical evidence of an association with AD in the studied population.

In a series of cases, AD was reported as being more prevalent in sterilized animals than in intact ones (Zur et al. 2002). In the present study, sterilization and breed were significantly associated with AD in the bivariate analysis (Table 2) but not in the final model (Table 3). Breed has been implicated as a predisposing factor for AD (Saridomichelakis

et al. 1999, Pocta & Svoboda 2007, Whilhem et al. 2011). Although studies have reported a predisposition for AD due to breed, there are limitations regarding the statistical bivariate analysis (Picco et al. 2008), where the results may be influenced by confounding variables. In the present study, after the multivariable analysis, differences in AD prevalence according to breed were not observed (Nødtvedt et al. 2007). These results reinforce the need for the use of multivariate analyses when an event is multifactorial (Katz 2006).

Table 1. Comparison of the composition of the studied population with the total population.

| Variable | Category | Total Population | Study Population |
|---|---|---|---|
| | | % | % |
| Gender | Male | 44.8 | 43.8 |
| | Female | 55.2 | 56.2 |
| Age | Puppy | 15.0 | 14.7 |
| | Adult | 58.3 | 59.4 |
| | Elderly | 22.5 | 25.9 |
| Breed | DB | 67.9 | 68.8 |
| | WDB | 32.1 | 31.2 |
| Time of year (Season) | Rainy | 52.9 | 54.0 |
| | Dry | 45.4 | 46.0 |

DB: defined breed; WDB: without a defined breed.

Table 2. Bivariate analysis of factors that predispose dogs to acquire canine atopic dermatitis.

| Variable | Categories | AD | | Total | Prevalence | p-value | PR (I.C.) |
|---|---|---|---|---|---|---|---|
| | | Yes | No | | (%) | | |
| Gender | | | | | | 0.00 | 1.26 (1.09-1.45) |
| | Males* | 202 | 438 | 640 | 31.6 | | |
| | Females | 326 | 496 | 822 | 39.7 | | |
| | Total | 528 | 934 | 1462 | 36.1 | | |
| Sterilized | | | | | | 0.00 | 1.77 (1.55-2.02) |
| | No* | 407 | 778 | 1185 | 34.3 | | |
| | Yes | 121 | 156 | 277 | 43.7 | | |
| | Total | 528 | 934 | 1462 | 36.1 | | |
| Age | | | | | | | |
| | Puppies* | 42 | 173 | 215 | 19.5 | - | |
| | Adults | 358 | 511 | 869 | 41.2 | 0.00 | 2.11 (1.59-2.80) |
| | Elderly | 128 | 250 | 378 | 33.9 | 0.00 | 1.73 (1.28-2.35) |
| | Total | 528 | 934 | 1462 | 36.1 | - | - |
| Breed | | | | | | 0.05 | 1.16 (1.00-1.36) |
| | DB* | 148 | 308 | 456 | 32.5 | | |
| | WBD | 380 | 626 | 1006 | 37.8 | | |
| | Total | 528 | 934 | 1462 | 36.1 | | |
| Time of year (Season) | | | | | | 0.02 | 0.84 (0.74- 0.97) |
| | Rainy* | 307 | 483 | 790 | 38.9 | | |
| | Dry | 221 | 451 | 672 | 32.9 | | |
| | Total | 528 | 934 | 1462 | 36.1 | | |
| Perfume | | | | | | 0.00 | 1.36 (1.17- 1.59) |
| | No* | 414 | 802 | 1216 | 34.0 | | |
| | Yes | 114 | 132 | 246 | 46.3 | | |
| | Total | 528 | 934 | 1462 | 36.1 | | |
| Cleaning products | | | | | | 0.21 | 1.23 (0.89-1.70) |
| | No* | 27 | 64 | 91 | 29.7 | | |
| | Yes | 501 | 870 | 1371 | 36.5 | | |
| | Total | 528 | 934 | 1462 | 36.1 | | |

PR: Prevalence Ratio; CI: Confidence Interval; DB: Defined Breed; WDB: Without Defined Breed; *References.

Rev. Bras. Med. Vet., 37(Supl.1):13-17, dezembro 2015

15

Table 3. Multivariate analysis of factors that predispose dogs to canine atopic dermatitis.

| Variable | B | *P-value* | PR | CI (95%) | |
|---|---|---|---|---|---|
| Age (adult) | 0.715 | 0.000 | 2.045 | 1.542 | 2.711 |
| Use of perfume (yes) | 0.240 | 0.003 | 1.271 | 1.089 | 1.483 |
| Gender (female) | 0.186 | 0.004 | 1.204 | 1.048 | 1.384 |
| Time of year (Dry season) | -0.174 | 0.019 | 0.840 | 0.734 | 0.962 |
| Constant | -1.693 | 0.00 | | | |

PR: Prevalence Ratio; CI: Confidence Interval.

The results of the present study were consistent with the results of previous studies, which demonstrated that females were more affected then males (Halliwell & Schwartzman 1971, Scott 1981). However, other authors found no significant differences between different gendered animals (Saridomichelakis et al. 1999, Zur et al. 2002, Nødtvedt et al. 2007, Pocta & Svoboda 2007). The observation that the levels of IgE in the serum of non-spayed females were higher than in non-neutered males could be a possible biological explanation for the statistical evidence demonstrating an association with AD in females (Racine et al. 1999).

AD was diagnosed in animals ranging from two months to 18 years (median = five years) of age and had a prevalence that was 2 times higher in adult animals (Table 3) when compared with puppies. The prevalence of AD by age group was as follows: 19.5% in puppies, 33.9% in seniors, and 41.2% in adults (Table 2). Among those affected, 7.95% were less than one year old (2.72% were less than 6 months old), and 21.97% were less than three years old (data not shown). These results conflict with the results of a prospective study that found that the age of the dogs at disease onset was less than one year in 60% and less than three years in 78% of the dogs studied (Picco et al. 2008), respectively. A greater frequency in the diagnosis of AD has also been reported in dogs between six months and three years of age (48.9%), whereas in animals between 3.1 and six years of age, the frequency was lower (39.3%) (Pocta & Svoboda 2007). However, there have also been reports that 95% of dogs exhibit the clinical signs of AD by the age of five years and that the age at which the allergic test was performed varied between one and 11 years (median = 4.3 years) ( Zur et al. 2002). In the present study, the median of five years refers to the age of diagnosis and treatment, including laboratory tests, which does not necessarily reflect the age of onset of clinical symptoms. Despite the different methodologies and sample sizes used in these studies, there is an agreement that dogs in adulthood are more affected than puppies. Some hypotheses can be raised to attempt to explain the different results in regards to the age of diagnosis. The first hypothesis considers that several owners may have delayed seeking a diagnosis for their animals or have previously received an erroneous diagnosis. The second hypothesis is that, when dealing with a chronic disease such as AD, the animal's age tends to be more advanced. Studies show that adult dogs are more affected due to the time required for allergen exposure that can then trigger the disease (Saridomichelakis et al. 1999). Thus, it is likely that puppies have not had enough exposure time to the same agents for clinical symptoms to appear, whereas in elderly dogs, an immunological equilibrium would have already been reached or their immunity would already be declining.

In the present study, in contrast to what has been shown by other authors (Scott 1981, Volsset 1985, Saridomichelakis et al. 1999), the time of year in which the diagnosis was made was a factor that influenced AD. Previously, seasonal variation was also observed in cases of atopic dermatitis, which occurred more frequently in the spring and summer (Zur et al. 2002, Picco et al. 2008), agreeing with the results of the present study, in which the frequency of AD was significantly higher in the rainy season, which corresponds to the months of spring and summer in Brazil. The rainy season coincides with the pollination of flowers, although the dry season is when the dust and pollution particles are more present in the atmosphere. In the present cross-sectional study, the onset of clinical symptoms was uncertain. Only the date of veterinary assistance was known.

Although statistical evidence of association of AD with the use of cleaning products such as degreasers, wax, disinfectants, soap powder, among others, were expected, the absence of this association in the present study can be explained by the fact that the use of such products is not itself a risk as long as no residues remain in the environment and they are not used in the presence of the animal. However, the use of beauty products such as perfumes is a factor that has been significantly associated with a higher prevalence of AD. Beauty products are usually considered to be environmental allergens, which may cause animals to produce IgE antibodies (Halliwell 2006).

Despite the internal validity of the present study, any extrapolation of these results should consider that the animal sample was examined by veterinary dermatologists in a veterinary hospital of a University that has technological capabilities

16

Rev. Bras. Med. Vet., 37(Supl.1):13-17, dezembro 2015

that surpass those of most private clinics. However, despite the intrinsic limitations to the research design, observational studies such as the present study can be used to assess supposedly causal associations.

## CONCLUSIONS

A multivariate analysis indicated that, within the studied population, AD was associated with adult females during the rainy season and with the use of perfumes in animals. The present study constitutes a new approach to epidemiological aspects of canine AD in Brazil, but a deeper understanding of the relationships observed between the explanatory variables and the outcome is required and can be achieved through longitudinal studies.

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